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Diversity of Rodent-Borne Zoonotic Pathogens at the Human-Animal-Environment Interface in Qatar

By

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2. **Islam MM,** Farag E, Eltom K, Hassan MM, Bansal D, Schaffner F, Medlock JM, Al-Romaihi H, Mkhize-Kwitshana Z. Rodent Ectoparasites in the Middle East: A Systematic Review and Meta-Analysis. Pathogens. 2021 Jan 31;10(2):139. doi: 10.3390/pathogens10020139.
3. **Islam MM,** Farag E, Mahmoudi A, Hassan MM, Mostafavi E, Enan KA, Al-Romaihi H, Atta M, El Hussein ARM, Mkhize-Kwitshana Z. Rodent-Related Zoonotic Pathogens at the Human-Animal-Environment Interface in Qatar: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021 May 31;18(11):5928. doi: 10.3390/ijerph18115928.
4. **Islam MM**, Farag E, Mahmoudi A, Hassan MM, Atta M, Mostafavi E, Alnager IA, Farrag HA, Eljack GEA, Bansal D, Haroun M, Abdeen R, Al-Romaihi H, Al-Zeyara AA, Almalki SA, Mkhize-Kwitshana Z. Morphometric Study of Mus musculus, Rattus norvegicus, and Rattus rattus in Qatar. Animals (Basel). 2021 Jul 22;11(8):2162. doi: 10.3390/ani11082162.
5. **Islam MM**, Farag E, Hassan MM, Enan KA, Mohammad Sabeel KV, Alhaddad MM, Smatti MK, Al-Marri AM, Al-Zeyara AA, Al-Romaihi H, Yassine HM, Sultan AA, Bansal D, Mkhize-Kwitshana Z. Diversity of bacterial pathogens and their antimicrobial resistance profile among commensal rodents in Qatar. Vet Res Commun. 2022 Jan 27. doi: 10.1007/s11259-021-09876-2.

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1. **Islam MM,** Farag E, Hassan MM, Enan KA, Mohammadi MA, Aldiqs AK, Alhussain H, Musalmani E, Al-Zeyara AA, Al-Romaihi H, Yassine HM, Sultan AA, Bansal D, Mkhize-Kwitshana ZL. Detection of rodent-borne parasites in Qatar: a potential risk for public health. *Manuscript under review*
2. **Islam MM,** Farag E, Hassan MM, Khaled MFI, Ahmed MA, Abdeen R, Al-Romaihi H, Kwitshana ZMK. Ameloblastoma in the mandible of Rattus norvegicus from Qatar: a case report
3. **Islam MM,** Farag E, Hassan MM, Bansal D, Al-Romaihi H, Kwitshana ZMK. Rodent-borne zoonoses in Qatar: a possible One-Health framework for intervention of future epidemic

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1. Farag E, Nour M, **Islam MM**, Mustafa A, Khalid M, Sikkema RS, Alhajri F, Bu-Sayaa A, Haroun M, Van Kerkhove MD, Elkholy A, Malik SMR, Reusken C, Koopmans M, AlHajri MM. Qatar experience on One Health approach for middle-east respiratory syndrome coronavirus, 2012-2017: A viewpoint. One Health. 2019 Apr 4;7:100090. doi: 10.1016/j.onehlt.2019.100090.
2. Farag E, Sikkema RS, Vinks T, **Islam MM**, Nour M, Al-Romaihi H, Al Thani M, Atta M, Alhajri FH, Al-Marri S, AlHajri M, Reusken C, Koopmans M. Drivers of MERS-CoV Emergence in Qatar. Viruses. 2018 Dec 31;11(1):22. doi: 10.3390/v11010022.
3. Sikkema RS, Farag EABA, **Islam M**, Atta M, Reusken CBEM, Al-Hajri MM, Koopmans MPG. Global status of Middle East respiratory syndrome coronavirus in dromedary camels: a systematic review. Epidemiol Infect. 2019 Jan;147:e84. doi: 10.1017/S095026881800345X.
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imported into Qatar, a case report. Int J Infect Dis. 2020 Jul;96:323-326. doi: 10.1016/j.ijid.2020.04.070.

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6. Kalam MA, Alim MA, Shano S, Nayem MRK, Badsha MR, Mamun MAA, Hoque A, Tanzin AZ, Khan SA, Islam A, **Islam MM**, Hassan MM. Knowledge, Attitude, and Practices on Antimicrobial Use and Antimicrobial Resistance among Poultry Drug and Feed Sellers in Bangladesh. *Veterinary Sciences* **2021**, *8*(6), 111, doi:10.3390/vetsci8060111.
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8. Triggle CR, Bansal D, Ding H, **Islam MM**, Farag EABA, Hadi HA, Sultan AA. A Comprehensive Review of Viral Characteristics, Transmission, Pathophysiology, Immune Response, and Management of SARS-CoV-2 and COVID-19 as a Basis for Controlling the Pandemic. Front Immunol. 2021 Feb 26;12:631139. doi: 10.3389/fimmu.2021.631139.
9. Farag EA, **Islam MM**, Enan K, El-Hussein AM, Bansal D, Haroun M. SARS-CoV-2 at the human-animal interfase: A review. Heliyon. 2021 Dec;7(12):e08496. doi: 10.1016/j.heliyon.2021.e08496
10. Kalam MA, Rahman MS, Alim MA, Shano S, Afrose S, Jalal FA, Akter S, Khan SA, **Islam MM**, Uddin MB, Islam A, Magalhães RJS, Hassan MM. Knowledge, Attitudes, and Common Practices of Livestock and Poultry Veterinary Practitioners Regarding the AMU and AMR in Bangladesh. Antibiotics (Basel). 2022 Jan 10;11(1):80. doi: 10.3390/antibiotics11010080

List of presentation

1. **Islam MM.** Risk analysis of rodent-borne zoonotic diseases in Qatar. School of Laboratory Medicine and Medical Science Academic Day April **2021**, University of KwaZulu-Natal, Durban, South Africa, Oral presentation.

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Abstract

Rodents are the most diversified terrestrial mammals in the world. These animals assist with maintaining a healthy ecosystem through the soil structure modification, aeration, and hydration, although 5-10% are regarded as pests and carry zoonotic pathogens. Besides consumption and damage of our food and property, they are responsible for the transmission of several diseases, including plague, typhus, and leishmaniasis. Commensal rodents are the primary source of these pathogens because of their close proximity to humans. Qatar is a small country in the Arabian Peninsula. Four rodent species have been recorded in this country, that includes three commensal (*Mus musculus, Rattus norvegicus,* and *Rattus rattus*) and one wild (*Jaculus jaculus*) species. The zoonotic importance of rodents is yet to be explored. Knowing the pathogens originating from rodents is essential for early preparedness, prevention, and control. Therefore, the current study was undertaken on commensal rodents, rodent-borne zoonotic pathogens, and the factors that are associated with pathogen prevalence among rodents, such as rodent sex, age, and trapping location in Qatar. A cross-sectional study was conducted between August 2019 and February 2020, which trapped rodents from different facilities, such as livestock and agricultural farms, bachelor and family accommodations, and industrial and commercial areas of Qatar. After studying the morphological and morphometric characters, blood samples, ectoparasites and visceral samples were collected from the captured rodents. Parasitic, bacterial, and viral pathogens were identified and characterized using gross, necropsy, microscopic, culture, biochemical, immunologic, and molecular methods. Descriptive statistics and univariate analysis were conducted to detect rodents, rodent-borne pathogens abundance, and the related risk factors. The study trapped 148 rodents, most of which were adults (*n* = 138, 93.2%, 95% CI: 87.92–96.71), and from livestock farms (*n* = 79, 49%, 95% CI: 41.02–57.65). *R. norvregicus* was the most prevalent (*n* = 120, 81%, 95% CI: 73.83–87.05), followed by *R. rattus* (n=24, 16%, 95% CI:10.68–23.16) and *M. musculus* (n=4, 3%, 95% CI: 0.74–6.78) with an average body weight of 18.8 ± 2.2 gm, 264.3 ± 87.5 gm, and 130 ± 71.3 gm, respectively. This is the first morphologic and morphometric study of commensal rodents in Qatar and the Arabian Peninsula that detected the Qatari rodents are relatively smaller than those of Turkey, Tunisia, and Iran. About 63.5% of the rodents were infected with at least one of the 9 species of parasites, viz. *Xenopsylla astia, Ornithonyssus bacoti, Hymenolepis diminuta, Taenia taeniaeformis, Capillaria annulosa, Strongyloides* spp., *Giardia* spp., *Toxoplasma gondii*, *Trypanosoma lewisi*, and *Leishmania* spp. Helminths were the most prevalent (46.0%), followed by ectoparasites (31.8%) and protozoa (29.1%). Going by individual species prevalence, *X. astia* ranked the highest (31.8%), where the lowest prevalent parasite was *C. annulosa* (0.7%). The prevalence of *H. diminuta* was positively correlated (OR=4.13; p = 0.00) with the prevalence of *X. astia*. The study also identified thirteen bacterial species, namely *Acinetobacter baumannii, Aeromonas salmonicida, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Hafnia alvei, Klebsiella pneumoniae, Providencia stuartii, Proteus mirabilis, Pseudomonas aeruginosa,* and *Salmonella enterica,* from the intestine samples. The majority of the bacteria were *E. coli* (54.63%, 95% CI: 44.76-64.24), followed by *P. mirabilis* (17.59%, 95% CI: 10.94-26.10), and *K. pneumoniae* (8.33%, 95% CI: 3.88-15.23). The study detected 31.58% (6/19, 95% CI: 12.58-56.55) of the flea pools, and one (1/1) mite pool was positive with *Rickettsia* spp. *S. enterica* showed the highest antimicrobial resistance (100% resistant to 8 antimicrobials). The top resistant antimicrobials were from cephalosporin, followed by penicillin and tetracycline groups. *E. coli* (26.92%, 95% CI:11.57-47.97) and *K. pneumonia* (50%, 95% CI: 6.76-93.24) were ESBL (extended-spectrum beta-lactamases) producers. The studied rodents are indicators of the presence and dispersal of zoonotic pathogens in Qatar. Urgent action is needed to prevent future spillover of these pathogens at the human-animal-environment interface. It is essential to understand the biology, epidemiology, and transmission dynamics of these pathogens. Farm biosecurity and integrated pest management approach should be implemented in the farm premises. Implementing the One Health approach to combat rodent-borne zoonoses in order to reduce the risk of the future epidemic in Qatar is strongly recommended.

Isihloko: Ukwehluka kwezindalasifo ezithelelwanayo ezisemagundaneni endaweni ehlala abantu nezilwane eQatar

Iqoqa

Amagundane ahlukene kakhulu ayizilwane ezincelisayo ezihlala ezweni. Lezi zilwane ziwusizo ngokugcina ihlanzekile inhlalo yemvelo ngokuguquka kwesimo somhlabathi, ukuguquguquka okwenziwa wumoya, ukumunceka kwamanzi, nakuba u-5-10% uthathwa njengezilwanyana eziyingozi/khathazayo nezithelelana ngendalasifo. Ngaphandle kokuba amagundane adle esikudlayo futhi onokalise ukudla kwethu, yiwona kanye athelelana ngezifo eziningi, kubandakanya ubhubhane, utwayi, nezilonda ezijulile. Ofeleba bamagundane ayisizinda salezi zindalasifo ngenxa yokusondelana kakhulu nabantu. I-Qatar iyizwana elise- Arabian Peninsula. Zine izinhlobo zamagundane ezitholwe kuleli lizwe, kubandakanya izilwane ezindlandawonye (amagundane ahlala endlini, amagundane ansundu, namagundane amnyama kanye namanye asendle anomsila omude nezinyawo ezinde. Ukubaluleka kokuthelelana kwamagundane kusazohlolwa. Ukwazi ngendalasifo evela emagundaneni kusemqoka ukuma ngomumo, ukuvikela, nokulawula. Ngakho-ke, lolu cwaningo lwenziwe kuqondwe amagundane adla ndabawonye/aluhlobofana, indalazifo ngokuthelelwa ngamagundane, nokunye okusondelene nendalasifo esabalele phakathi kwamagundane, njengobulili begundane, iminyaka, nalapho ande khona eQatar. Ucwaningo olugxile sakusabalala lwenziwe phakathi kukaNcwaba wezi-2019 noNhlolanja wezi-2020, ngamagundane agcinwe ezindaweni ezehlukahlukene, njengasemfuyweni nasemasimini ezolimo, ezindaweni ezihlala ngayedwana, ezemindeni, embonini kanye nasezindaweni zokuhweba eQatar. Emuva kokucwaninga ngafanayo nangokulinganisa umumo nesakhiwo, izibonelo zegazi, izimuncagazi nezibonelo zezibilini kwathathwa emagundaneni ayebanjiwe. Okuphila ngokudla emzimbeni wokunye, ibhakitheriya, ukusabalala kwendalasifo, kwahlonzwa futhi kwachazwa ubunjalo kusetsheniswa igrosi, ukuhlolwa kwesilwane sesifile noma ukusabalala kwesifo, ukupopola, isikompilo, ukusebenza kwekhemikhali emzimbeni, ukufunda ngezivikelimzimba, nangezindlela zemolekhula. Inani elichazwayo nokuhlaziywa kohlobolunye lweminingwane kwenziwa ukuthola amagundane nendalasifo yamagundane ethelelwanayo ngobuningi nokunye kwalokho okungaba yingozi. Ucwaningo lugcine amagundane ayi-148, iningi layo ebesemadala, (*n* = 138, 93.2%, 95% CI: 87.92–96.71), kuthi athathwe emapulazini emfuyo abe (*n* = 79, 49%, 95% CI: 41.02–57.65). Amagundane ansundu yiwona ebemaningi (*n* = 120, 81%, 95% CI: 73.83–87.05), kulandele amnyama (n=24, 16%, 95% CI:10.68–23.16) kube ansundumpunga (n=4, 3%, 95% CI: 0.74–6.78) avame ukuba nomzimba osisindo singu-18.8 ± 2.2 gm, 264.3 ± 87.5 gm, and 130 ± 71.3 gm, ngokulandelana. Lolu cwaningo lungolokuqala lomumo nokwakheka kwamagundane adla ndawonye eQatar nase-Arabian Peninsula oluhlole amagundane aseQatar, mancane kunawaseTurkey, awaseTunisia nawase-Iran. Cishe ngama-63.5% wamagundane abetheleleke okunganani ngolulodwa kweziyi-9 eziphila ngokuncela ezinye, okungamazenze, izimbungulu, izikelemu emagundaneni, izikelemu ezisamisundu, okusashongololocimbi, izinhlobonhlobo zemisundu, igciwane elincu elenza uhudo, ithazopulasma gondi, itrayipanosoma lewisi, namashandazilonda. Imisundu iyona ebimininingi kakhulu ingu-46.0%, kulandele imiqhaza/izintwala (31.8%) nezilwane ezinamagqamuzana amancu/amaphrothozowa (29.1%). Ngokubheka ngalunye uluhlobofana ngobuningi, amazenze asemagundwaneni akleliswe phezulu ngo-31.8%, kuthi izincelagazi ezimaphansi ngobuningi kube yi-C. Anulosa (0.7%). Obekukuningi kwezikelemu ezisemagundwaneni kuhambisana bekungu (OR=4.13; p = 0.00) kuhamba phambili amazenze emagundwaneni. Ucwaningo luphinde lwahlonza uhlobofana lwebhaktheriya, imbulungandilinga, etholakala enhlanzini, emisanduku, ehambisana kakhulu nesifo imenenjathisi, iqoqondalazifobhaktheriya, ibhaktheriyasanduku, ibhaktheriyazibilini, iHafiniya aliveyi, iklebisiyela yumoniya, *ibhaktheriya edala ukuchama kabuhlungu nohudo, iprothewusi mirabilisi, ibhaktheriyasanduku,* ne*bhaktheriyambulungaboya***,** okuthathwe emathunjini kwaba yizibonelo. Iningi lazo bekuyibhaktheriyazibilini ebingu (54.63%, 95% CI: 44.76-64.24), kulandele ibhaktheriya eshwizashwizayo (17.59%, 95% CI: 10.94-26.10), ibhaktherimaphaphu/oyithola usesemtholampilo (8.33%, 95% CI: 3.88-15.23). Ucwaningo luthole 31.58% (6/19, 95% CI: 12.58-56.55) wamazenze

asemadamini okubhukuda, kwathi elilodwa (1/1) okusazicabucabu edamini kutholakale kunebhaktheriya ethelelwanwayo. Ibhaktheriya yamathumbu ikhombise ngamandla ukungagobi uphondo nge (100% kwezingu-8 izibulalibhaktheriya). Amabhaktheriya ebelingathi shu ikhambi kuwo abesukela kusephalosporini, kulandele amakhambi akhiqizwe ngokwemvelo bese kuba yiqoqo lamakhambi okwelapha ukutheleka kwebhaktheriya. Ibhaktheriya evame ukuhlala emathunjini ibingama (26.92%, 95% CI:11.57-47.97) kuthi ibhaktheriyamaphaphu ibe ngu (50%, 95% CI: 6.76-93.24) obekungama-enziyamu athile akhiqhizwa ngamabhaktheriya) bekuyizikhiqizi. Ucwaningo ngamagundane ahloliwe beluyizinkomba zokuba khona nokusabalala kwendalazifo evela ezilwaneni eQatar. Umnyakazo ophuthumayo uyadingeka ukunqanda ukusabalala kwendalazifo ngomuso endaweni ehlala abantu nezilwane. Kusemqoka ukuqonda ngempilo yokuphilayo, izimbangela zempilo nangezifo kubantu/ngokwenzeka kubantu, nezindlela okwenzeka ngazo ukuthelelana ngalezi zindalazifo. Iningi lezindalazifo litholwe livela emagundaneni afuyiwe nasemasimini ezolimo. izindlela zokuphatha kwabakhiqizi ukugwema ukusabalala kwezifo kwezolimo, ukusebenzisa izindlela zemvelo ukulawula izinambuzane kufanele kwenziwe ezindaweni zolimo. Ukusebenzisa indlela eyodwa yezempilo ukulwa nokuthelelwa ngamagundane ngezifo ukuze kunciphe ukuba sengcupheni kwekusasa ngokubhebhetheka kokuthelelana ngesifo eQatar kuyisincomo esiqave kakhulu.

Chapter 1: Introduction

Rodent overview

Rodents are the most represented mammalian order in the world. The Class Mammalia consists of 27 orders, which comprises 1314 genera and 6495 species. The order Rodentia has 36 families that include 513 genera and 2552 species. The prominent rodent families are Muridae (157 genera and 834 species), Cricetidae (145 genera and 792 species), and Sciuridae (62 genera and 298 species) [1]. Rodents are distributed in every terrestrial ecosystem, from the desert to the arctic, except Antarctica and some islands [2]. These animals have evolved from the Clade Glires over 100 million years ago [3,4]. They have rapid evolution abilities, such as high prolificacy, short gestation period, easy adaptability to unusual environment, which made them capable of surviving in different ecosystems [5]. With extreme phenotypic differences, they are the most diversified mammals in the terrestrial ecosystems. The majority of the rodents are small and have a unique body shape. However, some are very small (Pygmy mouse: *Mus minutoides*, having only 5 g body weight) and others are big sized (Capybara: *Hydrochoerus hydrochaeris*, 35-66kg body weight) [6]. The adaptations of lesser jerboa (*Jaculus jaculus*), such as their ability to jump, live with minimal water, and run up to 10-14 kilometers searching for food has enabled them to survive in the harsh conditions of the desert [7]. Muskrat (*Ondatra zibethicus*) are semi-aquatic rodents, found in the wetlands [6,8]. On the other hand, Tundra vole (*Microtus oeconomus*) are capable of living in cold weather, including in the Arctic. Some have flying/gliding ability (*Idiurus zenkeri* and *Petaurus breviceps*) [6], while others can regenerate their tissues (Spiny mouse: *Acomys* spp.) [9]. Moreover, the African crested rat (*Lophiomys imhausi*) carries poison on their hair to protect them from predators and possess the microbial digestion capabilities in their guts [10]. Generally, rodents are classified as herbivorous as they eat flowers, fruits, grain, leaves, roots, seeds, and stems. However, some rodents are known to be omnivorous (*Gracilimus radix* [11]), while others are carnivorous (Grasshopper mouse, *Onychomys leucogaster* [12]). Most of the rodents are restricted to their ecological territory, except some commensal rodents, such as *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* from the Muridae family, which are distributed globally in the similar ecologies, including residential, agricultural, and commercial areas [2,13].

Rodents in the ecosystem

The introduction of rodents in different ecosystems in the world usually happened either accidentally or purposefully. *Rattus norvegicus* and *Rattus rattus* are the two major invasive rodent species that originated from Asia and currently have global distribution. *Rattus rattus* was accidentally introduced to the Galapagos islands by pirates or whalers. The distribution of these commensal rodents has been influenced by human movement around the world [13]. As a member of the land habitat ecosystems, rodents serve several benefits, such as modification of the soil structure, soil aeration and hydration, energy and nutrition cycling, seed and spore dispersal, pollination, and source of feed for other animals (Figure 1) [14]. In some places, rodents are a source of meat (*Thryonomys swinderianus* and *Hydrochoerus hydrochaeris*) and fur (*Myocastor coypus*) for humans [15,16]. Despite their many benefits, 5-10% of the rodent population are known to act as pests and disease sources [14,17]. Rodents consume and damage our food, contaminate and spoil it with urine, feces, and fur [18]. Their gnawing and burrowing habit destroys property (clothes and valuable documents) and structure (floor and networking facilities), and sometimes cause accidents (damage to the electrical wire) [18]. Although it is not clearly estimated, the International Rice Research Institute states that rodents damage 1% of the world cereal crops every year. In the developing countries, the estimate is 3-5%, which can increase up to 60% in some countries, like Bangladesh [18,19]. In Asia, rodents destroy around 30 million tons of rice which can feed 180 million people for a year [20].

Rodents as a source of zoonotic pathogens

Rodents are significant sources of zoonoses transmission worldwide. These animals caused many epidemics in history, such as plague, leishmaniasis, and typhus [21-24]. In recent years, many rodent-borne diseases are causing illness in humans and animals in different parts of the world, such as leishmaniasis and monkeypox [25-28]. Rodents move from sewage to kitchen, therefore can serve in disease transmission efficiently. There are at least 70 rodent-borne zoonotic diseases [29]. Rodents act either as carriers or reservoirs in transmission of these disease pathogens to humans through direct or indirect contact (Figure 2A) [30]. Rodent-borne zoonoses occur through three mechanisms of

biodiversity: spillover of pathogens from rodents to humans, spillback of pathogens from humans to rodents, and dilution of pathogens at the human-animal-environment interface [31]. Many factors are associated with rodent-borne pathogens transmission and to increase the disease prevalence, such as direct and indirect exposure between humans and animals, climatic events, and war and famine (Figure 2B).

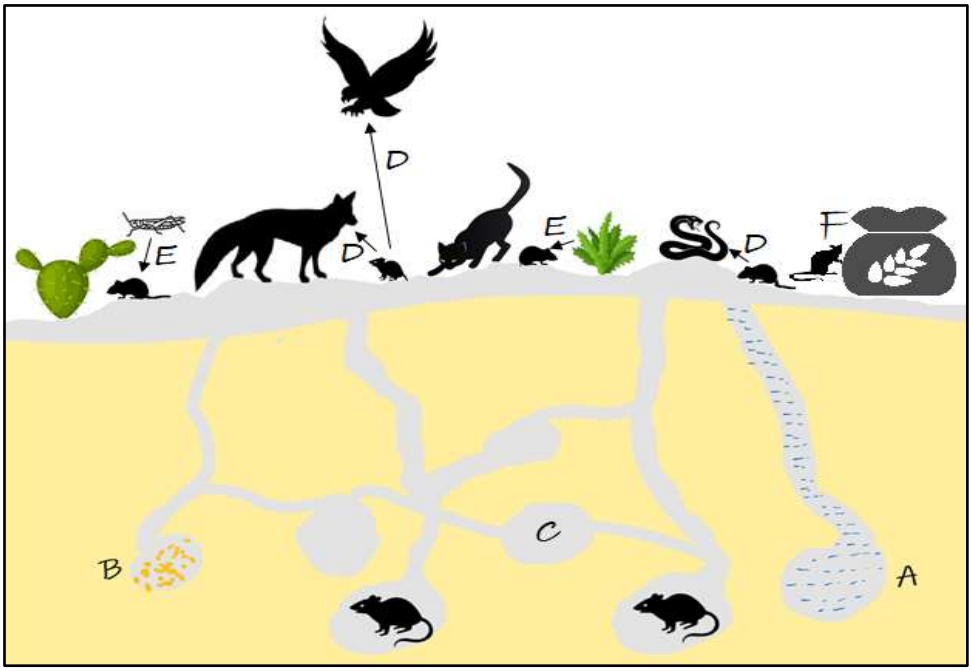

Figure 1: Rodent ecosystem. Rodents help in soil hydration (A), mineral-nutrition cycle (B), soil aeration (C). Cats, dogs, foxes, snakes, and falcons eat rodents (D). Rodents eat seeds, grains, and insects (E). They also cause crop and property damage (F).

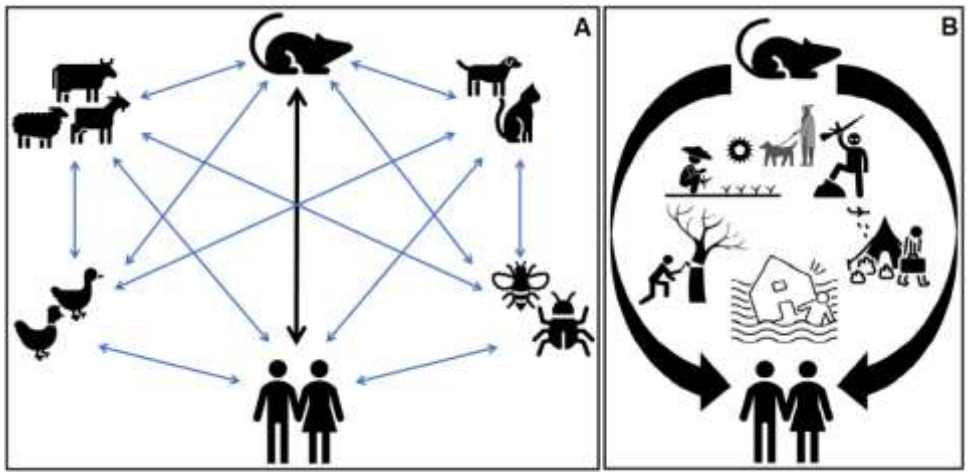

Figure 2: (A) Transmission dynamics of rodent-borne zoonoses at the human-animal-environment interface through direct or indirect contact. The direct transmission includes contamination of human food and water with rodent excreta, rodent bite, and physical contact with rodents, whereas the indirect contact includes the transmission of a pathogen through ectoparasite vectors, livestock, and pets; (B) Some risk factors that can increase rodent-borne disease prevalence, such as people working in the agriculture facilities or with animals get more contact with rodents or rodent excreta [32]; deforestation and climatic events (floods) result in rodent ecosystem damage [33,34]; war and famine forces mass population movement and leads to live more people in small confined premises with poor socio-economic conditions (in the refugee camps) [35,36],.

Qatar

Qatar is a small country situated in the Arabian Peninsula (Figure 3) [37], which is characterized by hot summer (42.7–48.1°C) and warm winter (10.7 °C) with minimal annual rainfall (114.1 mm in 2015)

[10,12]. It is a cosmopolitan country with about 2.6 million population. The local citizens constitute only 11% of the population, and the rest 89% are migrants. The majority of the population are males (72%), adults (82%) [38,39], and originate from South Asia (India, Bangladesh, Nepal, Pakistan, and Sri Lanka) [38]. The economy of the country is exclusively based on fossil fuels (petroleum and natural gas). The economic boom by fossil fuels invited large number of people from the developing countries in Qatar. Due to the harsh climate and landscape, agriculture is minimal in this country. Hence it imports food products from different parts of the world [40,41]. There is chance of importation of rodent-borne pathogens from the developing countries through migrant workers and imported agricultural products. The country has only four points of entry and exit that include two seaports (Hamad port and Al Ruwais port), one land port (Abusamara port), and one airport (Hamad international airport), which can be considered as potential routes of entry of rodents and rodent-borne pathogens to the country.

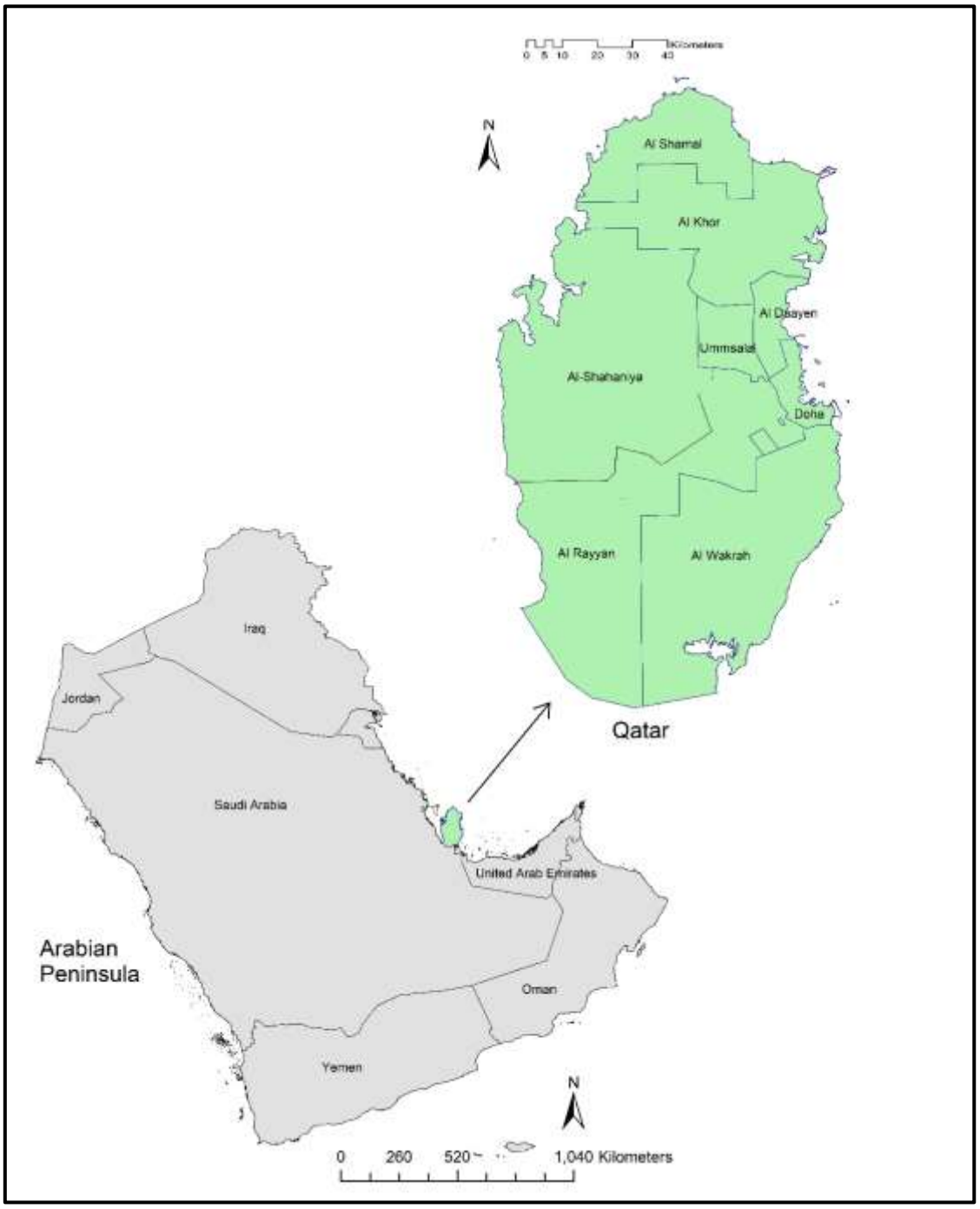

Figure 3: The location of Qatar in the Arabian Peninsula.

There are only four rodent species recorded in this country: *J. jaculus, M. musculus, R. norvegicus,* and *R. rattus* [42-45]. One previous study reported that approximately 70% of the livestock farms are infested with rodents in Qatar [43]. Rodents of Qatar were found to be infested with *Hymenolepis diminuta* and *Xenopsylla astia* [44,45]. Many zoonotic diseases, such as toxoplasmonis, hymenolepiasis, leishmaniasis, Q-fever, hepatitis E, and salmonellosis, were reported among humans, livestock, and pets in Qatar [46,47]. With the current surge of emerging and reemerging zoonoses, some of these have immense global impacts. The country gets increased risk of rodent-borne zoonoses transmission by international travel and tourism [48] and imported animal, food, and agricultural products [49-51]. As there were minimal studies done on rodent-borne pathogens in Qatar, there is a knowledge gap in such pathogens, their prevalence and risk factors of prevalence in this country. Proper infection prevention and control for infectious and zoonotic diseases cannot be taken if the etiology, source, risks, and dynamics of the pathogens are adequately known.

Research objectives

Based on the paucity of such knowledge, the current study was conducted to understand rodents and rodent-borne zoonotic pathogens in Qatar. The specific objectives were to identify the commensal rodent morphology and morphometry, determine the rodent-borne zoonotic pathogens, and assess their risk factors associated with the prevalence of these pathogens.

To address the objectives, we assessed the following questions: (1) What are the rodent-borne zoonotic pathogens dispersed at the human-animal-environment interface in Qatar and the region? (2) What is the spatial distribution and characteristics of commensal rodents? (3) What are the burdens of rodent-borne zoonotic pathogens among commensal rodents? and (4) Which are the drivers and risk factors of rodent-borne zoonoses in Qatar?

The objectives and questions were addressed with the following tasks:

1. To conduct systematic reviews on rodent-borne pathogens previously reported in Qatar and the region (Chapter 2.1, Chapter 2.2, and Chapter 2.3)
2. To identify the characteristics of commensal rodents collected from different facilities (Chapter 3)
3. To investigate the burden of rodent-borne pathogens with public health importance (Chapter 4.1, Chapter 4.2, and Chapter 4.3)
4. To study the related drivers and risk factors for rodent and rodent-borne zoonoses in Qatar (Chapter 6)

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Chapter 2: Literature Review

A background study is essential prior to any research. Therefore, before starting the field and laboratory work in the current study, we conducted three systematic reviews and meta-analysis on rodent-borne pathogens in Qatar and in the Middle Eastern region. These studies helped us to understand the prevailing rodent-borne zoonotic pathogens in this country and the region.

Chapter 2.1: Rodent Ectoparasite in the Middle East: A Systematic Review and Meta-Analysis

Rodent-borne ectoparasites include flea, louse, mite, and tick. These ectoparasites are important in two ways: some have the potential to infect humans and other animals, and some ectoparasites act as vectors or reservoirs of many zoonotic pathogens. To understand the overall situation of rodent ectoparasites in Qatar and the region, we reviewed the available data of rodent ectoparasites in the Middle East. This chapter compiles over 100 years published reports of rodent ectoparasites in the Middle Eastern countries.

Islam, M.M.; Farag, E.; Eltom, K.; Hassan, M.M.; Bansal, D.; Schaffner, F.; Medlock, J.M.; Al-Romaihi, H.; Mkhize-Kwitshana, Z. Rodent Ectoparasites in the Middle East: A Systematic Review and Meta-Analysis. *Pathogens* **2021**, *10*(2):139, doi:10.3390/pathogens10020139

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Systematic Review

Rodent Ectoparasites in the Middle East: A Systematic Review and Meta-Analysis

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Abstract: Rodents carry many ectoparasites, such as ticks, lice, fleas, and mites, which have potential public health importance. Middle Eastern countries are hotspots for many emerging and re-emerging infectious diseases, such as plague, leishmaniasis, Crimean Congo hemorrhagic fever, and Q fever, due to their ecological, socioeconomic, and political diversity. Rodent ectoparasites can act as vectors for many of these pathogens. Knowledge of rodent ectoparasites is of prime importance in controlling rodent ectoparasite-borne zoonotic diseases in this region. The current systematic review and meta-analysis performs a comprehensive synthesis of the available knowledge, providing an evidence-based overview of the ectoparasites detected on rodents in Middle Eastern countries. Following a systematic search in Pubmed, Scopus, and Web of Science, a total of 113 published articles on rodent ectoparasites were studied and analyzed. A total of 87 rodent species were documented, from which *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* were found to be the most common. Fleas were the most reported ectoparasites (87 articles), followed by mites (53), ticks (44), and lice (25). *Xenopsylla cheopis*, *Polyplax spinulosa*, *Ornithonyssus bacoti*, and *Hyalomma rhipicephaloides* were the most commonly described fleas, lice, mites, and ticks, respectively. Based on the reviewed articles, the median flea, louse, mite, and tick indices were highest in Israel (4.15), Egypt (1.39), Egypt (1.27), and Saudi Arabia (1.17), respectively. Quantitative meta-analysis, using a random-effects model, determined the overall pooled flea prevalence in the Middle East as 40% (95% CI: 25–55, $I^2 = 100\%$, $p < 0.00001$), ranging between 13% (95% CI: 0–30, $I^2 = 95\%$, $p < 0.00001$) in Iran and 59% (95% CI: 42–77, $I^2 = 75\%$, $p < 0.00001$) in Israel. The overall pooled louse prevalence was found to be 30% (95% CI: 13–47, $I^2 = 100\%$, $p < 0.00001$), ranging between 25% in Iran (95% CI: 1–50, $I^2 = 99\%$) and 38% in Egypt (95% CI: 7–68, $I^2 = 100\%$). In the case of mites, the pooled prevalence in this region was 33% (95% CI: 11–55, $I^2 = 100\%$, $p < 0.00001$), where the country-specific prevalence estimates were 30% in Iran (95% CI: 4–56, $I^2 = 99\%$) and 32% in Egypt (95% CI: 0–76, $I^2 = 100\%$). For ticks, the overall prevalence was found to be 25% (95% CI: 2–47, $I^2 = 100\%$, $p < 0.00001$), ranging from 16% in Iran (95% CI: 7–25, $I^2 = 74\%$) to 42% in Egypt (95% CI: 1–85, $I^2 = 100\%$). The control of rodent ectoparasites should be considered to reduce their adverse effects. Using the One Health strategy, rodent control, and precisely control of the most common rodent species, i.e., *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus*, should be considered to control the rodent-borne ectoparasites in this region.

Keywords: rodents; ectoparasites; fleas; lice; mites; ticks; Middle East; systematic review; meta-analysis

1. Introduction

Ectoparasites are organisms that infest the exterior surface, such as skin or its integument, of a host [1,2]. The vast majority of human and animal ectoparasites are arthropods. Ectoparasites can cause multiple health problems for the host, such as anemia, hypersensitivity, irritability, and skin lesions [2]. They also act as vectors of many pathogens of public and animal health importance, such as *Crimean-Congo hemorrhagic fever virus* (CCHFV), *Coxiella*, *Rickettsia* and *Hymenolepis* [3–6].

Rodents are the largest and most diverse group of animals among mammals in the world [7]. These animals are one of the major causes of crop and resource damage worldwide [8]. Moreover, after bats, rodents have the highest importance for carrying zoonotic pathogens [9]. Since the middle ages, rodents have contributed to the spread of many disease pandemics, such as plague, murine typhus, and leishmaniasis. Rodents carry different ectoparasites, which act as vectors of these pathogens [10]. There are many other zoonotic pathogens, such as *Hymenolepis diminuta*, *Bartonella* sp., *Coxiella burnetii*, and *Rickettsia* sp., which have been identified from rodent-borne fleas, mites, and ticks [4,11,12]. Rodents carry many ectoparasites, such as lice, fleas, ticks, and mites [10], that are associated with low socioeconomic status, war, famine, climatic events (e.g., floods), and environmental changes, facilitating the transmission of pathogens among the human and animal populations [13–15].

The Middle East is centered on Afro-Eurasia, and includes member countries of the Gulf Cooperation Council (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, and United Arab Emirates (UAE)), in addition to Cyprus, Iran, Iraq, Israel, Jordan, Lebanon, Palestine, Syria, Turkey, and Yemen [16,17]. Countries in the Middle East are hotspots for emerging and re-emerging infectious diseases, partly because of their ecological, cultural, socioeconomic, and political diversity, but also due to the unrest, conflict, and wars in this region [18,19]. The lack of relevant information on infectious diseases, their sources, and their diversity is a major drawback for public health studies in this area, possibly misguiding both civilians and governments in their attempts at mitigation [20].

In the past, the Middle East experienced several rodent ectoparasite-associated disease epidemics that caused the loss of millions of lives, such as plague and murine typhus [21–23]. Even today, many Middle Eastern countries remain at risk of particular rodent ectoparasite-associated infectious diseases, such as leishmaniasis [24]. As such, it is of the utmost importance for regional health authorities to control the spread of rodents and their ectoparasites, and fully-characterize their ecological niche and diversity. To date, several studies have been undertaken on rodent ectoparasites and related diseases in this region. However, to the best of our knowledge, this is the first systematic review that aims to summarize, analyze and interpret the available baseline data to provide an in-depth understanding of the presence and abundance of rodent ectoparasites in this region.

2. Methods

This systematic review was conducted in full accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines (Figure 1 and Supplementary Table S1) [25]. One author performed the search in electronic databases, two authors cross-examined the titles, abstracts, and full-texts of the retrieved citations against a set of predetermined selection criteria, and then one author compiled the relevant data. Subsequently, three authors organized the data and conducted the meta-analysis. The review protocol was registered in Open Science Framework (OSF) Registries under the following DOI: 10.17605/OSF.IO/RPYK8.

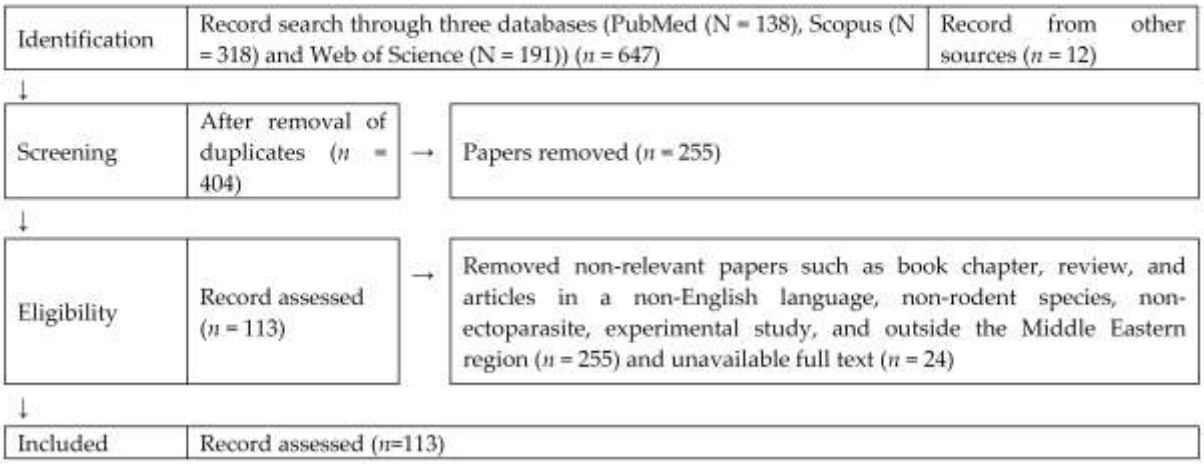

Figure 1. Systematic review preferred reporting items for systematic reviews and meta-analysis (PRISMA) flow diagram describing the selection of published articles on rodent ectoparasites in the Middle East and the inclusion/exclusion process used in the study.

2.1. Search Strategy

Systematic searches on PubMed, Scopus, and Web of Science were performed by 16 October 2020. The search covered every original research article published in English containing field information on rodent ectoparasites in the Middle Eastern countries without any restrictions on publication dates. Following a previous systematic review [26], the keywords included (Rodent OR Rat OR Jird OR Gerbil OR Vole OR Mouse OR Hamster OR Porcupine OR Squirrel OR Jerboa) AND (Ectoparasite OR Flea OR Mite OR Lice OR Tick) AND (17 Middle Eastern countries name linked with OR). We used advanced search strategies, i.e., [Title/Abstract] in PubMed, [TITLE-ABS-KEY] in Scopus, and [Topic] in Web of Science, to screen the searches.

2.2. Search of Relevant Articles

At first, EndNote X9 (Clarivate Analytics, Philadelphia, PA, USA) was used to identify and exclude duplicate studies. Imported citations were then transferred to Rayyan (https://rayyan.qcri.org/) for title and abstract screening. If any article's title and abstract were ambiguous in terms of relevance to our study, it was subjected to full-text analysis.

2.3. Quality Assessment of the Selected Articles

The quality assessment of all included articles was conducted using a modified version of the critical appraisal tool for prevalence studies created by the Joanna Briggs Institute and reported by Munn et al. [27]. A checklist with 10 questions was used (Supplementary Table S2) to assess the risk of confounding bias, selection bias, and bias related to measurement and data analysis. Each question was answered either with "yes", "no", "unclear" or "not/applicable". A score was calculated as the number of questions answered with a "yes" for each study. According to this score, studies were categorized into three groups based on their quality: low (a score of 0–4), intermediate (5–6), and high quality (7–10). Representative samples were those with basic characteristics that mimic our targeted population (rodents and ectoparasites) selected through the fieldwork. For practical reasons, the adequate sample size for each study was estimated in a case-by-case manner, taking into account the geographical area it represents, study type, and the rodent species in question. The sampling location and other details of the setting of fieldwork had to be described appropriately. Studies had to explain how they identified different rodents and ectoparasite species in detail, or use valid references of identification methods. Additionally, articles had to explicitly report the calculations of ectoparasite indices and prevalence, or provide

enough baseline data for the reviewers to calculate these measures on their behalf. The appropriateness of statistical analysis was evaluated in relation to the objectives of each study. Important subgrouping was expected according to the type and species of rodents and ectoparasites.

2.4. Data Extraction

We considered only the field reports on rodent ectoparasites for data extraction. The extracted variables were the country and year of sampling, rodent-specific data (species, gender, total rodent count, and the number of ectoparasite-infected rodents), ectoparasite-specific data (type, species, and total number), and the associating factors for ectoparasite abundance on rodents (Supplementary Table S3). The taxonomy of all reported rodents and ectoparasites were verified through online databases, namely the National Center for Biotechnology Information (NCBI) Taxonomy Browser, the Global Biodiversity Information Facility (GBIF), Animal Diversity Web (ADW), and the Zoological Institute of Russian Academy of Sciences.

2.5. Data Analysis

The extracted data were organized and stored in Microsoft Excel (MS Office, 2019) spreadsheets. The initial descriptive analysis of the included studies was conducted using the same application. Ectoparasite indices were calculated for each of the four types of ectoparasites (fleas, lice, mites, and ticks) by dividing the total numbers detected for the specific ectoparasite by the total number of sampled rodents [28]. Central tendency and dispersion were calculated for country-specific ectoparasite indices and illustrated in Boxplots using the BoxplotR web tool [29]. An ectoparasite's prevalence was calculated by dividing the total number of ectoparasite-positive rodents over the total number of sampled rodents, and was expressed in decimals. Quantitative meta-analysis was conducted by one co-author (K.E.) using Review Manager 5.3 (The Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark), and the results were verified by another co-author (MMH) using STATA/IC-13.0 (Stata Corp, 4905 Lakeway Drive, College Station, Texas 77845, USA). In both instances, a random-effects model was applied to calculate the pooled prevalence of all types of ectoparasites with 95% confidence intervals (CI). Studies were weighted according to the inverse of variance. The prevalence reported by each study was used as the effect estimate, and its standard error (SE) was calculated using the formula $SE = SQRT(p(1-p)/n)$, where p is the reported prevalence, and n is its sample size. The Inconsistency Index (I^2) was used to assess the degree of heterogeneity among studies, as it is known to be less influenced by the number of included studies. According to the country and rodent species, subgroup meta-analyses were performed to investigate possible explanations of significant heterogeneity ($I^2 > 75\%$). However, each subgroup had to be represented by at least three studies to be included for analysis. The results of all meta-analyses were illustrated in forest plots. Finally, funnel plots were generated and visually-examined to assess the possibility of publication bias.

3. Results

3.1. Descriptive Analysis

The literature search resulted in 113 articles (Figure 1) published from 1914 to 2020 [3–5,11,12,14,24,30–135]. The articles were covering 11 out of 17 Middle Eastern countries (Figure 2). However, no information was available from the countries Bahrain, Iraq, Jordan, Oman, Syria, or the UAE. Among the 113 published articles, 82 articles focused on rodent fleas, 38 on rodent lice, 53 on rodent mites, and 44 on rodent ticks. A total of 61 (54%) articles were of high quality, followed by 29 (26%) with intermediate quality, and 23 (20%) were low-quality articles (Supplementary Table S2). The visual examination of funnel plots revealed evidence of possible publication bias in all meta-analyses, as more articles were near the top, with an asymmetrical distribution on both sides of the overall pooled prevalence estimate (Supplementary Figure S1).

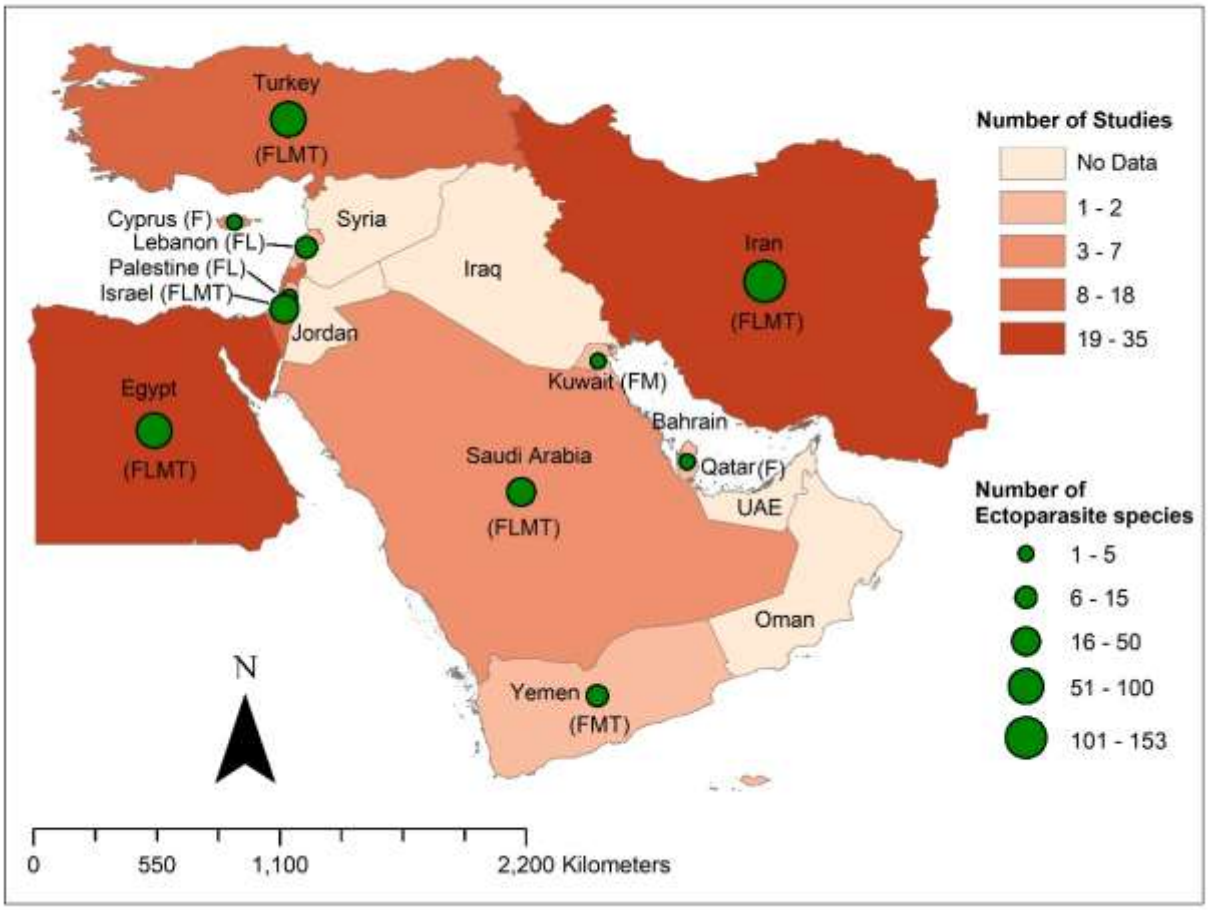

Figure 2. The map describes the Middle Eastern countries with the total number of studies and the number of ectoparasite species detected on rodents (the letters F, L, M, and T indicate information available about fleas, lice, mites, and ticks, respectively).

The 113 studies examined at least 26,003 rodents from 87 rodent species belonging to seven families (Supplementary Table S4a). Among these, *Mus musculus* (9% of total examined rodents), *Rattus norvegicus* (48%), and *Rattus rattus* (19%) were found to be the most common and widely-distributed rodents. Moreover, *Acomys cahirinus*, *Acomys dimidiatus*, *Apodemus mystacinus*, *Apodemus sylvaticus*, *Cricetulus migratorius*, *Gerbillus nanus*, *Jaculus jaculus*, *Meriones crassus*, *Meriones libycus*, and *Meriones tristrami* were reported from at least three countries of the Middle East, and can be considered as widely-distributed rodents in this region.

Based on the reviewed articles, the Boxplots (Figure 3) summarize the results of the reported ectoparasite indices in some of the Middle Eastern countries. The median flea index was the highest in Israel (4.15) and lowest in Iran (0.95). In the case of louse, it ranged from a median of 0.09 in Iran to 1.39 in Egypt. The median mite index was 0.42 in Iran, 0.94 in Saudi Arabia, and 1.27 in Egypt, whereas the median tick indices in Middle Eastern countries were 0.19 in Egypt, 0.28 in Iran, 0.36 in Israel, and 1.17 in Saudi Arabia.

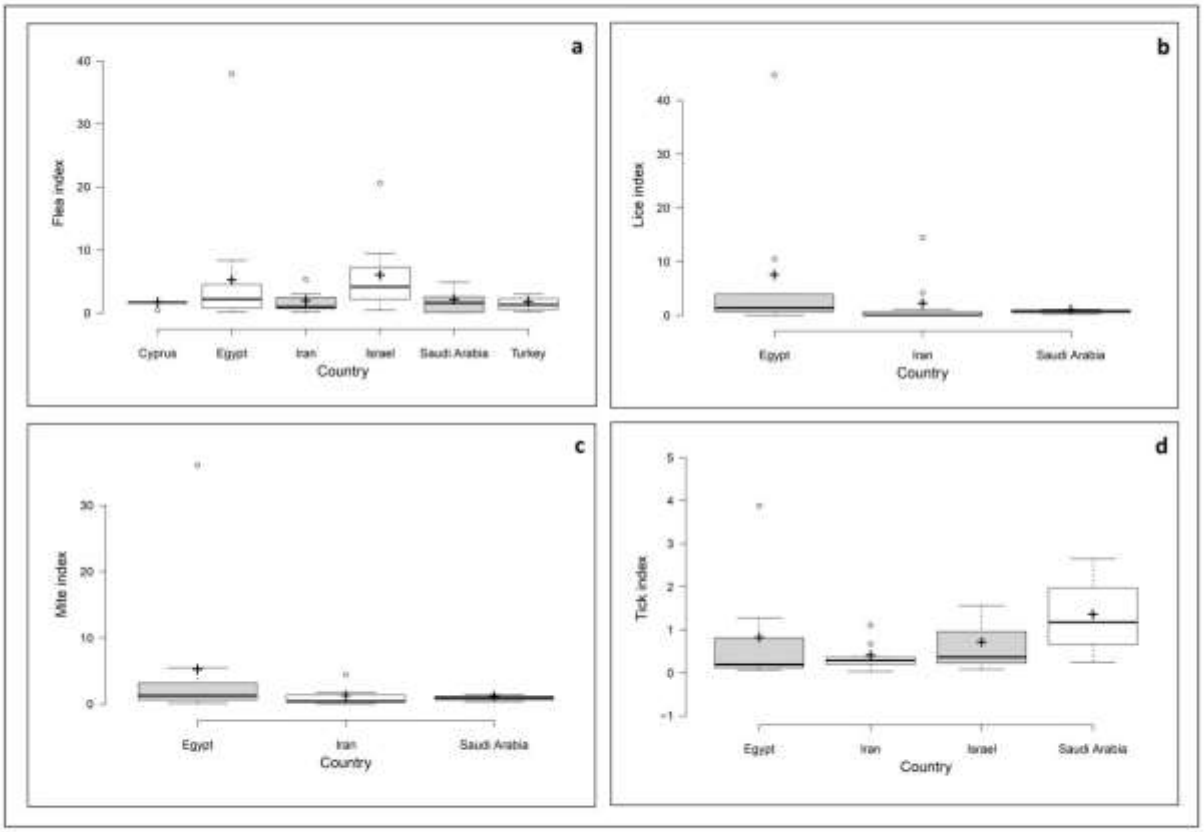

Figure 3. Ectoparasite indices in the Middle Eastern countries; (**a**) flea index, (**b**) louse index, (**c**) mite index, and (**d**) tick index. Centerlines indicate the medians; box limits indicate the 25 to 75 percentiles as determined by R software; whiskers extend the interquartile range 1.5-fold from the 25 to the 75 percentiles; outliers are represented by dots; crosses represent sample means.

3.2. Fleas Carried by Rodents in the Middle East

Based on the records of 82 articles with rodent fleas, a total of 67,057 fleas were examined, which were from 104 flea species (Supplementary Table S4b), of which most of the fleas were *Xenopsylla cheopis*, *Echidnophaga gallinacea*, and *Xenopsylla cleopatrae* (23.6%, 16.3%, and 14.9% of total fleas, respectively). The most frequently reported species of fleas were *Xenopsylla cheopis* (41 reports), *Leptopsylla segnis* (22), and *Ctenocephalides felis* (19). Fifteen species of fleas were reported from at least three countries, such as *Echidnophaga murina*, *Leptopsylla segnis*, *Leptopsylla taschenbergi*, *Nosopsyllus fasciatus*, *Nosopsyllus iranus*, *Parapulex chephrenis*, *Pulex irritans*, *Stenoponia tripectinata*, *Xenopsylla astia*, *Xenopsylla cheopis*, *Xenopsylla cleopatrae*, *Xenopsylla conformis*, *Xenopsylla nubica*, and *Xenopsylla ramesis*.

The overall pooled flea prevalence in the Middle East was found to be 40% (95% CI: 25–55, $I^2 = 100\%$, $p < 0.00001$), ranging between 13% (95% CI: 0–30, $I^2 = 95\%$, $p < 0.00001$) in Iran and 59% (95% CI: 42–77, $I^2 = 75\%$, $p < 0.00001$) in Israel (Figures 4 and 5). Species-specific prevalence was calculated only for three rodent species: *Mus musculus* (27%, 95% CI: 6–48, $I^2 = 98\%$), *Rattus norvegicus* (48%, 95% CI: 14–81, $I^2 = 100\%$) and *Rattus rattus* (35%, 95% CI: 0–75, $I^2 = 100\%$) (Figure 6).

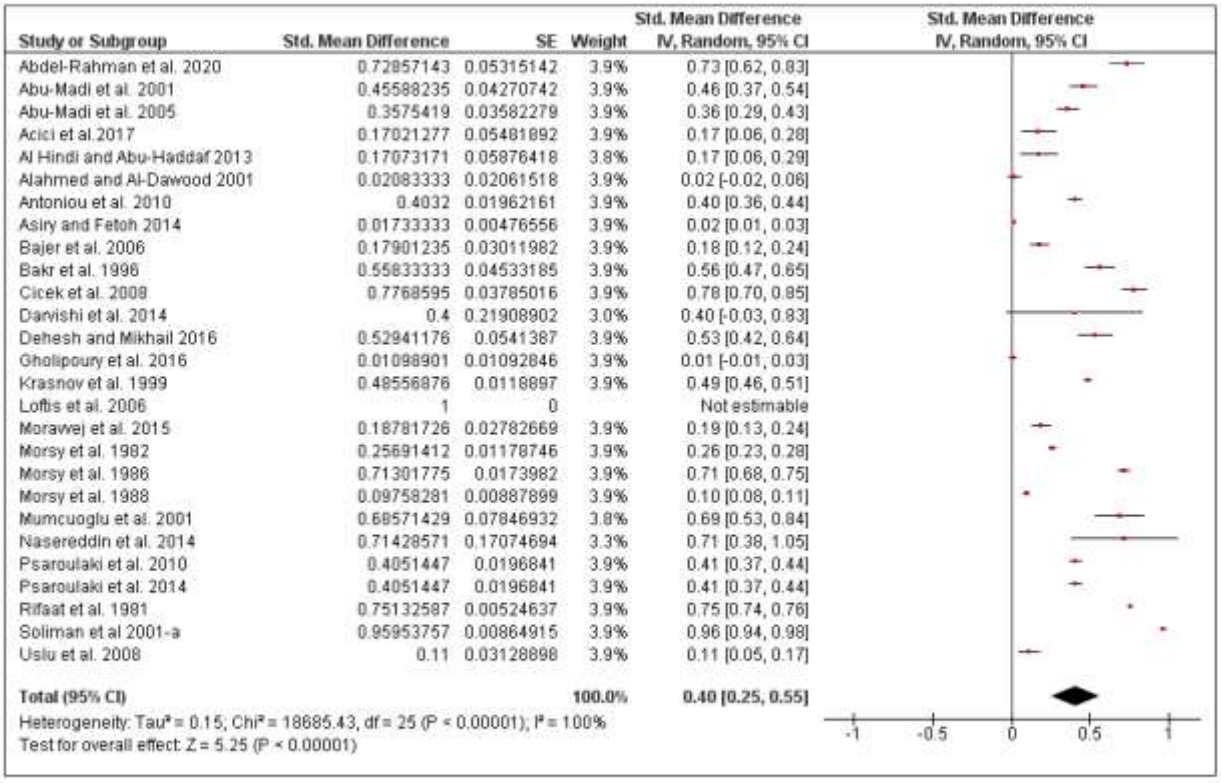

Figure 4. Forest plot of the pooled overall flea prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

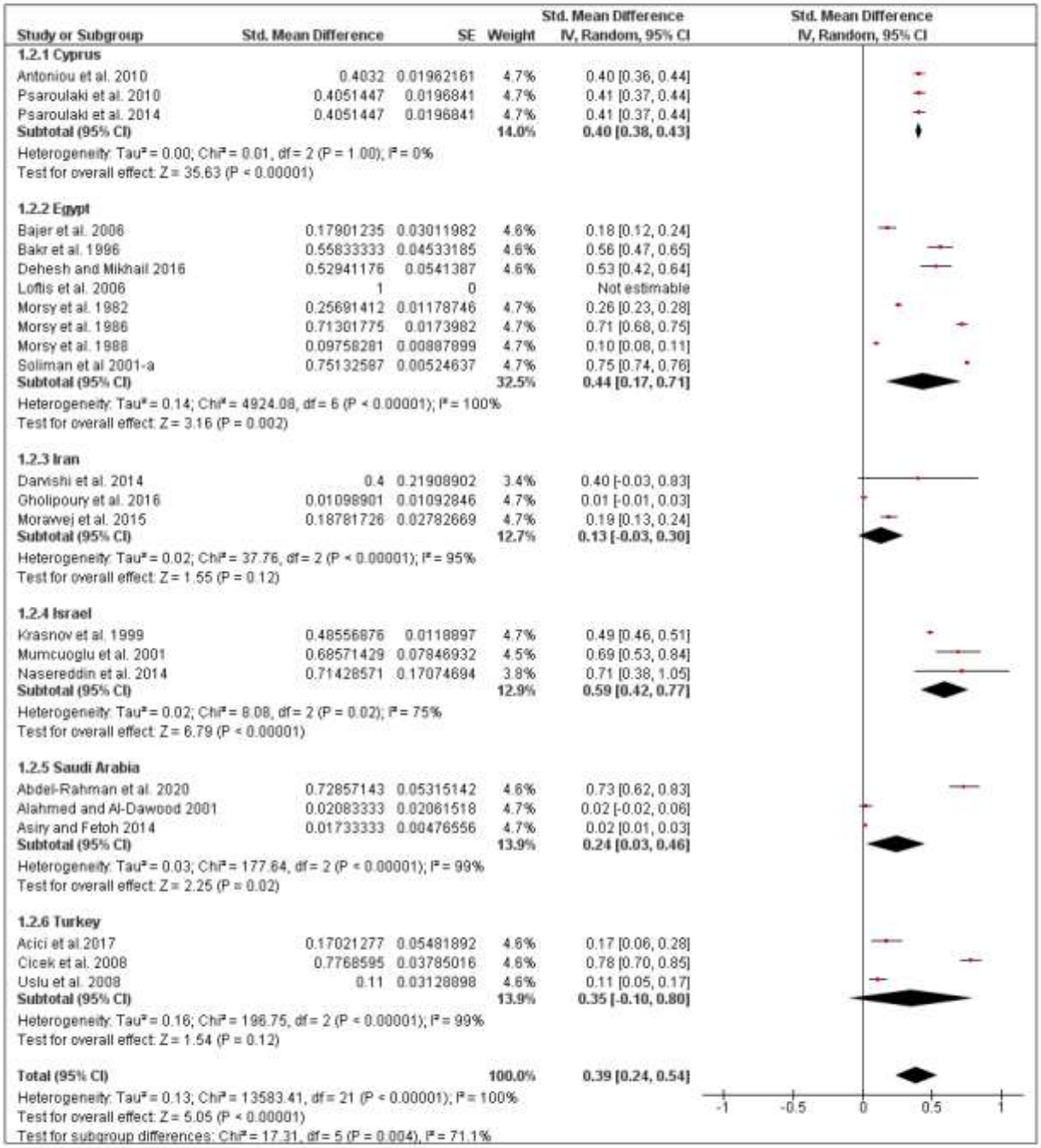

Figure 5. Forest plot illustrating subgroup meta-analysis of country-specific flea prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

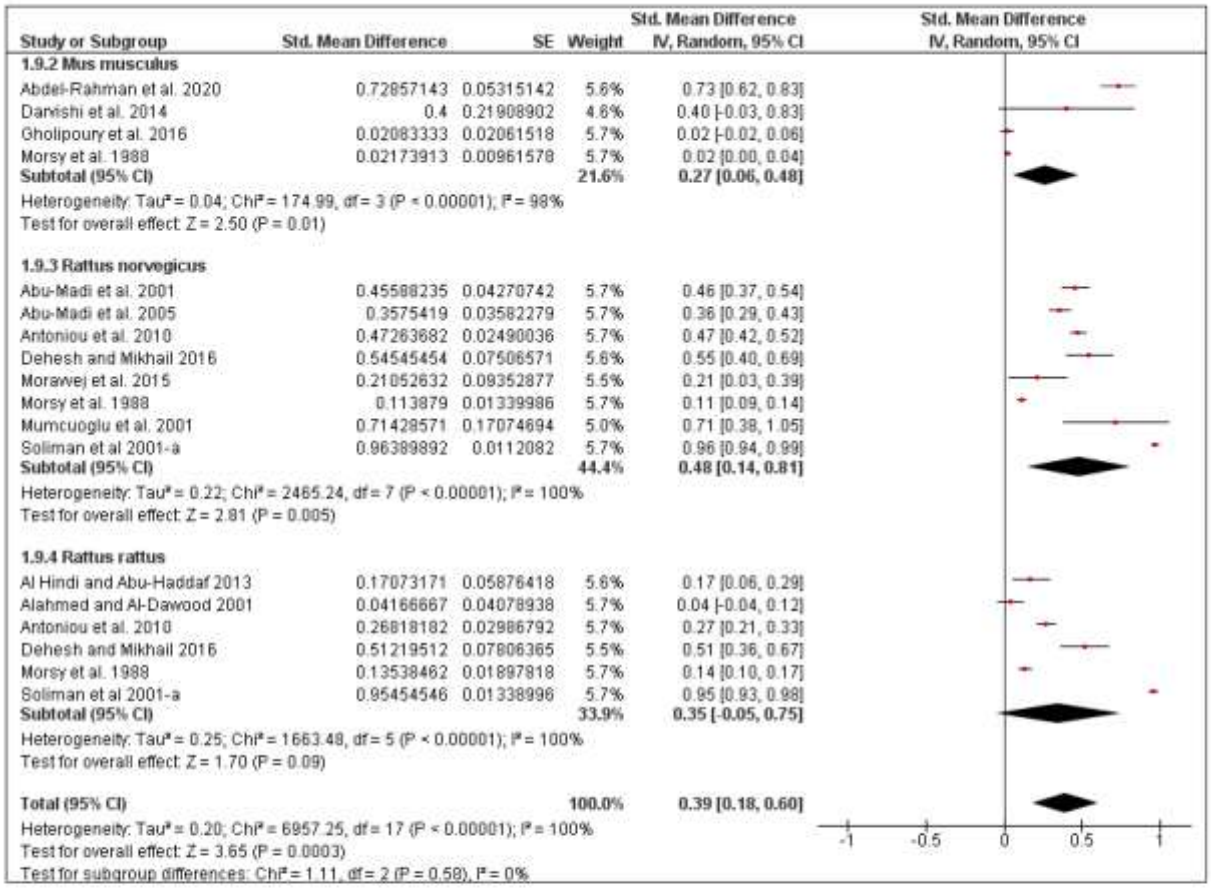

Figure 6. Forest plot illustrating subgroup meta-analysis of flea prevalence according to rodent species in Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

3.3. Lice Carried by Rodents in the Middle East

The 39 articles studied a collective 31,543 lice on rodents, and detected 28 species of lice in the Middle Eastern rodents (Supplementary Table S4c). However, *Polyplax spinulosa* represented 88.79% of the total lice, and was reported by 25 articles from Egypt, Iran, Kuwait, Palestine and Saudi Arabia.

For rodents in this region, the overall pooled louse prevalence was 30% (95% CI: 13–47, $I^2 = 100\%$, $p < 0.00001$), ranging between 25% in Iran (95% CI: 1–50, $I^2 = 99\%$) and 38% in Egypt (95% CI: 7–68, $I^2 = 100\%$) (Figures 7 and 8). Moreover, the louse prevalence was 23% in *Mus musculus* (95% CI: 7–68, $I^2 = 100\%$), and 53% in *Rattus rattus* (95% CI: 7–68, $I^2 = 100\%$) (Figure 9).

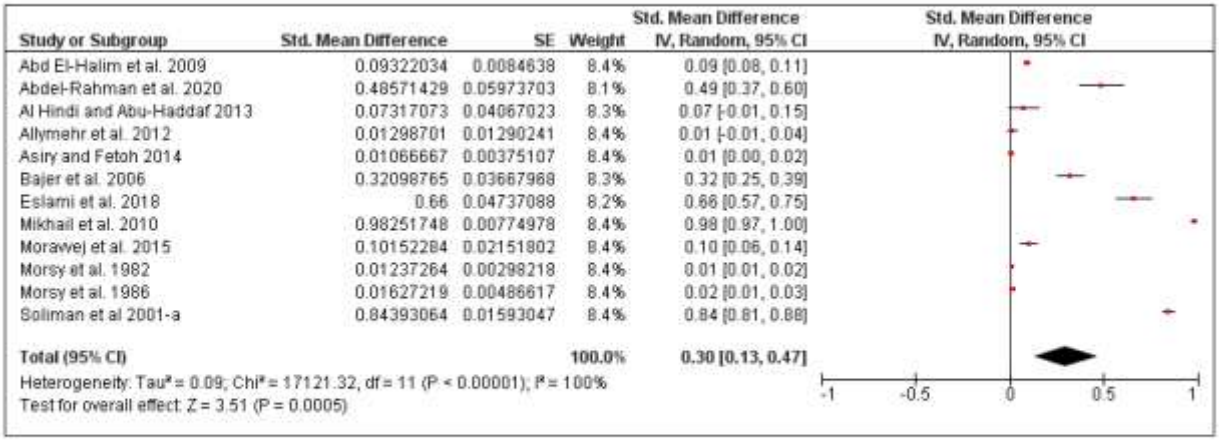

Figure 7. Forest plot of the pooled overall louse prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

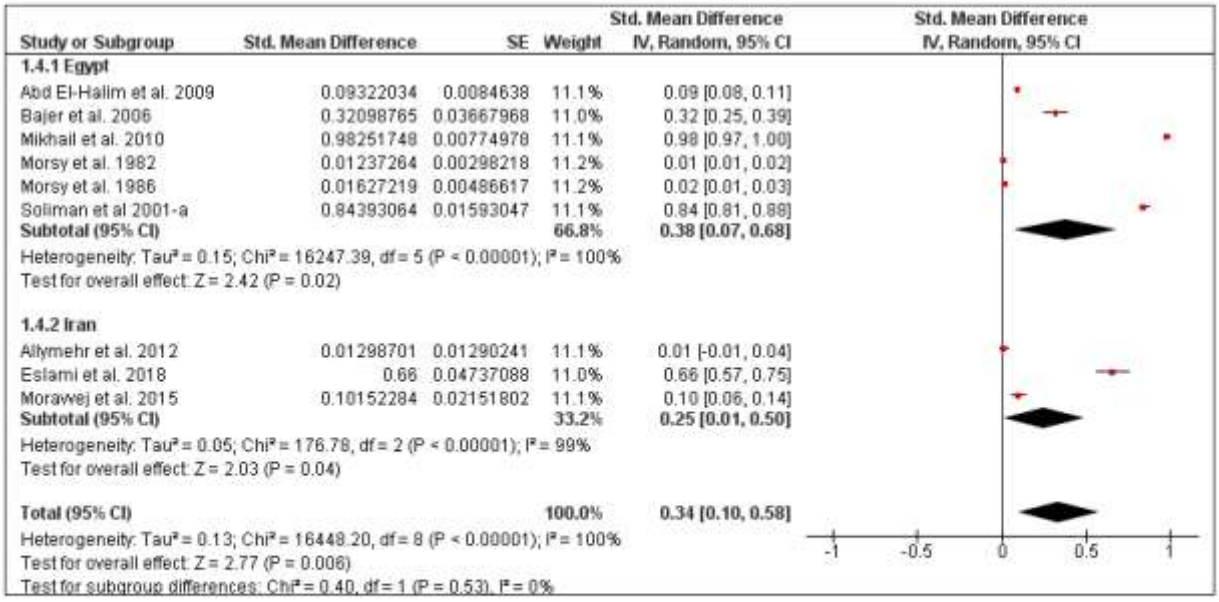

Figure 8. Forest plot illustrating subgroup meta-analysis of country-specific louse prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

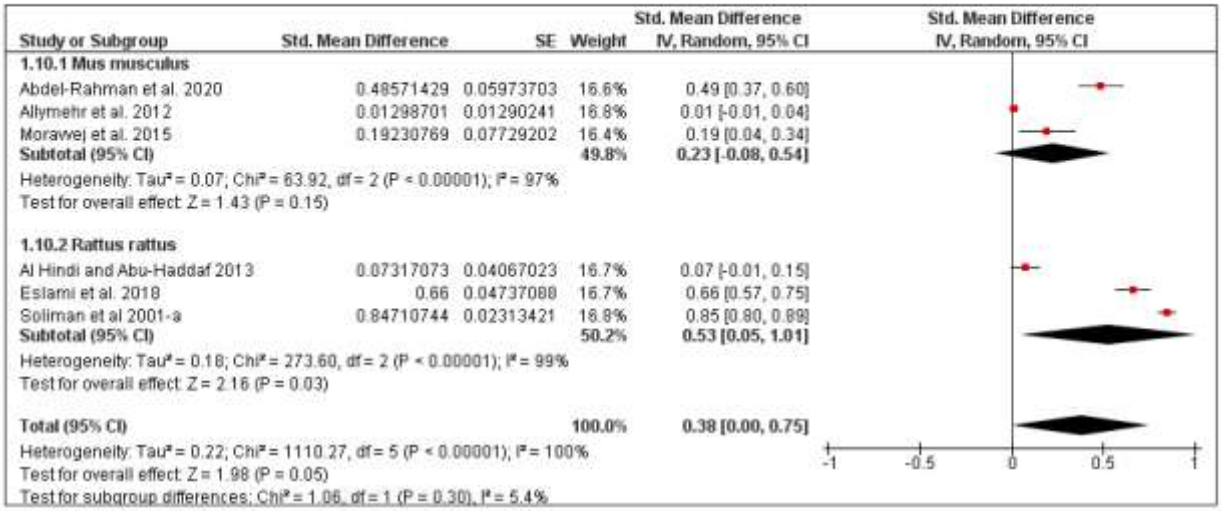

Figure 9. Forest plot illustrating subgroup meta-analysis of country-specific louse prevalence on rodents in Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

3.4. Mites Carried by Rodents in the Middle East

The review detected 134 species (Supplementary Table S4d) of mites (n = 26,476) on rodents in Middle Eastern countries, of which 73% were from three species, i.e., *Laelaps nuttalli* (29%), *Ornithonyssus bacoti* (34%), and *Radfordia ensifera* (10%). However, *Echinolaelaps echidninus*, *Eulaelaps stabularis*, *Haemolaelaps glasgowi*, *Laelaps nuttalli*, and *Ornithonyssus bacoti* were reported from at least three countries of the Middle East, whereas *Ornithonyssus bacoti* and *Laelaps nuttalli* were the highest reported mites (24 and 20 studies respectively out of 51 total studies on mites).

The overall pooled mite prevalence in the Middle East was 33% (95% CI: 11–55, $I^2 = 100\%$, $p < 0.00001$) (Figure 10). Country-specific prevalence was calculated for Iran (30%, 95% CI: 4–56, $I^2 = 99\%$) and Egypt (32%, 95% CI: 0–76, $I^2 = 100\%$) (Figure 11). The prevalence also varied according to rodent species, from 29% in *Mus musculus* (95% CI: 9–49, $I^2 = 96\%$) to 56% in *Rattus rattus* (95% CI: 1–100, $I^2 = 100\%$) (Figure 12).

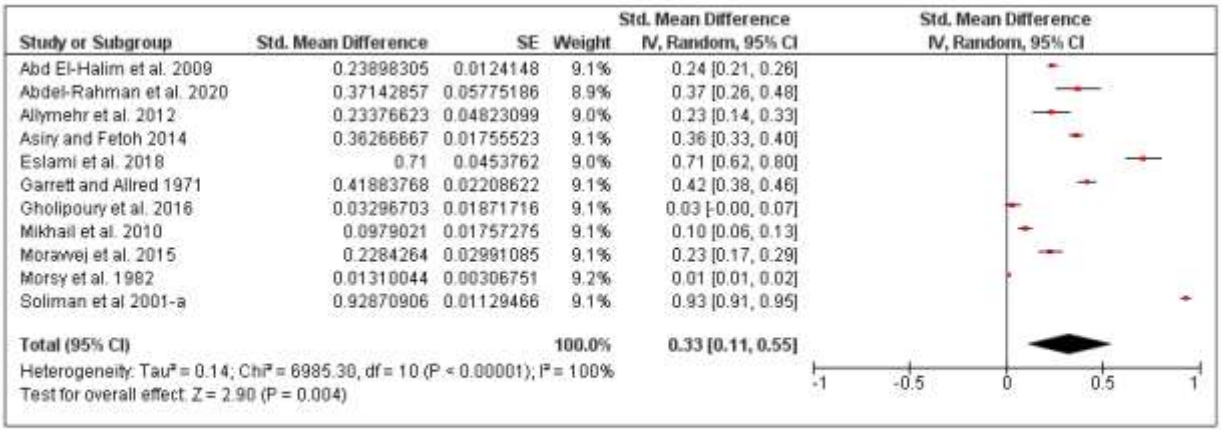

Figure 10. Forest plot of the pooled overall mite prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

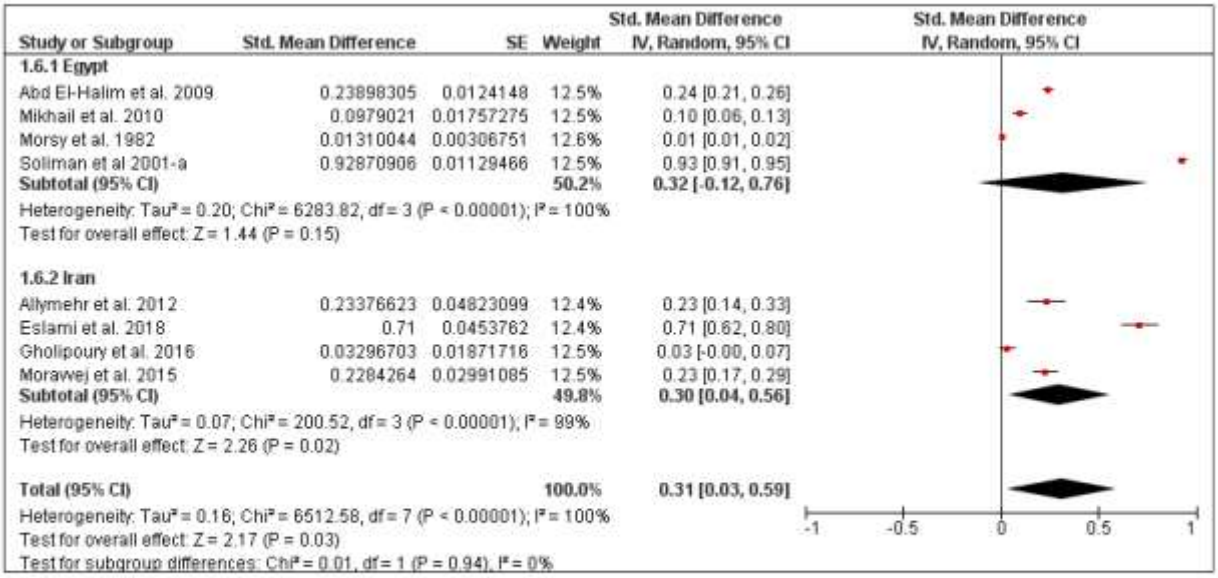

Figure 11. Forest plot illustrating subgroup meta-analysis of country-specific mite prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

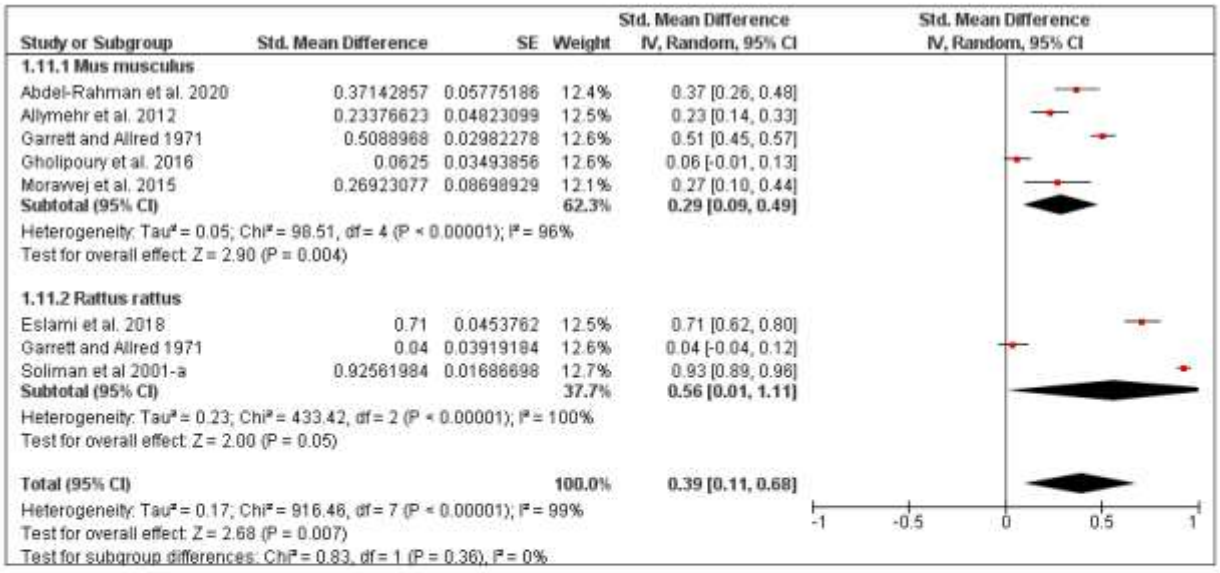

Figure 12. Forest plot illustrating subgroup meta-analysis of country-specific mite prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

3.5. Ticks Carried by Rodents in the Middle East

The reviewed studies identified 2897 ticks from at least 27 species (Supplementary Table S4e), of which 69.7% and 15.7% were *Hyalomma rhipicephaloides* and *Ixodes eldaricus*, respectively. Three species of ticks were reported from more than three countries, such as *Ixodes* spp., *Rhipicephalus sanguineus*, and *Rhipicephalus turanicus*.

The overall tick prevalence in this region was 25% (95% CI: 2–47, $I^2 = 100\%$, $p < 0.00001$) (Figure 13), ranging from 16% in Iran (95% CI: 7–25, $I^2 = 74\%$) to 42% in Egypt (95% CI: 1–85, $I^2 = 100\%$) (Figure 14). The tick prevalence also varied according to rodent species, from 11% in *Rattus norvegicus* (95% CI: 0–25, $I^2 = 82\%$), to 24% in *Mus musculus* (95% CI: 0–52, $I^2 = 91\%$) (Figure 15).

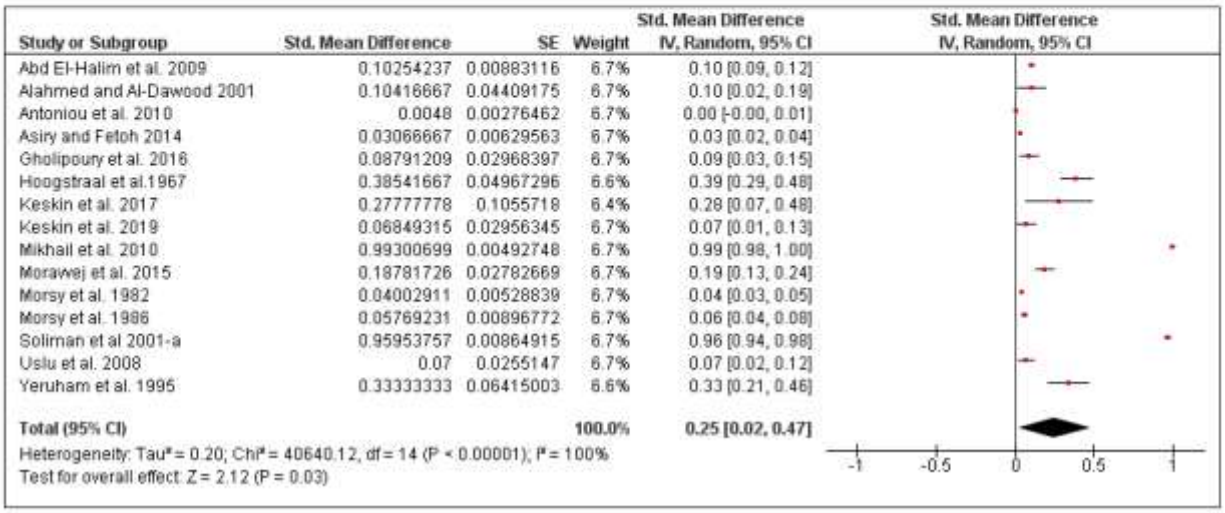

Figure 13. Forest plot of the pooled overall tick prevalence on rodents in Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

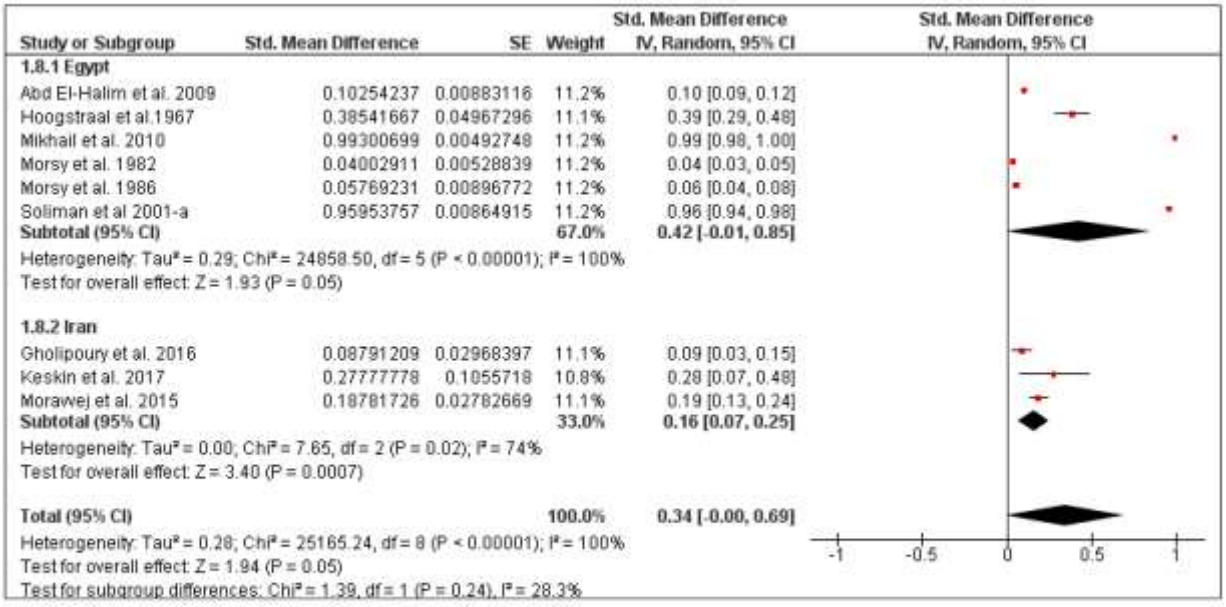

Figure 14. Forest plot illustrating subgroup meta-analysis of country-specific tick prevalence on rodents in Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

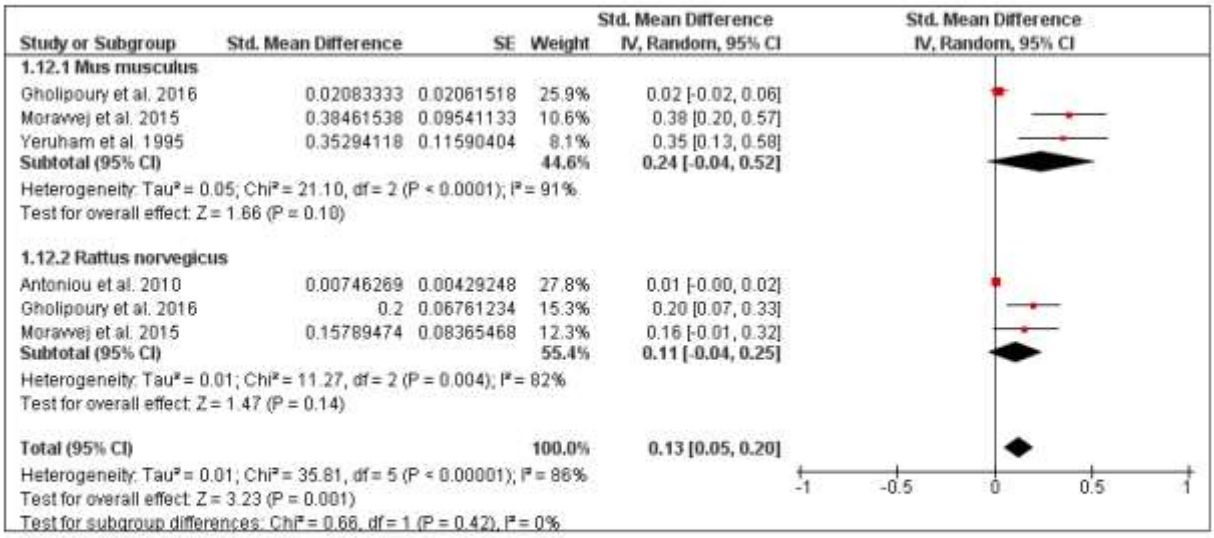

Figure 15. Forest plot illustrating subgroup meta-analysis of country-specific tick prevalence on rodents in the Middle Eastern countries. The central red square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

4. Discussion

Our study reviewed the published literature on rodent ectoparasites in the Middle Eastern countries to provide a comprehensive overview of rodent ectoparasites in this region. Most of the studies were from Iran, Egypt, and Israel (82 out of 113). A previous history of rodent-borne disease epidemics, such as plague, leishmaniasis, and murine typhus, may be behind the increased interest in rodent-related pathogens by researchers in these countries [26]. Ectoparasite index and prevalence are suitable descriptors to quantify parasites in a host or estimate ectoparasite abundance [136,137]. These indices are essential to use in conjunction with rodent and vector surveillance to estimate human and epizootic risks [28]. However, the current review failed to calculate the pooled abundance of most Middle Eastern countries, possibly affecting the generalizability of our results and emphasizing the need for further detailed studies to understand the rodent ectoparasite abundance in this region, the resultant threat to the local population, and the necessary control measures.

Although there were no rodent ectoparasite reports from Bahrain, Iraq, Jordan, Oman, Syria, and UAE in our systematic review, there are rodent-related ectoparasites reported in some of these countries from non-rodent hosts. The brown dog tick, *Rhipicephalus sanguineus*, is abundant on stray dogs in Jordan [138]. *Rhipicephalus sanguineus* and *Xenopsylla astia* were identified on domestic cats in UAE [139]. This indicates that there is a considerable gap in the knowledge in these countries where rodent-borne zoonoses are concerned. A previous review reported a knowledge gap as regards rodent-borne helminths in some of these countries, such as Bahrain and Oman [26], suggesting that it is essential to conduct more comprehensive studies on rodent-borne diseases, including ectoparasites, in certain countries such as UAE, Jordan, Oman, Iraq, and Bahrain.

The present review listed a total of 87 species of rodents that occur in the Middle Eastern region. In Iran, 79 species of rodents have been described, of which 15 are considered common, i.e., *Allactaga* sp., *Apodemus witherbyi*, *Dryomys nitedula*, *Gerbillus nanus*, *Jaculus blanfordi*, *Meriones crassus*, *Meriones libycus*, *Meriones persicus*, *Microtus socialis*, *Mus musculus*, *Nesokia indica*, *Rattus norvegicus*, *Rattus rattus*, *Rhombomys opimus*, *Tatera indica* [140,141]. Seventeen species of rodents are reported in Sinai, Egypt: *Acomys cahirinus*, *Acomys russatus*, *Dipodillus dasyurus*, *Eliomys quercinus*, *Gerbillus andersoni*, *Gerbillus gerbillus*, *Gerbillus pyramidium*, *Jaculus jaculus*, *Jaculus orientalis*, *Meriones crassus*, *Meriones sacramenti*, *Meriones tristrami*,

Mus musculus, *Psammomys obesus*, *Rattus norvegicus*, *Rattus rattus*, *Sekeetamys calurus* [142]. All these common rodents in Iran and Egypt have been reported in this present review.

Some of the rodent ectoparasites addressed in this review have high public and animal health importance. Similar to their impact on humans and other animals, they can also cause certain diseases in the host rodents. Nevertheless, the ectoparasites identified in this review are not always rodent-specific. The host specificity of ectoparasites generally falls within one of three broad categories: (i) ectoparasites specific to rodents, which do not, or only accidentally, infest other mammals (including humans) and birds; (ii) ectoparasites specific to other species that accidentally attack rodents; or (iii) ectoparasites with a broad host range. Rodent fur mites *Radfordia musculi*, *Radfordia musculinus*, *Radfordia affinis*, and *Radfordia ensifera* are mainly found in laboratory rodents [143–145]. *Dermanyssus gallinae* and *Ornithonyssus sylviarum* are poultry mites [82,135,146–149]. They attack humans and other mammals accidentally when exposed to them [150,151]. Some mites were detected on rodents from Egypt, Iran, and Turkey [54,98,121], such as *Macrocheles* spp. *Tryophagus* sp. and *Zygoribatula* sp., which are known as non-parasitic mites [152–154]. Reports of these mites parasitizing on rodents may be accidental infestations. On the other hand, some ectoparasites have a broad host range and can infect different birds or mammals, including humans and rodents. An excellent example is the soft tick *Ornithodoros* sp., which can parasitize humans, rodents, livestock, and poultry [155,156].

There is considerable public health importance attributed to ectoparasites with a broad host range, mainly if this includes humans, such as *Ctenocephalides canis* and *Ctenocephalides felis*, which can infest dogs, cats, rodents, and humans. These fleas carry multiple zoonotic pathogens, such as *Bartonella*, *Rickettsia felis*, *Dipylidium caninum*, and *Yersinia pestis*, which can be transmitted at the humans–animal interface [157–160]. The Oriental rat flea *Xenopsylla cheopis* is an essential vector of Bartonellosis, plague, and murine typhus [160,161]. The tropical rat mite *Ornithonyssus bacoti* can transmit numerous pathogens such as *Rickettsia typhi* (murine typhus), *Coxiella burnetti* (Q-fever), and *Trypanosoma cruzi* (Chagas' disease) [162]. The northern fowl mite *Ornithonyssus sylviarum* can bite humans and cause allergic reactions [163]. *Ornithodoros* sp. has been described to carry Alkhurma hemorrhagic fever virus in Saudi Arabia [164]; *Borrelia* sp. in Egypt [165–167], Iran [168,169], Israel [170,171], Jordan [172], Palestine [171] and Turkey [155]; and CCHFV in Iran [156]. *Rhipicephalus* spp. were also found to carry genomes of CCHFV in Iran [156] and Saudi Arabia [173], and *Coxiella*, *Francisella*, *Rickettsia*, *Babesia*, and *Theileria* in Turkey [174]. Moreover, many ectoparasites, such as the house dust mite *Cheyletus* sp., cause allergy in humans [175]. Infestation with *Dermanyssus gallinae* and *Dermanyssus americanus* can cause dermatitis in humans [151,176].

However, meticulously-designed and well-implemented control programs against rodent ectoparasites are of the utmost importance to regional health authorities to control rodent ectoparasite-borne zoonotic diseases effectively. A useful approach would be to limit the spread of rodents themselves. Many of the reviewed articles in this study [30,34,40] stated that rodent abundance is a crucial contributing factor to rodent-borne ectoparasites abundance. The season and location of trapping are other significant determinants of ectoparasites abundance [43,44,47]. More concentration is required to control the three commensal rodents, i.e., *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus*. These rodents have been identified as the most common and extensively-distributed rodent species in the Middle Eastern countries by a previous study [26], and the current study as well. However, rodents are essential components of an ecosystem [140,177], with undeniable benefits for their environment. Therefore, multidisciplinary teams working under the One Health umbrella are necessary to control rodents and rodent-borne ectoparasites with public health importance.

5. Conclusions

Rodent ectoparasites, including rodent fleas, lice, mites, and ticks, in Middle Eastern countries, including Cyprus, Egypt, Iran, Israel, Kuwait, Lebanon, Palestine, Qatar, KSA, Turkey, and Yemen, have been reported. In total, 104 flea species, 28 louse species, 134 mite species, and 27 tick species have been detected on 87 rodent species in these countries. Some

rodent ectoparasites have substantial public health importance as they are known to carry a broad spectrum of zoonotic pathogens. Besides the One Health approach for rodent control, some other factors such as rodent abundance, season of the year, and trapping location should be considered during the rodent ectoparasite control program. Our systematic review reveals knowledge gaps on rodent ectoparasites in this region, suggesting that it is essential to conduct countrywide in-depth studies on rodent ectoparasites and their public health importance. As the threats of zoonotic diseases increase, including rodent-borne diseases, it is crucial to expand all efforts from all angles to mitigate these threats.

Supplementary Materials: The following are available online at https://www.mdpi.com/2076-0817/10/2/139/s1, Figure S1: Funnel plots of overall rodent ectoparasite prevalence and subgroup analysis, Table S1: Prisma 2009 checklist, Table S2: Quality assessment of the 113 studied articles, Table S3: Extracted data from the selected 113 studies, Table S4: Rodents, fleas, lice, mites, and ticks on prevailing rodents in the Middle East.

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Chapter 2.2: Helminth Parasites among Rodents in the Middle East Countries: A Systematic Review and Meta-Analysis

Rodents carry different parasites including cestodes, nematodes, and trematodes, some of which has zoonotic potential. The current study compiled all the published articles in the history of the Middle East that studied rodent-borne helminths. The study also identified the rodent-borne zoonotic helminths in the region.

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Review

Helminth Parasites among Rodents in the Middle East Countries: A Systematic Review and Meta-Analysis

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Simple Summary: The review was conducted to establish an overview of rodent helminths in the Middle East as well as their public health importance. Following a systematic search, 65 field research were identified, studied, and analyzed. The overall prevalence of cestodes, nematodes, and trematodes were 24.88%, 32.71%, and 10.17%, respectively. The review detected 21 species of cestodes, 56 nematodes, and 23 trematodes, from which 22 have zoonotic importance. *Capillaria hepatica*, *Hymenolepis diminuta*, *Hymenolepis nana*, and *Cysticercus fasciolaris* were the most frequent and widespread zoonotic helminths. The review identified that there is an information gap on rodent helminths at the humans-animal interface level in this region. Therefore, the public health importance of rodent-borne helminth parasites is not fully recognized. Countrywide detailed studies on rodent helminths, along with the impact on public health, should be conducted in this region.

Abstract: Rodents can be a source of zoonotic helminths in the Middle East and also in other parts of the world. The current systematic review aimed to provide baseline data on rodent helminths to recognize the threats of helminth parasites on public health in the Middle East region. Following a systematic search on PubMed, Scopus, and Web of Science, a total of 65 research studies on rodent cestodes, nematodes, and trematodes, which were conducted in the countries of the Middle East, were analyzed. The study identified 44 rodent species from which *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* were most common (63%) and recognized as the primary rodent hosts for helminth infestation in this region. Cestodes were the most frequently reported ($n = 50$), followed by nematodes (49), and trematodes (14). The random effect meta-analysis showed that the pooled prevalence of cestode (57.66%, 95% CI: 34.63–80.70, $I^2\% = 85.6$, $p < 0.001$) was higher in Saudi Arabia, followed by nematode (56.24%, 95% CI: 11.40–101.1, $I^2\% = 96.7$, $p < 0.001$) in Turkey, and trematode (15.83%, 95% CI: 6.25–25.1, $I^2\% = 98.5$, $p < 0.001$) in Egypt. According to the overall prevalence estimates of individual studies, nematodes were higher (32.71%, 95% CI: 24.89–40.54, $I^2\% = 98.6$, $p < 0.001$) followed by cestodes (24.88%, 95% CI: 19.99–29.77, $I^2\% = 94.9$, $p < 0.001$) and trematodes (10.17%,

95% CI: 6.7–13.65, $I^2\%$ = 98.3, $p < 0.001$) in the rodents of the Middle East countries. The review detected 22 species of helminths, which have zoonotic importance. The most frequent helminths were *Capillaria hepatica*, *Hymenolepis diminuta*, *Hymenolepis nana*, and *Cysticercus fasciolaris*. There was no report of rodent-helminths from Bahrain, Jordan, Lebanon, Oman, United Arab Emirates, and Yemen. Furthermore, there is an information gap on rodent helminths at the humans-animal interface level in Middle East countries. Through the One Health approach and countrywide detailed studies on rodent-related helminths along with their impact on public health, the rodent control program should be conducted in this region.

Keywords: rodent; helminth; cestode; trematode; nematode; Middle East; meta-analysis

1. Introduction

Helminths are among the most diverse and geographically widespread groups of parasites that infect both humans and animals [1]. Although they are from different phyla or class (nematode, cestode, and trematode), the mode of transmission, infection, and pathogenesis, as well as host immune-responsiveness of these pathogens, follows a typical pattern. Approximately one-third of the world population is infected with one or more types of helminths. From amongst 300,000 species of helminths that typically infect vertebrates, 287 of them infect humans, from which 95% are either zoonoses or have evolved from animal parasites [2]. About 100 of the zoonotic helminths cause asymptomatic infection or mild symptoms in humans, while only a small percentage of them cause severe or even fatal infections [1]. In resource-poor countries, livestock is a source of food, production, income source, and deposit of wealth. Parasite infections in animals indirectly affect human health through financial hardship and malnutrition. Based on the burden of death, sickness, and treatment cost for both humans and animals for helminth infestation, the zoonotic parasites' socioeconomic burden was presented as high or low socioeconomic impact [3].

Rodents are significant sources of parasitic zoonosis in humans, serving as reservoirs and vectors of at least 70 zoonotic diseases, of which 16 are helminth parasites [4]. Consumption of uncooked/improperly cooked food contaminated with the infective larvae, eggs, or metacercariae is the primary source of humans infestation with helminth parasites [5,6]. When pilfering humans food, rodents pass stool or urine that contaminates said food, leading to transmission of zoonotic helminths from rodents to humans [7].

The Middle East is an intercontinental region with a total population of over 411 million [8] in 17 sovereign countries, including Bahrain, Cyprus, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Palestine, Qatar, Kingdom of Saudi Arabia (KSA), Syria, Turkey, United Arab Emirates (UAE), and Yemen. The majority of people in this region live in poverty [9], with the highest percentage being specific to Yemen, Syria, Egypt, Palestine, and Iraq [10,11]. Cultural diversity, weak economic policy, poor governance, rapid population growth, low educational structure, gender discrimination, underdeveloped infrastructure, and war and conflict have turned the region into a hot spot for many emerging and re-emerging diseases, including rodent-borne parasitic infections [9,12,13]. In the past, rodent-borne infections have led to multiple instances of a fatal epidemic, in part due to a lack of relevant information available on the subject, which makes it difficult to maintain public health sustainability [14,15].

Helminth infestations are mostly neglected diseases [16]. Therefore, the complete picture of zoonotic helminths is not well known in the Middle East area. Despite several studies being done on helminths in this region, no systematic review or meta-analysis was performed on rodent helminths, including zoonotic importance in the Middle East region. Our objective is to summarize baseline information on rodent helminths in this region using evidence-based records of the helminths detected

in rodents in the Middle Eastern countries. The review also identifies the rodent helminths with public health importance in this region.

2. Materials and Methods

We followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [17] to conduct the systematic review using a four-step approach: database search, evaluating relevant articles, data extraction, and summarizing. One author conducted the data search. Two authors were involved in critical evaluation and data extraction from the selected articles, while one author managed the compilation of said data. Afterward, two authors arranged the data and conducted the meta-analysis (Figure 1, Supplementary Table S1).

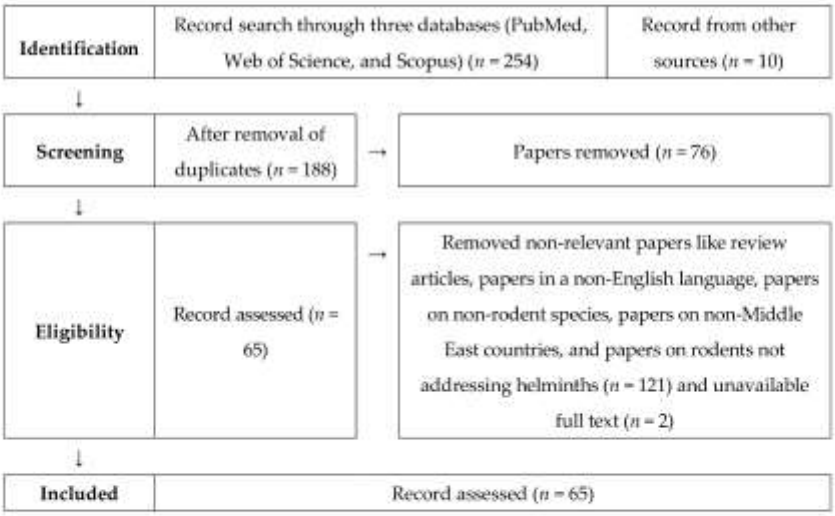

Figure 1. Systematic review PRISMA flow diagram describing the selection of published articles on rodent helminths in the Middle East and inclusion/exclusion process used in the study.

2.1. Search Strategy

A literature search on rodent helminth parasites in the Middle East was performed on 17 June 2019 through PubMed, Web of Science, and Scopus (Figure 1). The search included all the original research articles containing field evidence of helminth parasites (trematode, nematode, cestode) among rodents in the Middle East countries. The search did not have any date range of publication. The keywords included (Rodent OR Rat OR Jird OR Gerbil OR Vole OR Mouse OR Hamster OR Porcupine OR Squirrel OR Jerboa) AND (Endoparasite OR Helminth OR Cestode OR Trematode OR Nematode) AND (17 Middle East country names individually). Screening on the search was conducted as [Title/Abstract] in PubMed, [TITLE-ABS-KEY] in Scopus, and [Topic] in Web of Science.

2.2. Search of Relevant Articles

The data search results were processed using EndNote X9 (clarivate analytics, Philadelphia, PA, USA), which was also used to identify and exclude duplicate studies. Then we proceeded to peruse through the titles and abstracts to find the relevant articles. However, articles that were ambiguous regarding their relevance by their title and abstract were subjected to full-text analysis. Only documents published in English were considered for the review [18–82].

2.3. Data Extraction and Summarizing

Evidence-based field reports give a clear picture of any pathogen's availability, diversity, and dynamics in a locality [83,84]. We considered only the field reports containing rodent helminths

for data abstraction. The extracted data included several variables such as country and location of sampling, season, year of sampling, rodent information (rodent species, sex, total rodent count, and the number of infected), helminth species and type, and possible associating factors of rodent infestation with helminth (Supplementary Table S2). The zoonotic rodent-borne helminths in this region were identified from the list of rodent helminths from this review with the support of published articles.

2.4. Data Analysis

The aggregated data was transcribed and stored in a Microsoft Excel spreadsheet, and then the data was forwarded to STATA/IC-13.0 (Stata Corp, 4905 Lakeway Drive, College Station, TX 77845, USA) for statistical analysis. Crude prevalence estimation was performed by dividing the total number of helminth-positive rodents with the total number of rodents sampled and expressed as a percentage. The crude estimate of prevalence was used throughout, the 95% confidence interval (CI), and the *p*-value were calculated on different types of helminths among the countries. Study variations among the studies were evaluated using the Chi-square (χ^2) test on Cochran's *Q* statistics (with *p*-value) followed by I^2 statistics to determine the study's degree of heterogeneity. Standard Error (SE) was calculated using a standard formula for proportion calculation. A random-effect meta-analysis model was applied using the "mean" command specifying random due to the study's high degree of heterogeneity ($I^2 > 75\%$). The output has been illustrated using a forest plot [85].

3. Results

3.1. Descriptive Analysis

The literature search returned 65 articles (Figure 1, Supplementary Table S2) published from 1969 to 2019. These articles were from 11 out of 17 Middle East countries, such as Cyprus, Egypt, Iran, Iraq, Israel, Kuwait, Palestine, Qatar, Saudi Arabia, Syria, and Turkey (Figure 2). No report on rodent helminths was available from Bahrain, Jordan, Lebanon, Oman, United Arab Emirates, and Yemen. Cestodes were the most frequently reported (50 articles) helminths in the Middle Eastern rodents, followed by nematodes (49), and trematodes (14).

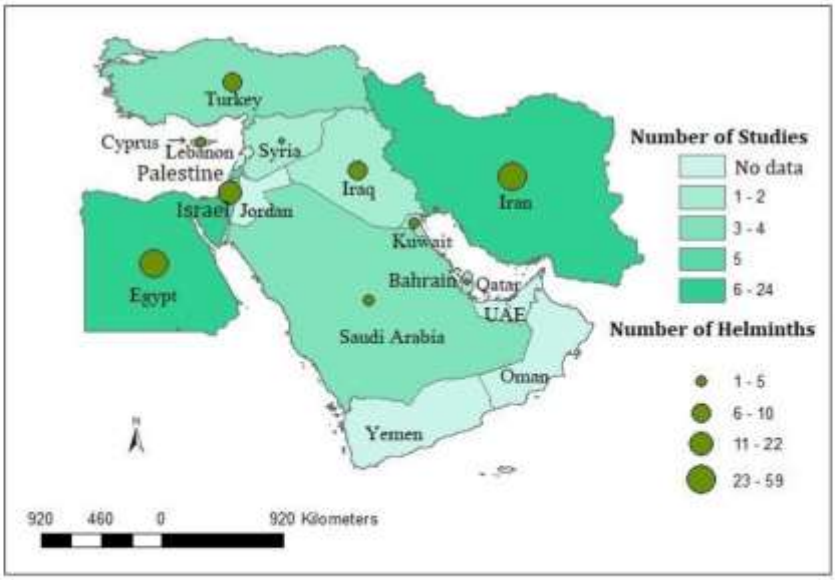

Figure 2. The map depicted the Middle East countries with the total number of studies and the number of helminths detected in rodents.

All 65 studies reported at least 9628 rodents (47% females and 53% males). A total of 44 rodent species from 6 families were listed (Supplementary Table S3). The analysis identified *Acomys dimidiatus*, *Jaculus jaculus*, *Meriones crassus*, *Mus musculus*, and *Rattus norvegicus*, *Rattus ratus* were widely distributed as these rodents were reported from where *Mus musculus* (n = 1251, 12.6%), *Rattus norvegicus* (n = 3325, 33.6%), and *Rattus rattus* (n = 1694, 17.1%) as the most common. Besides, three sub-species of *Rattus rattus*, such as *Rattus rattus alexandrines*, *Rattus rattus frugivorous*, and *Rattus rattus rattus*, are prevalent in the Middle East. Moreover, the review found some other rodents, which are important as zoonotic helminth carrier. These include *Acomys cahirinus*, *Acomys dimidiatus*, *Apodemus sylvaticus*, *Apodemus witherby*, *Arvicanthus niloticus*, *Calomyscus elburzensis*, *Cricetulus migratorius*, *Gerbillus cheesmani*, *Gerbillus gerbillus*, *Meriones libycus*, *Meriones persicus*, *Mesocricetus auratus*, *Microtus socialis*, *Microtus transcaspicus*, *Mus domesticus*, *Rhombomys opimus*, and *Tatera indica*. A total of 100 species of rodent helminths were identified. Based on the available data, the estimated pooled prevalence of the different types of parasites in rodents has been presented in Table 1. The random effect meta-analysis showed that the pooled prevalence of cestode ranged from 12.87% (95% CI: 5.17–20.57, $I^2\%$ = 80.6, $p < 0.001$) in Turkey to 57.66% (95% CI: 34.63–80.70, $I^2\%$ = 85.6, $p < 0.001$) in Saudi Arabia. The nematode prevalence was varying from 0.16% (95% CI: −0.15–0.47, $I^2\%$ = 0.0) in Cyprus to 56.24% (95% CI: 11.40–101.1, $I^2\%$ = 96.7, $p < 0.001$) in Turkey. Moreover, the prevalence of trematode ranged from 0.24% (95% CI: −0.11–0.59 $I^2\%$ = 0.0, $p < 0.001$) in Iran to 15.83% (95% CI: 6.25–25.1, $I^2\%$ = 98.5, $p < 0.001$) in Egypt.

Table 1. Estimated pooled prevalence of the rodent helminths in the Middle East countries.

Country	Parasite	Pooled Estimates (%)	95% CI	Heterogeneity Chi-Squared (χ^2)	$I^2\%$	p-Value
Cyprus	Nematode	0.160	−0.15–0.47	0.00	0	-
	Cestode	14.72	11.94–17.50	0.00	0	-
Egypt	Nematode	31.81	19.83–43.78	259.62	97.3	<0.001
	Cestode	27.49	23.72–31.26	17.18	70.9	<0.001
	Trematode	15.827	6.56–25.1	344.74	98.5	<0.001
Iran	Cestode	18.21	11.59–24.83	56.08	87.5	<0.001
	Nematode	33.93	16.52–51.35	154.53	96.8	<0.001
	Trematode	0.24	−0.11–0.59	0.19	0	<0.001
Palestine	Nematode	24.39	11.25–37.54	0.00	0	-
	Cestode	36.59	21.84–51.32	0.00	0	-
Qatar	Cestode	26.64	8.89–44.39	13.94	92.8	<0.001
Saudi Arabia	Cestode	57.66	34.63–80.70	6.74	85.6	<0.001
	Trematode	14.685	8.88–20.49	0.00	0	-
Turkey	Nematode	56.24	11.40–101.1	30.10	96.7	<0.001
	Cestode	12.87	5.17–20.57	10.34	80.6	<0.001

CI: confidence interval; I^2: inverse variance index; χ^2: Cochran's Q chi-square.

3.2. Rodent Cestodes in the Middle East Countries

Rodent cestodes information was available from all 11 Middle Eastern countries (Supplementary Table S3). A total of 21 rodent cestode species that belongs to 8 families have been reported in this review. Most of the cestodes were from Egypt and Iran (12 cestode species from each county). Out of 44 rodent species, *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* were frequently identified with the cestode infestation. Three species of cestodes have been frequently reported, viz: *Hymenolepis diminuta* (20 reports from 5 countries), *Hymenolepis nana* (30, 9), and *Cysticercus fasciolaris* (23, 4). Figure 3 shows the prevalence estimates from individual studies on cestodes in rodents of the Middle East countries,

which ranged from 7.69 (95% CI: 2.22–13.17) to 68.57 (95% CI: 59.69–77.45) with an overall estimated prevalence 24.88 (95% CI: 19.99–29.77, $I^2\% = 94.9$, $p < 0.001$).

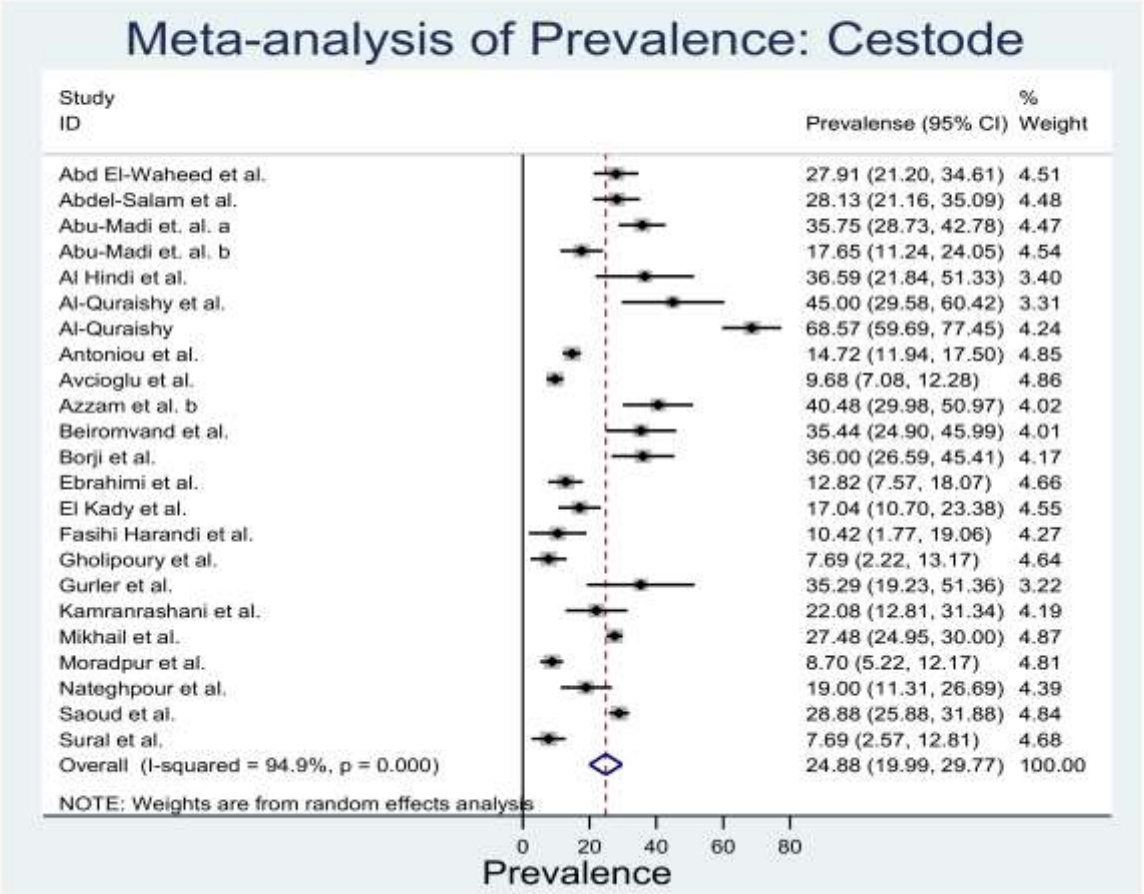

Figure 3. Forest plot of the prevalence estimates of cestode in rodents among the Middle East countries (the center dot representing point estimates whereas Gray Square representing the weight of each study to the meta-analysis).

3.3. Rodent Nematodes in the Middle East Countries

Rodent nematodes were studied in 8 countries in the Middle East, namely Cyprus, Egypt, Iran, Iraq, Israel, Kuwait, Palestine, and Turkey (Supplementary Table S3). Nematodes from 23 families represented the 56 nematode species in this region. Most of the rodent nematodes were reported from Egypt ($n = 24$) and Iran ($n = 31$) and the rodent species such as *Mus musculus*, *Rattus norvegicus*, *Rattus rattus*, *Meriones persicus*, *Acomys dimidiatus*, and *Tatera indica*. However, the nematodes, *Aspiculuris tetraptera*, *Capillaria hepatica*, *Syphacia obvelata*, *Streptopharagus kuntzi*, and *Trichuris muris* were most frequently reported and widely distributed. These nematodes were reported from three or more countries in the Middle East. Figure 4 shows the prevalence estimates from individual studies on nematodes in rodents of the Middle East countries, which ranged from 0.16 (95% CI: −0.15–0.47) to 79.41 (95% CI: 65.82–93.0) with an overall estimated prevalence of 32.71 (95% CI: 24.89–40.54, $I^2\% = 98.6$, $p < 0.001$).

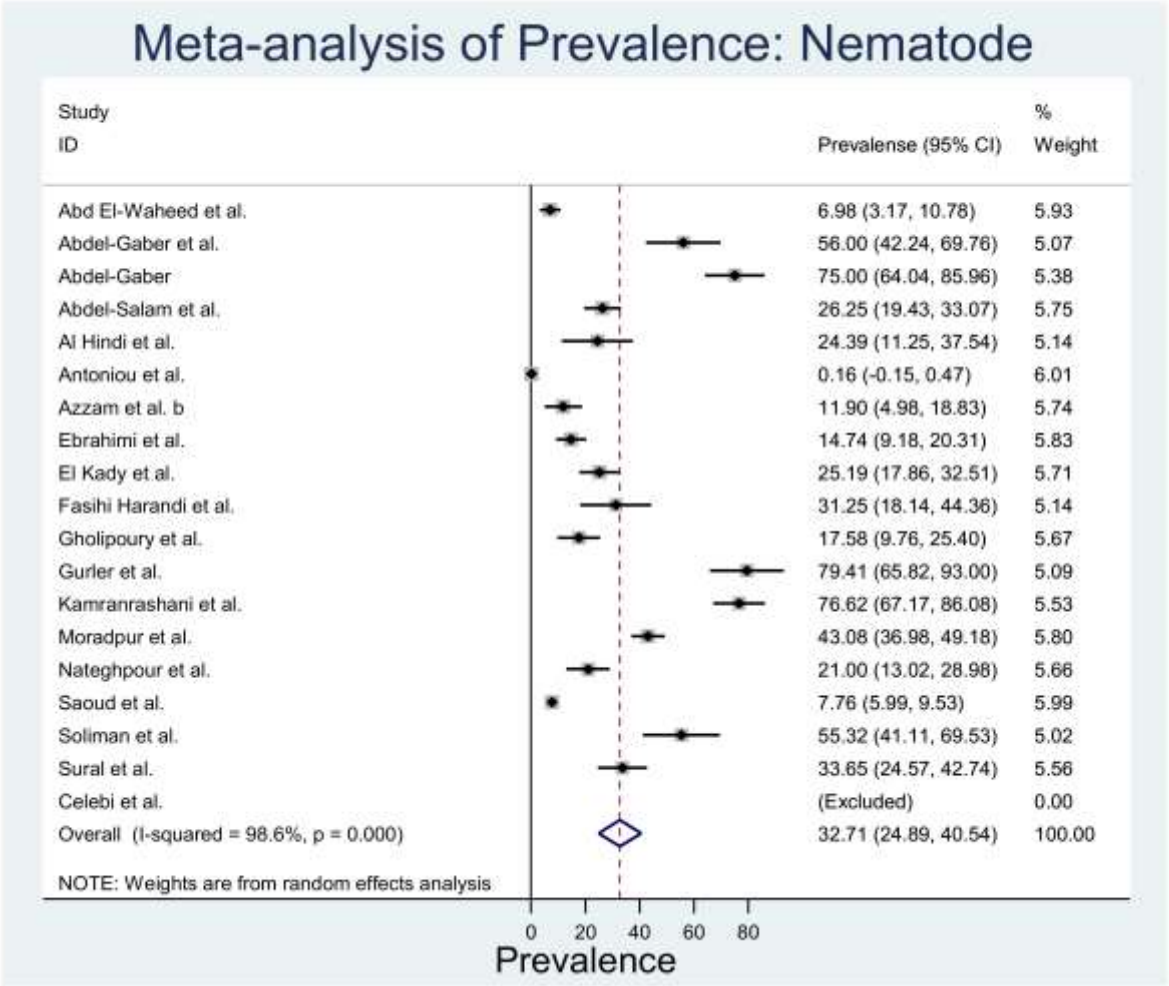

Figure 4. Forest plot of the prevalence estimates of nematode in rodents among the Middle East countries (the center dot representing point estimates whereas Gray Square representing the weight of each study to the meta-analysis).

3.4. Rodent Trematodes in the Middle East Countries

The reviewed studies reported rodent trematodes in Egypt, Iran, Israel, and Saudi Arabia (Supplementary Table S3). At least 23 trematode species from 11 families of trematodes were reported in the Middle Eastern rodents. Reports from Egypt (n = 21) were more descriptive of these trematodes. Moreover, *Fasciola* sp. was detected in Saudi Arabia, *Scaphiostomum* sp. in Israel, and *Notocotylus neyrai* and *Plagiorchis muris* were identified in Iran. The review found *Arvicanthus niloticus*, *Rattus norvegicus*, and *Rattus rattus* are three rodent species important for trematode infestation. Figure 5 shows the prevalence estimates from individual studies on trematode in rodents of the Middle East countries, which ranged from 0.20 (95% CI: −0.19–0.59) to 36.90 (95% CI: 26.59–47.22) with an overall estimated prevalence of 10.17 (95% CI: 6.7–13.65, I^2% = 98.3, $p < 0.001$).

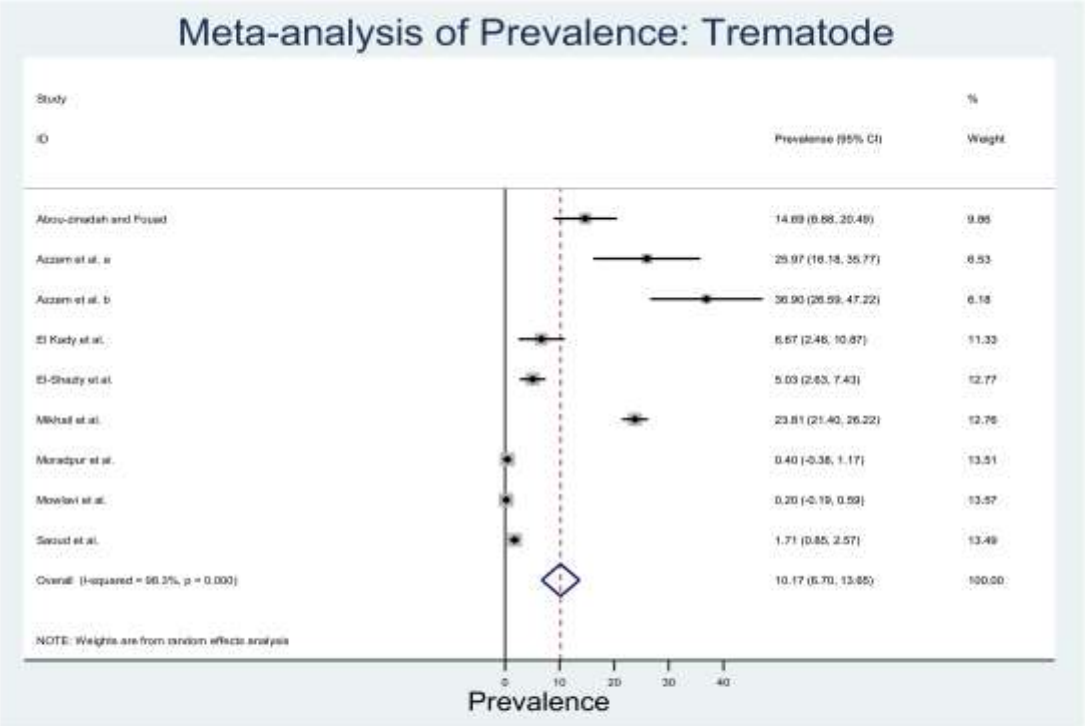

Figure 5. Forest plot of the prevalence estimates of trematode in rodents among the Middle East countries (the center dot representing point estimates, whereas Gray Square representing the weight of each study to the meta-analysis).

3.5. Zoonotic Importance of the Rodent Helminths in the Middle East Countries

Out of the 100 species of rodent helminths detected in this review, 22 species have zoonotic importance; 7 cestodes, 6 nematodes, and 9 trematodes. The zoonotic helminths, their hosts, and possible human infection sources have been illustrated in Table 2.

Table 2. Rodent-borne zoonotic helminths in the Middle East countries.

Parasites	Host	Source of Human Infection	Reference
Rodent-borne zoonotic cestodes:			
Raillietina celebensis and *R. demerariensis*.	DH: rodent; IH: ant and beetle	Ingestion of food contaminated with infected insects	[5,6]
Hymenolepis diminuta and *H. nana*	DH: rodent; IH: *H. diminuta*: flea and beetle. *H. nana* does not require IH.	Consumption contaminated food with rodent feces containing parasitic egg	[6,86,87]
Mesocestoides sp.	DH: dog and cat; 1st IH: ant and mite, 2nd IH: rodent, bird, amphibian, and reptile	Consumption of undercooked meat of amphibians and reptiles containing infective larva (tetrathyridium)	[5,6]
Taenia taeniaeformis	DH: cat; IH: rodent	There is a report that *Taenia taeniaformis* can infect humans	[88]
Echinococcus multilocularis	DH: dog, fox; IH: rat	Ingestion of embryonated eggs	[86]

Table 2. *Cont.*

Parasites	Host	Source of Human Infection	Reference
Rodent-borne zoonotic nematodes:			
Angiostrongylus cantonensis	DH: rat and mollusk; IH: snail, prawn, crab, and frog	Ingestion of uncooked IH or vegetables contaminated with infected larvae	[6]
Gongylonema pulchrum	DH: ruminant, pig, wild boar, non-human primate, carnivore, and rodent; IH: beetles and cockroaches	Ingestion of IH or drinking of water contaminated with infective larvae	[5,6]
Trichinella spp.	Pig, wild boar, and rodent	Ingestion of uncooked muscle with encysted larvae	[6]
Trichostrongylus spp.	Herbivorous animal	Consumption of food and water contaminated with animal feces containing infective larvae	[6]
Capillaria hepatica	Rat, carnivore, and humans	Consumption of food contaminated with feces containing embryonated eggs	[5]
Trichuris trichiura	Humans	Consumption of food contaminated with feces containing *Trichuris* egg.	[5]
Rodent-borne zoonotic trematodes:			
Echinochasmus sp., *Echinoparyphium recurvatum*, and *Echoinostoma* sp.	DH: humans, rat, duck 1st IH: snail, 2nd IH: snail, amphibian, bivalve, fish	Ingestion of uncooked fish containing metacercariae	[2,89]
Fasciola hepatica	DH: herbivore; IH: snail	Ingestion of metacercariae contaminated vegetable	[6,34]
Haplorchis *pumilio*, *Pygidiopsis genata*, *Stictodora tridactyla*, *Prosthodendrium* spp., and *Plagiorchis muris*	DH: dog, cat, rat, duck, humans; 1st IH: snail, 2nd IH: fish	Eating uncooked fish harboring viable metacercariae	[88,90]
Schistosoma mansoni	DH: Vertebrate animal; IH: snail	Penetrate the DH skin	[6,86]

Note: DH: Definite host, IH: Intermediate host.

4. Discussion

This study reviewed the literature published in English on helminths-infested rodents in the Middle East region. The majority of the studies (47 of 65) were from Iran and Egypt, most likely due to their long history of rodent-borne zoonotic disease (like murine typhus, plague, tularemia) epidemics, which resulted in millions of death [4,91–94]. Thus, this topic became a central focus of public health research in these countries. The present review found three commensal rodent species: *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* to be more common and carrying most of the zoonotic helminths within this region. Previous literature described that these species occupy different habitats with higher population density than the other species and pose considerable risk to public health [4]. Although rodent cestodes were most frequently reported (n = 50) helminth in this review, the meta-analysis detected the overall rodent nematode prevalence was highest (32.7%) compared to cestodes (24.88%) and trematodes (10.17%) prevalence. Out of the 22 zoonotic helminths detected in this review, *Capillaria hepatica*, *H. diminuta*, *H. nana*, and *C. fasciolaris* have been found as widespread distribution. Furthermore, some non-zoonotic helminths such as *Aspiculuris tetraptera*, *Syphacia obvelata*, *Streptopharagus kuntzi*, and *Trichuris muris* were reported from three or more countries in this region.

Rodents have several beneficiary activities in ecology, such as soil aeration and water absorption ability, biotic recovery, and insect control [4,95]. In this regard, the presence of healthy rodents is essential

for ecology [96]. Helminths infestation in rodents affects their own health and can subsequently alter the rodent-environment ecology to a considerable degree. Moreover, rodent helminths are important for humans, livestock, and pet animal health. Hymenolepiais is a major zoonotic rodent cestode [6]. Fascioliasis is hazardous for livestock health as well as for humans [6,97]. The definite host of *Taenia taeniaeformis* is the cat, where a stage of this cestode lifecycle (the cystic form, *Cysticercus fasciolaris*) is completed in rodents. An increase of *Cysticercus fasciolaris* in rodents can increase the health risk of cats [98]. Thus, rodent helminths have an impact on the ecology as well as humans and animal health.

Rodent-borne zoonotic helminths incur significant socioeconomic losses, although the zoonotic helminths' socioeconomic burden can differ from species to species [3]. *Hymenolepis diminuta* and *Hymenolepis nana* are major zoonotic cestodes [3,99]. *Trichostrongylus* sp. and *Trichuris trichiura* are generally considered as major nematode threats [100]. The socioeconomic burden caused by *Angiostrongylus cantonensis*, *Gongylonema pulchrum*, *Trichinella* sp., and *Capillaria hepatica* are likely to be very low [3].

There is an information gap on rodent-borne zoonotic helminths in the Middle East countries. Some zoonotic cases of helminths infestation were reported in rodents by some countries in the Middle East, but none involved humans who might have been infected with the same helminths. Humans hymenolepiasis were reported in Bahrain [101], Cyprus [102], Jordan [103], Oman [104], Palestine [105], Qatar [106], and Yemen [107]. The *Hymenolepis nana* is a common zoonotic helminth transmitted from rodents to humans and the prevalence ranged from 0.15% to 12.2% in some Middle East countries with prevalence of specific countries such as Jordan (1.8%) [103], Oman (5.9%) [104], Palestine (1.0%) [105], Qatar (0.15%) [106], and Yemen (12.2%) [107]. Egg of *Hymenolepis diminuta* was detected from soil samples of school playgrounds of Jordan [108]. There is no report of rodent hymenolepiasis within these countries. *Echinococcus* spp. is a major helminth for human health, which was detected in rodents of Egypt, Iran, and Turkey. Human cases of alveolar hydatid cysts were reported from Iran, Kuwait, Saudi Arabia, and Turkey [109,110].

The rodent lungworm, *Angiostrongylus cantonensis*, causes eosinophilic meningomyelitis in humans, reported in Israel [111]. Gongylonema infection is reported in humans [112] and dromedaries [113] from Iran. *Trichinella* was a widespread parasite infecting humans and other mammals, although the former makes for a poor host for said organism [6]. There are reports of humans trichinellosis from Iran [114], Israel [115], Lebanon [116], and Turkey [117]. Human cases of trichostrongyliasis infestation were reported in Egypt [118], Iran [119], Israel [120], and Turkey [121]. Eggs of *Trichostrongylus* sp. were detected from soil samples of public places of Jordan [108] and Iraq [122]. Humans reports of *Trichuris trichiura* are available from Bahrain [123], Egypt [118], Israel [120], Jordan [103], Oman [104], Palestine [105], Qatar [124], Saudi Arabia [125], Turkey [126], and Yemen [107]. *Trichuris muris*, the rodent whipworm, does not have any zoonotic importance. Eggs of *Trichuris* were found in the soil of the public place of Iraq [122]. *Trichuris trichiura* is not a rodent specific nematode. The report of *Trichuris trichiura* in Iranian rodents [67] may be a case of accidental infestation.

Schistosoma and *Fasciola* are two major humans trematodes globally [3]. The high prevalence of *Fasciola* was recorded in Egypt, Iran, and Yemen [127]. Human cases of schistosomiasis were noted in Egypt [3], Iran [128], Israel [129], Jordan [103], Saudi Arabia [130], Turkey [131], and Yemen [3,132], whereas *Heterophyes heterophyes* were reported from Egypt and Saudi Arabia [133,134]. There are non-humans (fish, dogs, and cats) reports of *Pygidiopsis genata*, *Haplorchis pumilio*, *Haplorchis yokogawai*, and *Heterophyes heterophyes* from Egypt, Iran, Iraq, Israel, Palestine, Kuwait, Saudi Arabia, Turkey, UAE, and Yemen [135–138]. However, these rodent trematodes in the current review were mostly reported from Egypt and Iran.

Based on the meta-analysis, the overall prevalence of rodent trematodes was less than that of nematodes and cestodes in the Middle East, which had received more emphasis in other similar reports [110,127]. Efficient management of water resources are important factor for prevalence of trematode prevalence [139,140]. The presence of deserts means shortage of surface water in some of the countries of Arabian Peninsula such as Bahrain, Kuwait, Oman, Qatar, Saudi Arabia,

and United Arab Emirates [141], which may be the cause of shortage of aquatic intermediate hosts of trematodes in these countries. Therefore, rodent trematodes are less reported in these countries. More research should be conducted to find rodent-borne trematodes in the countries of this region.

The reviewed articles in the current study described some of the factors that can influence the population of rodent-borne helminths within the Middle East, necessitating a need to develop a plan of action to control rodent helminths. The abundance of rodent-borne helminths depends on the host organism's prevalence and its distribution [29,44]. An increase in the rodent population may increase the risk of humans getting infected by rodent parasites [142]. Rodents who inhabit animal farms have easy access to animal feed, and thus, they can be considered a potential vector and reservoir of animal and zoonotic diseases where animals serve as hosts [26]. *Hymenolepis diminuta* in the rodent are linked with some insects as intermediate hosts, such as *Xenopsylla astia*, which has a clear seasonal pattern. In Qatar, a research found that rodents are more infested with *Hymenolepis diminuta* in summer due to the *X. astia* abundance [24]. Several studies reported that the prevalence of rodent helminths is increased with rodent age [23,24,35,51]. Rodent helminths infestation can change with rodent host species [48]. The nematode, *Syphacia obvelata*, was reported to be most abundant in *Mus musculus* [64].

Rodent population control is a primary way to control rodent zoonotic diseases [143,144]. The other contributing factors, such as rodent species, seasons of the year, intermediate host, rodent control management in the residential areas, and animal farms, should also be considered on rodent related zoonoses control. As most of the rodent-related zoonotic helminths are linked to herbivores and carnivores [5,6,86,88], it is vital to manage dogs, cats, and livestock animals to avoid the spread of helminth infestation. Thus, One Health practice comes as a practical approach to control rodent-borne helminth prevalence [145]. "One Health is a collaborative, multisectoral, and transdisciplinary approach - working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment" [146]. One Health practice by linking veterinary, medical, ecology, entomology, parasitology, zoology fields, and local people are essential for rodent helminths prevention and control.

5. Conclusions

Rodent helminths in the Middle Eastern countries have been documented, which also highlighted rodent-borne zoonotic helminths. *Rattus norvegicus*, *Rattus rattus*, and *Mus musculus* were the most frequently reported rodents and infected with helminth parasites. Out of the 22 rodent-related zoonotic helminths, *Capillaria hepatica*, *H. diminuta*, *H. nana*, and *C. fasciolaris* were most frequent in this region. The current study illustrates that there is an information gap on the availability, diversity, and dynamics of rodent helminths and their interaction between humans and animals in the Middle East. Thus, the public health importance of rodent-borne helminth parasites is not fully recognized. However, rodent control should be the primary concentration by a One Health approach to control the spread of these helminths at the humans-animal-environmental interface in the countries of this region. We also suggest countrywide and detailed studies be conducted on rodent-borne helminths along with their impact on public health in this region.

Supplementary Materials: The following are available online at http://www.mdpi.com/2076-2615/10/12/2342/s1, Table S1: Prisma checklist, Table S2: Extracted data from the selected 65 studies, Table S3: Prevailing rodents and common cestodes, nematodes, and trematodes in the Middle East.

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Chapter 2.3: Rodent-Related Zoonotic Pathogens at the Human–Animal–Environment Interface in Qatar: A Systematic Review and Meta-Analysis

One objective of the PhD research was to know the zoonotic pathogens carried by rodents in Qatar. It was essential to document the reported rodent-related zoonotic pathogens among humans, other animals, and environmental interface in this country. Therefore, the current study was undertaken to review and compile all reports of rodent-related zoonotic pathogens in the history of Qatar.

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Rodent-Related Zoonotic Pathogens at the Human–Animal–Environment Interface in Qatar: A Systematic Review and Meta-Analysis

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Abstract: Rodents are one of the most diversified terrestrial mammals, and they perform several beneficial activities in nature. These animals are also important as carriers of many pathogens with public health importance. The current systematic review was conducted to formulate a true depiction of rodent-related zoonoses in Qatar. Following systematic searches on PubMed, Scopus, Science Direct, and Web of Science and a screening process, a total of 94 published articles were selected and studied. The studied articles reported 23 rodent-related zoonotic pathogens that include nine bacterial, eleven parasitic, and three viral pathogens, from which the frequently reported pathogens were *Mycobacterium tuberculosis* (32 reports), *Escherichia coli* (23), and *Salmonella* spp. (16). The possible pathway of entry of the rodent-borne pathogens can be the land port, seaports, and airport of Qatar through carrier humans and animals, contaminated food, and agricultural products. The pathogens can be conserved internally by rodents, pets, and livestock; by agricultural production systems; and by food marketing chains. The overall estimated pooled prevalence of the pathogens among the human population was 4.27% (95%CI: 4.03–4.51%; $p < 0.001$) with significant heterogeneity ($I^2 = 99.50\%$). The top three highest prevalent pathogens were *M. tuberculosis* (30.90%; 22.75–39.04%; $p < 0.001$; $I^2 = 99.70\%$) followed by *Toxoplasma gondii* (21.93%; 6.23–37.61%; $p < 0.001$; $I^2 = 99.30\%$) and hepatitis E virus (18.29%; 11.72–24.86%; $p < 0.001$; $I^2 = 96.70\%$). However, there is a knowledge gap about the listed pathogens regarding the occurrence, transmission pathways, and rodent role in transmission dynamics at the human–animal–environment interface in Qatar. Further studies are required to explore the role of rodents in spreading zoonotic pathogens through the One Health framework, consisting of zoologists, ecologists, microbiologists, entomologists, veterinarians, and public health experts in this country.

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1. Introduction

Rodentia is one of the most diversified mammalian orders in the world [1]. With 2552 known species, they make up 39.3% of mammals and are the essential components of many terrestrial ecosystems. These animals have several beneficial activities in nature, such as soil aeration and insect control [2–4]. However, rodents are also sources of zoonotic pathogens [4–6]. Almost 10% of the global rodent population are either carriers or reservoirs of pathogens with public health importance [5,6]. Rodents transfer infectious agents to humans by direct contact with humans and animals or through contamination of human or animal food and water with rodent stool, hair, and urine. Arthropod vectors on rodent skin are also able to carry several zoonotic pathogens [5–8]. Rodent-borne diseases and their prevalence are associated with several factors, including the rodent population, human socio-economic lifestyle, human conflict, and war [7,9–11]. Human-related activities such as migration, large-scale traveling, trade, urbanization, and agricultural activities can also be facilitating factors in transferring rodent-borne pathogens from one community to another [12,13].

Qatar is a small desert country located on the coast of the Arabian Peninsula [14]. The country is inhabited by multinational people from around 94 countries around the world [15]. The current population of the country is 2.8 million [16], of whom only 10.5% are Qatari nationals. The people who make up around 80% of the Qatar population are mainly from India, Bangladesh, Nepal, Egypt, the Philippines, Pakistan, Sri Lanka, Sudan, Syria, Jordan, Lebanon, Kenya, and Iran [15]. Approximately 83% of these non-Qatari residents are primarily construction workers, housemaids, drivers, and retail market workers [17]. As a desert country, agriculture is limited [18], and the country imports live animal and food products from nearby countries such as Iran, Turkey, India, Pakistan, and Bangladesh [19,20].

The rodent fauna of the country is limited to four species, which include three commensal species (*Mus musculus, Rattus norvegicus,* and *Rattus rattus*) and a single wild rodent species (*Jaculus loftusi*, previously known as *Jaculus jaculus*) [21–24]. *M. musculus, R. norvegicus*, and *R. rattus* are reported to spread rodent-borne zoonoses among the human population throughout the world [8,25]. The countries from where most of the Qatari residents originated and some of the countries from where food and agricultural products are imported are endemic with several rodent-borne diseases, including leishmaniasis, enteric fever, echinococcosis, and hepatitis E virus [26–28]. For effective prevention and control measures of such diseases, it is essential to know the status of these pathogens in Qatar. However, to the authors' knowledge, no studies have been performed to understand the rodent-borne diseases in this country at the human–animal–environment interface. Therefore, the current study aimed to identify the rodent-related zoonotic pathogens detected in humans, animals, and environmental sources in Qatar and possible transmission pathways and to estimate the pooled prevalence of these pathogens among humans in this country.

2. Materials and Methods

We conducted a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [29]: (1) We conducted a database search to find relevant articles, (2) we assessed the relevance of the searched articles, and (3) we extracted data from the included articles (Figure 1, and Supplementary Table S1).

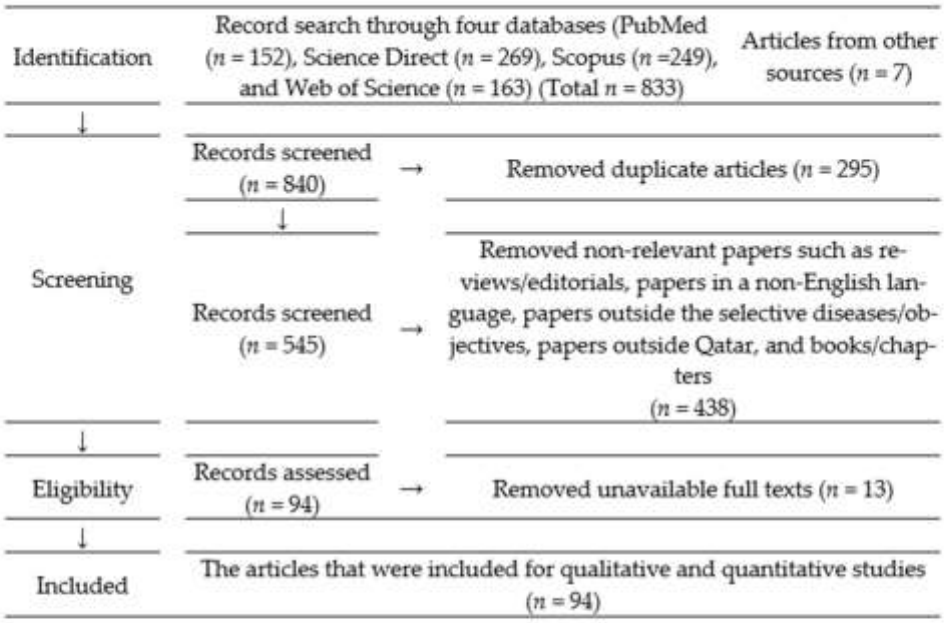

Figure 1. PRISMA flow diagram describing selection of published articles on rodent-related diseases with public health importance in Qatar and the inclusion/exclusion process used in the study.

2.1. Data Search

In the beginning, we conducted a mini-review to determine the list of rodent-borne diseases. We found a total of 88 diseases that can have public health importance (Supplementary Table S2). Among these, 26 were bacterial diseases, 2 fungal, 27 parasitic, and 33 viral diseases. Then, we conducted a systematic literature search from 20 to 26 March 2020 through four databases: PubMed, Scopus, Science Direct, and Web of Science. The search included all the original field reports for each of the 88 rodent-borne diseases individually in Qatar with no time limit of publication. The search terms included ((disease name OR synonym OR causal agent[s]) AND Qatar). We screened the searches as "Title/Abstract" in PubMed, "Find articles with these terms" in Science Direct, "TITLE-ABS-KEY" in Scopus, and "Topic" in Web of Science.

2.2. Assessing the Searched Articles

We compiled the searched document on the EndNote X9 system (Clarivate Analytics, Philadelph, PA, USA). Using EndNote X9, we identified and removed the duplicate articles. After that, two authors assessed the title and abstract of the articles. The articles that had unknown relevance based on the title and abstract study were subjected to full-text screening. We included only original research studies published in English. We excluded articles that did not fulfill the objective, were reviews/editorials, were outside the selective diseases, were from outside Qatar, or were books/chapters.

2.3. Data Extraction

The extracted data included the study type and season, the pathogen, target population, total sample tested and total positives, and associating factors of a disease prevalence and dynamics (Supplementary Table S3).

2.4. Data Analysis

We collected the relevant data in a Microsoft Excel spreadsheet and analyzed them using the statistical software STATA/IC-13.0 (Stata Corp, 4905 Lakeway Drive, College

Station, TX 77845, USA). Descriptive statistics of the selected articles were calculated and expressed as percentage (%) and 95% confidence interval (CI). Then, the crude prevalence estimation was calculated by dividing the total number of individual positive pathogens with the total number of sampled and expressed percentages (%). The crude estimate of prevalence was used for the 95% confidence interval (CI), the p-value, and heterogeneity (I^2). A random-effect meta-analysis model was applied using the "mean" command specifying random due to the study's high degree of heterogeneity(I^2 > 80%) [30]. The output was illustrated using a forest plot.

3. Results

3.1. Characteristics of the Studied Articles

The literature search resulted in a total of 94 articles published from 1991 to 2020 (Table 1). Many of the articles (n = 42, 44.68%, 95%CI: 34.41–55.29%) were published by last five years (2016–2020), and only one (n = 1, 1.06%; 0.027–5.79%) was published between 1991–1995. The studies were mostly conducted in human hosts (n = 80, 85.11%, 95%CI: 76.28–91.61), followed by animals (n = 10, 10.64%; 5.22–18.70), and the environment (n = 1, 1.06%, 95%CI: 0.027–5.79), with some studies on the human–animal–environment interface. The majority of the studies assessed rodent-related bacteria (n = 62, 65.96%, 95%CI: 55.46–75.42), followed by helminths (n = 10, 10.64%, 95%CI: 5.22–18.70), protozoa (n = 9, 9.57%; 95%CI: 4.47–17.40), and viruses (n = 5, 5.32%, 95%CI: 1.75–11.98). However, some articles described mixed infections.

Table 1. Characteristics of the reviewed articles.

Characteristics	Number of Articles (%; 95%CI)	References
Publication Year		
1991–1995	1 (1.06; 0.027–5.79)	[31]
1996–2000	3 (3.19; 0.66–9.04)	[32–34]
2001–2005	12 (12.77; 6.77–21.24)	[21,35–45]
2006–2010	13 (13.83; 7.57–22.49)	[46–58]
2011–2015	23 (24.47; 16.19–34.42)	[22,59–80]
2016–2020	42 (44.68; 34.41–55.29)	[81–122]
Host		
Humans	80 (85.11; 76.28–91.61)	[31–45,49–54,56–75,77–81,83–92,94–99,101,103,104,107–118,120–122]
Animals	10 (10.64; 5.22–18.70)	[21,22,46–48,55,82,93,105,106]
Environment	1 (1.06; 0.027–5.79)	[36]
Humans + Animals	1 (1.06; 0.027–5.79)	[119]
Animals + Environment	1 (1.06; 0.027–5.79)	[76]
Humans + Environment	1 (1.06; 0.027–5.79)	[104]
Pathogen		
Bacteria	62 (65.96; 55.46–75.42)	[31–45,53,54,57,58,62–67,69–82,87,88,92,94–98,102,103,105–111,114–117,120,121]
Helminth	10 (10.64; 5.22–18.70)	[21,22,46–48,60,63,68,86,122]
Protozoa	9 (9.57; 4.47–17.40)	[49,50,55,83,84,89,99–101]
Virus	5 (5.32; 1.75–11.98)	[45,56,90,113,119]
Helminth + Protozoa	4 (4.25; 1.17–10.54)	[51,52,61,85]
Bacteria + Protozoa	4 (4.25; 1.17–10.54)	[59,91,93,112]

CI: Confidence Interval.

3.2. Possible Transmission Pathways of the Pathogens in Qatar

The current review shows that besides humans, rodent-related zoonotic pathogens are available among livestock, stray (free on-street) and domesticated cats and dogs, big cats (cheetah), and environmental samples. In addition, rodents are usually available in every facility of an ecosystem, such as animal farms, agricultural farms, residential areas, desert ecosystems, restaurants, and sewage facilities in Qatar. Therefore, rodents can contribute to zoonotic pathogen transmission within and between these facilities. The possible transmission pathways of rodent-borne zoonotic pathogens in Qatar are illustrated in Figure 2. Moreover, the land port at the Qatar–Saudi Arabia border, the international airport, and the two seaports can also contribute to rodent-associated zoonoses transmission into Qatar by the human migration and transmission of live animals, rodents, and agricultural products from different parts of the world.

3.3. Estimated Pooled Prevalence of Pathogens

The overall estimated pooled prevalence of the rodent-related zoonotic pathogens within the human population in Qatar was 4.27% (95%CI: 4.03–4.51%; $p < 0.001$) with significant heterogeneity ($I^2 = 99.50\%$) and p-value ($p = 0.00$) (Figure 3). Among the individual pathogens, the estimated pooled prevalence of *Mycobacterium tuberculosis* was the highest (30.90%; 22.75–39.04%; $p < 0.001$; $I^2 = 99.70\%$) followed by *Toxoplasma gondii* (21.93%; 6.23–37.61%; $p < 0.001$; $I^2 = 99.30\%$), hepatitis E virus (18.29%; 11.72–24.86%; $p < 0.001$; $I^2 = 96.70\%$), *Escherichia coli* (16.34%; 13.08–19.59%; $p < 0.001$; $I^2 = 98.60\%$), *Campylobacter* spp. (8.09%; 3.48–12.70%; $p < 0.001$; $I^2 = 97.70\%$), *Salmonella* spp. (7.77%; 4.74–10.79%; $p < 0.001$; $I^2 = 94.10\%$), *Cryptosporidium* spp. (6.61%; 0.25–12.97%; $p < 0.001$; $I^2 = 98.60\%$), *Giardia duodenalis* (2.88%; 2.26–3.50%; $p < 0.001$; $I^2 = 95.10\%$), *Schistosoma* sp. (2.05%; 0.83–3.27%; $p < 0.001$; $I^2 = 99.00\%$), *Trichuris trichiura* (1.48%; 1.05–1.92%; $p < 0.001$; $I^2 = 97.50\%$), *Entamoeba histolytica/dispar* (0.62%; 0.366–0.87%; $p < 0.001$; $I^2 = 88.20\%$), *Hymenolepis nana* (0.21%; 0.12–0.31%; $p < 0.001$; $I^2 = 82.10\%$), and *Taenia* spp. (0.10%; −0.03–0.24%; $p = 0.02$; $I^2 = 74.30\%$). The overall prevalence by meta-analysis showed that bacterial organisms were the major group of pathogens followed by parasitic and viral pathogens.

3.4. The Pathogens at the Human—Animal–Environmental Interface

Of the 88 rodent-borne disease pathogens listed by mini-review at the beginning of the current systematic review, we identified 23 disease pathogens in Qatar. We described the interface of these pathogens in terms of humans, animals, and environmental hosts to determine the relationship with the One Health process in Qatar (Figure 4): we found 12 parasitic, 8 bacterial, and 3 viral pathogens. Our review revealed that *Campylobacter* spp. (including *Campylobacter coli* and *Campylobacter jejuni*) and *E. coli* are common in humans, animals, and the environment. *Salmonella* spp. (mainly *Salmonella enterica*), *Babesia* spp., *Taenia* spp., *T. gondii*, and rabies virus were reported from humans and animals. *Corynebacterium* spp. was the only pathogen reported from both humans and the environment.

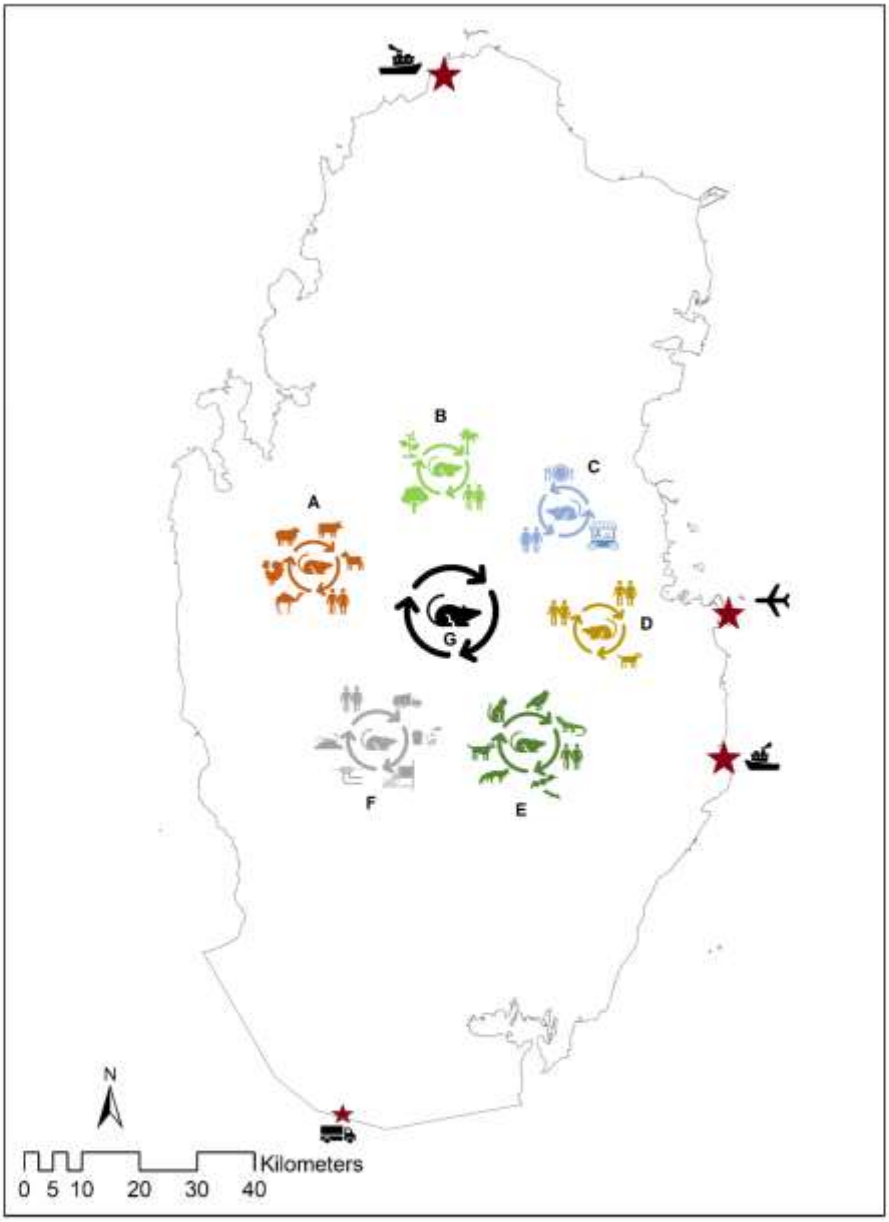

Figure 2. Possible transmission pathways of the rodent-related zoonotic pathogens at the human–animal–environmental interface in Qatar. The stars indicate the plausible routes of entry of rodent-related pathogens in Qatar via carrier immigrants and the importing of contaminated food and agricultural products. "A" indicates that rodents can be a source of transmission of pathogens among livestock animals and humans inside Qatar. Similarly, the figure illustrates how rodents can facilitate zoonotic pathogens transmission among agricultural products and humans "B", residential areas between humans and pet animal "C", in the environment between stray cats and dogs, wildlife, and humans "D", fresh food in households, restaurants, markets, and humans "E", and through the sewage system "F". Rodents can interlink zoonotic pathogens "G" between A, B, C, D, E, and F.

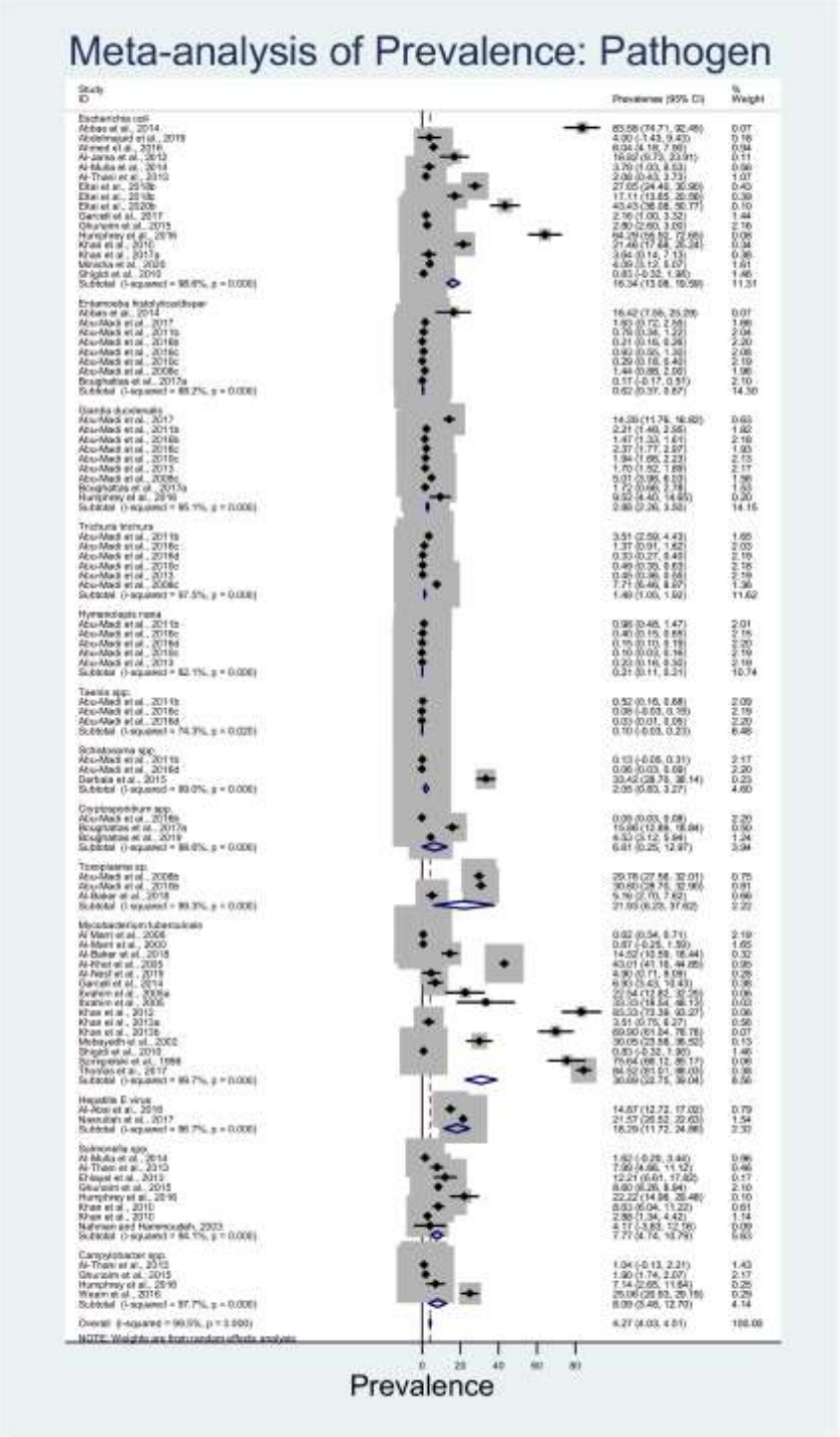

Figure 3. Forest plot of the pooled overall prevalence of rodent-related pathogens in Qatar. The central square represents point estimates, whereas the square size represents the weight of each study in the meta-analysis.

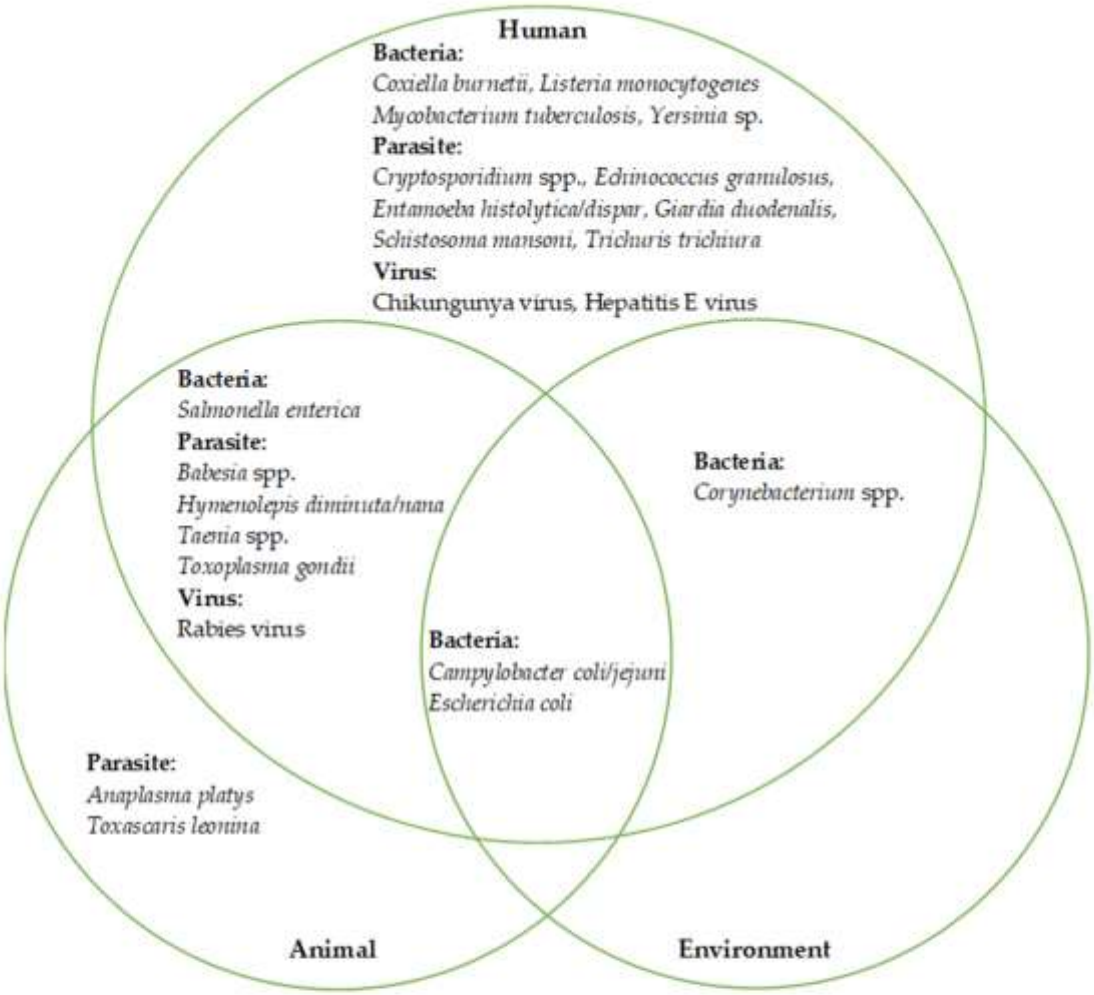

Figure 4. Rodent-related zoonotic pathogens identified at the human–animal–environmental interface in Qatar.

M. tuberculosis was detected within various forms in humans of Qatar, such as abdominal tuberculosis (TB), mastitis pulmonary TB, pleural TB, peritoneal TB, ocular TB, pancreatic TB, spinal TB, tuberculous adenitis, tuberculous arthritis, tuberculous meningitis, tuberculous peritonitis, military TB, latent TB, and multi-drug resistant TB. Moreover, childhood TB with many of the above forms has been detected in children in Qatar.

Supplementary Table S2 shows that the pathogenic *E. coli*, *Salmonella* spp., and *Campylobacter* spp. are three frequently reported causes of human gastroenteritis in this country. *E. coli*, including EAEC (enteroaggregative *E. coli*), EIEC (enteroinvasive *E. coli*), EPEC (enteropathogenic *E. coli*: EPEC 2, EPEC 3, and EPEC 4), ETEC (enterotoxigenic *E. coli*), STEC (Shiga-like toxin-producing *E. coli*), and *E. coli* O157: H7 were detected among humans. Besides human gastroenteritis, *E. coli* was found to cause surgical wound infection, arthritis, genital tract infection, meningitis, peritonitis, pneumonia, septicemia, skin infection, and urinary tract infection. *E. coli* O (O157: H7, O26, O45, O103, and O111) was identified from animal sources, such as camel, cattle, and sheep. *E. coli* was isolated in human food, such as fresh fruit juice; fresh vegetables; cattle and camel milk; meat animal carcasses, such as camel, cattle, chicken, and sheep carcasses; hand swabs of fresh product market workers; market environments; animal bedding; feed and water troughs; and abattoir environments.

S. enterica (type B, C1, C2, D, E), *S. enterica* paratyphi A, *S. enterica* Typhi were detected in humans. Among the non-human sources, *S. enterica* was isolated from animal bedding, camel carcasses, and cattle feces. In addition, *Campylobacter* spp., such as *C. coli, C. fetus, C. jejuni, C. laridis,* and *C. upsaliensis,* were confirmed from human diarrheagenic samples. Moreover, *C. coli* and *C. jejuni* were isolated from non-human sources, via camel and cattle milk; camel, cattle, and sheep feces; camel, cattle, chicken, and sheep carcasses; cattle udders; chicken abattoirs; feed water troughs; and bedding of animals in livestock farms.

Corynebacterium spp. was isolated from a fresh product market. *Listeria monocytogenes* was confirmed in children (<1 year), causing meningitis. In addition, soldiers at the US army base in Qatar were positive for *Coxiella burnetii* antibodies, and non-specific *Yersinia* was detected in fecal samples of humans with gastroenteritis.

The parasites that were detected in Qatar included 5 protozoa, 3 cestodes, 2 nematodes, and one trematode. *T. gondii* was reported to have vertically transmitted from mother to baby. Diarrheagenic protozoa, such as *Cryptosporidium parvum, Cryptosporidium hominis, Cryptosporidium meleagridis, G. duodenalis,* and pathogenic amoebae (*Entamoeba histolytica/dispar*), were reported among humans in Qatar. Besides gastroenteritis, *E. histolytica* was detected to cause a liver abscess. There was a case of non-specific human babesiosis in Qatar. However, *Babesia gibsoni* and *Babesia vogeli* are present among pet dogs in this country. Among the cestodes, *Hymenolepis diminuta* is a common parasite among rodents.

H. nana and *Echinococcus granulosus* were reported in humans. Non-specific *Taenia* and *Taenia taeniaeformis* were identified in humans and cats, respectively. Among the nematodes, *Toxascarsis leonina* was identified in cats, and *T. trichuria* was identified in humans. However, only the trematode *Schistosoma mansoni* was reported among humans in this country. The review found three viruses in Qatar, including chikungunya, hepatitis E, and rabies, of which rabies was reported in humans, camels, and foxes.

4. Discussion

4.1. Characteristics of Rodent-Borne Pathogens

The current review studied 94 research articles to understand the rodent-related zoonotic pathogens in Qatar. About 25% (23/88) of the rodent-related pathogens have been reported in this country. Most of the pathogens (20/23) were from humans, whereas only *H. diminuta* was from rodents. However, all these 23 infectious agents are important as they are zoonotic and can cross the species barrier at any time. In addition, some infectious agents have higher importance for public health in Qatar, such as *T. gondii, S. enterica,* which were reported multiple times or from multiple sources.

4.2. Bacterial Pathogens

We detected different types of bacterial pathogens in the current review. *M. tuberculosis* was the most studied pathogen, followed by *E. coli, Salmonella* spp., and *Campylobacter* spp. The overall estimated pooled prevalence (30.89%) suggests that tuberculosis is a high-risk disease in this country. However, the reviewed studies tested tuberculosis mostly among the suspected cases, which may not represent the population of Qatar. Rodents act as a reservoir of *Mycobacterium microti*, a member of the *M. tuberculosis* complex [123–125]. *M. microti* was not detected in rodents or humans in Qatar. Therefore, the rodent role in TB prevalence in Qatar remains to be confirmed. Previous studies suggested that immigrant workers can be a source of TB in Qatar [53], as TB is more prevalent among immigrants, especially newly arrived persons [37,40,43,65]. The review showed that *E. coli, Salmonella* spp., and *Campylobacter* spp. are the leading causes of human gastroenteritis in Qatar [121]. Pathogenic *E. coli, S. enterica, C. coli/jejuni* were reported from non-human samples [76,82,102,121]. Rodent can mediate these food-borne pathogens to humans and animals by contaminating the foods and water [5,126–128]. Enteric fever by *S. enterica* serovar Typhi was considered a border disease in Qatar, imported from the endemic countries, such as Bangladesh, India, Pakistan, and Nepal by immigrant workers [31,78]. *R. norvegicus* from the wholesale market of Doha was found to carry the oriental rat flea

Xenopsylla astia [21,22]. *Xenopsylla astia* is a carrier of *Bartonella* spp., *Coxiella burnetti*, and *Yersinia pestis* [129–131].

4.3. Parasitic Pathogens

The largest group of rodent-related pathogens in the current review was parasites, of which *T. gondii* was the most prevalent among humans in Qatar. *T. gondii* was reported with a vertical transmission from mother to fetus [50]. Besides free-living cats, *T. gondii* was detected in cheetahs [55]. Rodents might be involved with the transmission of *T. gondii* in Qatar, which needs to be confirmed. Qatar residents from Africa showed higher infection indices with *T. gondii*, *H. nana*, and *Taenia* spp. than did the residents from Asia [49,85]. *Cryptosporidium* spp., *H. nana*, and *Taenia* spp. are more prevalent in newly arrived residents [60,85,101]. Pathogenic amoebiasis are more prevalent among the immigrants from Asia than in those from Africa and other Arab countries [83–85]. Trichuriasis is mostly prevalent among residents from Asia [61,86], particularly from Eastern Asian countries [85], such as the Philippines and Indonesia [52]. Furthermore, cerebral schistosomiasis was reported in Filipino residents living in Qatar [122]. However, there is an information gap regarding rodent-borne diseases in humans, rodents, other animals, and the environmental interface in Qatar. *H. diminuta* was reported in *R. norvegicus* [21,22] with no report among humans. On the other hand, *H. nana* was reported from humans but not from rodents or other animals. In addition, the studies that identified rodent-related pathogens in animals and environmental sources may not represent the overall scenario at the non-human facilities in Qatar.

4.4. Viral Pathogens

Out of the three viruses identified in the current review, Hepatitis E showed high prevalence. Studies showed that hepatitis E in Qatar is imported by expatriates [56,90,118]. One study showed that Nepal could be a significant source of hepatitis E in Qatar [56]. Nepal is a hyperendemic country for the hepatitis E virus, where commensal rodents were found positive with hepatitis E virus [132]. Human cases of rabies in Qatar were confirmed in immigrants from Nepal [119]. Previous reports showed that rodents could be infected with rabies [133], with a low risk for transmitting the virus [134].

4.5. Possible Transmission of Rodent-Borne Pathogens at the Human–Animal–Environment Interface

The records of the Qatar Pest Control Company and the pest control unit of the Ministry of Municipality and Environments show that commensal rodents are more prevalent in livestock and agricultural farms than they are in residential, commercial, or industrial areas [135,136]. Most of the workers in these agriculture and livestock facilities are from South Asia [136]. The traditional livestock farms in Qatar are multi-species animal farms with poor biosecurity management [136,137]. A previous study showed that over 70% of the livestock farms are infested with rodents, such as *M. musculus*, *R. norvegicus*, and *R. rattus* [24]. In the residential area, rodents are more prevalent in bachelor accommodations [135]. It is plausible that immense ongoing efforts in urbanization and agricultural projects, in addition to climate change [138–140], may be conducive to a species-jump of rodent-borne pathogens from immigrant workers to livestock animals and rodents. Further, the introduction and establishment of new rodent species and their associated vectors in Qatar can increase such potential risks. However, the reports of *E. coli*, *Salmonella* spp., *M. tuberculosis*, *Cryptosporidium* spp., *T. gondii*, *Giardia* spp., and *Entamoeba* spp. among the residents from different nationalities, including native Qatari and children, means that there might be an autochthonous internal and dynamic transmission of these pathogens among the community.

The seaports and maritime shipping routes of Qatar are immensely linked to many countries to import foodstuffs, animals, crops, and animal feed and fodder. As the rodents, such as *R. norvegicus* and *R. rattus*, usually live in ships used for traveling and trades of agricultural food products [141], these rodents can move between the terminus countries

and Qatar and possibly can introduce unknown pathogens to Qatar. In this respect, international seaports may play a significant role in zoonotic disease spread [141,142]. The plague outbreak in Australia in 1900 [143] and Hong Kong in 1894 [144] was linked to rodent entry through the ports. Several rodent-borne disease agents reported from the central fresh product market in Qatar may indicate that pathogens are introduced into the country when fresh market products are imported from abroad. Further studies are required to find the link between the cross-border import of rodent-related pathogens through humans, animals, or agro-products spillover in Qatar.

4.6. Limitations

Our study is not without limitations. Some of the limitations were identified during our work. We only conducted a mini-review (at the beginning of the systematic review) to understand rodent-related zoonotic pathogens in general. In there, we emphasized only the descriptive articles [3,5,6] and 35 additional reports to list rodent-borne zoonotic diseases [123,124,127,128,133,145–174]. Therefore, there is a chance we missed pathogens that were not described by these studied articles. There has been limited rodent-related research done at the animal–environment interface in Qatar. Finally, some related information may be out of the scope of our current systematic review and meta-analysis.

5. Conclusions

This review showed pathogens at the human–animal–environment interface in Qatar for which rodents can become potential mediators in transmission. A total of 23 pathogens were listed, which were mostly reported from humans. *M. tuberculosis*, *E. coli*, *T. gondii*, and hepatitis E virus were the most prevalent pathogens among humans. Besides rodents, other animals such as dogs, cats, and livestock animals can be involved in the transmission cycle. However, as there is a lack of research on rodents and other animals in this country, the transmission cycle of the stated infectious agents remains unclear. Therefore, extensive studies are required to investigate rodents and rodent-borne zoonotic pathogens among the diverse human population, livestock and pet animals, rodents, and environments in various ecosystems in Qatar. Furthermore, these studies should pursue a multidisciplinary One Health approach with contributions from zoologists, ecologists, microbiologists, entomologists, veterinarians, and public health experts to understand rodent-related zoonoses in Qatar.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/ijerph18115928/s1, Table S1: Prima checklist, Table S2: List of the rodent-borne zoonotic diseases; mini-review, Table S3: Extracted data from the selected 94 studies.

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Chapter 3: Rodent Ecology and Morphology in Qatar

Commensal rodents have a high potential of transmitting zoonotic pathogens to humans and other animals. While working with the rodent-borne zoonoses, it is a prior necessity to understand the rodents and their ecosystem and distribution in the study area. As there was no previous research about commensal rodent identification and distribution in Qatar, the current study was undertaken to identify morphological and morphometric characteristics, and distribution of the commensal rodents in this country.

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Morphometric Study of *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* in Qatar

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Simple Summary: Rodents are the most abundant and diversified group of mammals. These animals show genetic and physical diversity in different ecosystems of the world, including the desert ecosystem. The current study was undertaken to check the morphometric pattern of three commensal rodent species, viz, *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus*, in Qatar. One hundred forty-eight rodents were captured and studied for body and cranio-mandibular measurements. The study found *R. norvegicus* as the most prevalent rodent in Qatar. Most of the rodents were collected from Al Rayan municipality, were adults, and were from livestock farms. The rodents' average body weights were 18.8 ± 2.2 gm, 264.3 ± 87.5 gm, and 130 ± 71.3 gm for *M. musculus*, *R. norvegicus*, and *R. rattus*, respectively. The average morphometric measurements of the external body and skull were normally distributed and can be used as a reference of *R. norvegicus* and *R. rattus* for Qatar.

Abstract: The current study was undertaken to estimate the morphometric pattern of three commensal rodents, i.e., *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* in Qatar. One hundred forty-eight rodents were captured from different facilities throughout Qatar. The captured rodents were used to identify the external body and cranio-mandibular morphometry. The study found that *R. norvegicus* was the most prevalent (n = 120, 81%, 95% CI: 73.83–87.05). Most of the rodents were collected from Al Rayan municipality (n = 92, 62%), were adults (n = 138, 93.2%, 95% CI: 87.92–96.71), and were from livestock farms (n = 79, 49%, 95% CI: 41.02–57.65). The rodents' average body weights were 18.8 ± 2.2 gm, 264.3 ± 87.5 gm, and 130 ± 71.3 gm for *M. musculus*, *R. norvegicus*, and *R. rattus*, respectively. The research found that the studied rodents are smaller than those of other countries

such as Turkey, Tunisia, and Iran. The study of morphometry is a useful tool for the traditional identification of small mammal species, including rodents. The average morphometric measurements of the external body and skull were normally distributed and can be used as a reference of *R. norvegicus* and *R. rattus* for Qatar. A further comprehensive study is required to investigate the rodent population index, eco-friendly control program, and public health importance in Qatar.

Keywords: rodents; small mammals; commensal species; morphometry; Qatar

1. Introduction

Rodents are the largest group of mammals, distributed on every continent of the world except Antarctica [1]. Globally, there are 2552 rodent species available, of which three species, i.e., house mice (*Mus musculus*), brown rat (*Rattus novegicus*), and black rat (*Rattus rattus*), occupy different habitats with higher density than other species of rodents [2,3]. These human commensals live in diverse ecosystems throughout the world, showing high morphological and genetic variation. For instance, the brown rat showed at least 13 evolutionary clusters globally [4]. Several evolutionary factors, such as climate and geography, predators, urbanization, and agricultural settlement, are behind these evolutionary changes [5–7]. The desert environment is also a factor for the phenotypic and genotypic evolutionary change of mammals. For example, fur coloration and its covariation with habitat have been reported for desert gerbils [8]. Genetic analysis and phenotypic and morphometric assessments provide unique ways of identifying different mammalian species and evaluating animal diversity evaluation [7,9]. The external and cranio-mandibular morphologies are valuable tools in the classification of rodent species. The bones of a skull have some variation between and within a mammalian species that lead their species or subspecies to a distinguished morphological identity [9].

The state of Qatar is a small country in the Arabian Peninsula, whose terrain comprises sand dunes and salt flats across a low barren plain [10,11]. The country has a dry, subtropical climate, with very low annual rainfall (33.1 mm in 2010 and 114.1 mm in 2015), intensely hot (42.7–48.1 °C) and humid (32–72% relative humidity) summer, and warm (10.7 °C) winter. Due to the climate and geography, agricultural practices are limited in Qatar [10,12]. Rodents have importance for animal and public health in this country [13]. Rodent-borne pathogens, such as *Coxiella* and *Toxoplasma*, are common causes of livestock abortion in Qatar [14]. *Taenia taeniaeformis*, *Toxoplasma godii*, and *Toxascaris leonina* were reported among pet animals [15,16]. Zoonoses that can be associated with rodents, such as *Escherichia coli*, *Giardia duodenali*, and *Hymenolepis nana*, were reported among human populations in this country [17,18]. Moreover, the zoonotic cestode, *Hymenolepis diminuta*, was identified among *R. norvegicus* in Doha city of Qatar [19,20]. The country has governmental [21] and non-governmental rodent control programs. Minimal research, however, has been done on rodents in this country [13,19,20]. There is no documented report of rodent identification guidelines, such as morphometry of rodents in Qatar. Therefore, the present research aimed to study three commensal rodents, such as *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus*, to identify the specific species of the rodents and to understand their physical and behavioral characteristics that are potentially found in the Qatar.

2. Materials and Methods

2.1. Study Season, Area, and Rodent Collection

A cross-sectional study was done from November 2019 to February 2020 as a part of routine pest control program in Qatar. A total of 250 traps were used, which include 150 single rodent traps (SRT) and 100 multi rodent traps (MRT). We used different types of baits such as bread (Arabian khubj), biscuits, potato chip, and cheese for capturing the rodents [22]. An SRT or MRT was used randomly, without targeting any specific rodent species or the species behavior. A water bottle containing 5% glucose was affixed

to each trap to reduce dehydration and stress of the captured animals in the harsh Qatari environment. The trappings covered six facilities: family residents, bachelor residents, agricultural farms, livestock farms, industrial areas, and commercial areas throughout Qatar (Figure 1). The traps were set for a single night. Successful traps were collected in the morning and transferred at the earliest convenience to the veterinary laboratory, Doha, Qatar. A comfortable temperature was maintained (20–25 °C) in the transportation car and veterinary laboratory rodent room. The traps were washed with soap and pressurized water and air-dried to avoid any residual contamination and transmission from the previous rodent to the next.

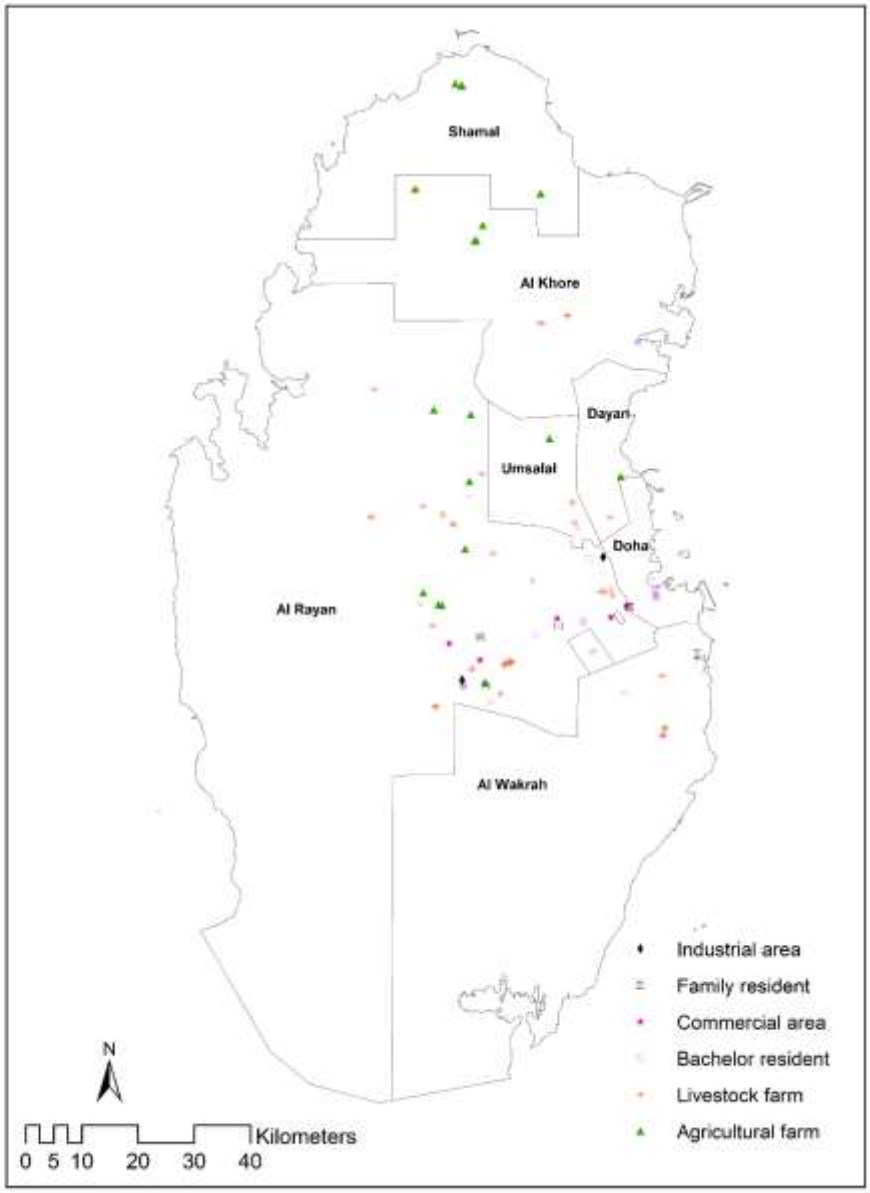

Figure 1. The map shows successful rodent trapping locations in different settings of Qatar.

2.2. Rodent Identification and Morphometric Assessment

The captured rodents were euthanized using 5% isoflurane inhalation for five minutes in a desiccator. After weighing with an electronic balance (Serial No. 057700082, Kern EG420-3NM, Kern & Sohn GmBH, Balingen, Germany), morphological appearance and external measurements were recorded as per species, age, sex, and pregnancy [22–25]. Rodent species were identified based on morphologic characteristics and measurements. The animals were assessed for sex (female or male) using external and internal aspects of reproductive organs such as testicles, penis, seminal vesicles, vagina, mammary teats, and possible pregnancy signs. For age detection, we only identified the adult rodents. Developed genital organs and pregnancy were the sign of an adult rodent. Additionally, we considered prominent temporal ridges and postorbital processes of the skull to determine a rodent as mature. The presence of a gravid uterus served as the indicator of pregnancy.

Five standard external measurements were made for the animals using a ruler (Figure 2). Following the morphological characterization, the rodents were dissected, skulls were collected, cleaned, and dried according to the standard procedure [26]. The cranium and mandible morphometric variables were recorded using a digital caliper (TESA TWIN-CAL IP67, Hexagon, Switzerland) described previously [9,27–29] and illustrated in Figures 3–6.

Figure 2. External view of a rodent body with linear measurement marks. General length (**A** to **C**, **C** is the last caudal vertebra), Tail length (**B** to **C**, **B** marks anus), Body (Head and body) length (**A** to **B**), Right ear length (**D** to **E**), and Right hind leg length (**F** to **G**).

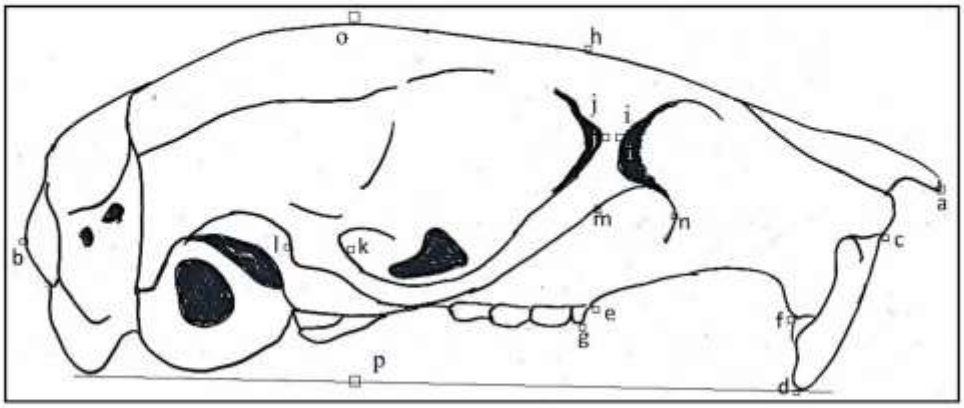

Figure 3. Lateral view of a rodent skull with linear measurements and identification marks. General cranial/Occipitonasal length (**a** to **b**), Length of upper incisor (**c** to **d**), Distance between upper incisor to alveolus molar tooth 1 (**d** to **e**), Length of diastema (**e** to **f**), Rostrum height (**g** to **h**), Breath of inferior ramus of zygomatic process of maxillary (**i** to **j**), Breath of base zygomatic process of squamosal (**k** to **l**), Breath of zygomatic plate (**m** to **n**), and General cranial height (**o** to **p**).

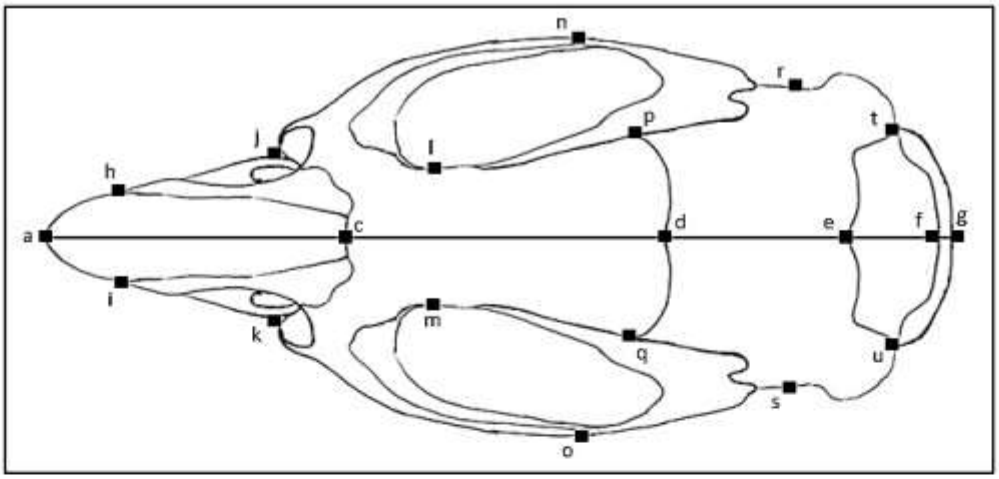

Figure 4. Dorsal view of a rodent skull with linear measurements and identification marks. Breath of nasal bones (**h** to **i**), Greatest rostrum breath (**j** to **k**), Smallest intraorbital breath (**l** to **m**), Zygomatic breath (**n** to **o**), Frontal bone width (**p** to **q**), Breath of brain cage (**r** to **s**), Interparietal bone width (**t** to **u**), Occipital bone length (**f** to **g**), Interparietal bone length (**e** to **f**), Parietal bone length (**q** to **u**), Frontal bone length (**c** to **d**), Nasal bone length (**a** to **c**).

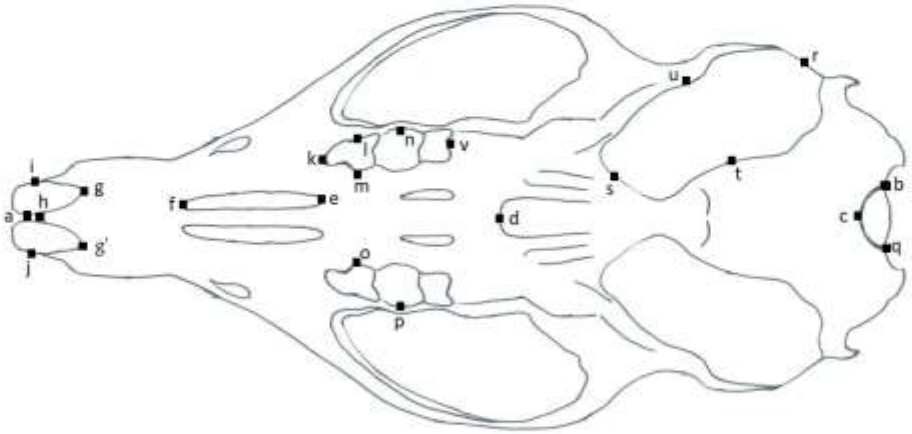

Figure 5. Ventral view of a rodent skull with linear measurements and identification marks. Condylobasala length (**a** to **b**), Henselion-basion distance (**h** to **c**), Henselion-palatial distance (**h** to **d**), Palatal foramen length (**e** to **f**), Smallest palatal breath (**m** to **o**), Upper cheek to teeth alveoli (**k** to **v**), Breath of upper dental arch (**n** to **p**), Breadth of molar tooth 1 (**m** to **l**), Width of upper incisor basal part (**i** to **j**), Width of the upper incisor apex part (**g** to **g'**), Tympanic bulla length (**r** to **s**), Tympanic bulla width (**t** to **u**), Foramen magnum width (**b** to **q**).

2.3. *Statistical Analysis*

The data were analyzed using statistical software StatSoft (2011) to study the descriptive analysis of the number of captured rodents and their morphometric variables that included mean, percentage (%), 95% confidence interval (CI), standard deviation (SD), skewness, standard error of skewness, kurtosis, and standard error of kurtosis. The data were tested with the Kolmogorov–Smirnov test, skewness, and kurtosis to validate the normality. If the skewness and kurtosis were outside −2 and +2, the measurement was considered significantly skewed or kurt [30,31]. The student *t*-test was performed to examine the variability of the morphometric traits among sex (female vs. male) and pregnancy

(pregnant vs. non-pregnant). The chi-square (χ^2) test was performed to examine the level of significance ($p < 0.05$) among the area (municipality) and trapping location types.

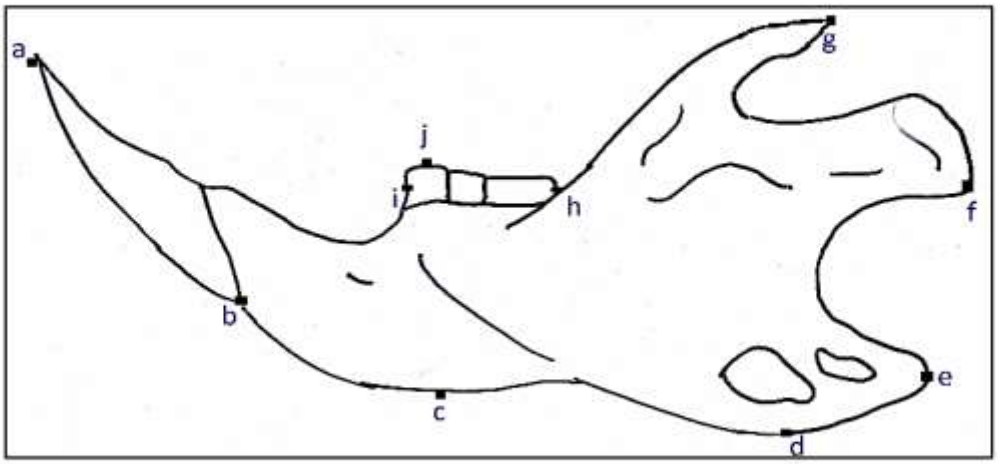

Figure 6. Lateral view of rodent mandible with linear measurements and identification marks. Length of lower incisor (**a** to **b**), Distance between lower incisor to coronoid process (**a** to **g**), Distance between lower incisor to condyloid process (**a** to **f**), Distance between lower incisor to angular process (**a** to **e**), Greatest jaw height (GJH) (**d** to **g**), Ramus to Molar tooth 1 (**c** to **j**), Distance between lower molar tooth 1 to molar tooth 3 (**h** to **i**), and Distance between lower incisor to molar tooth 1 (**a** to **i**).

3. Results

3.1. Demographic Information

The study captured 148 rodents from all seven municipalities of Qatar (Table 1, Figure 1). A total of 79 rodents were captured by SRT and 69 rodents by MRT. The thirty-two MRT captured more than one rodent (2–5) at a time. Based on the morphologic and morphometric characters of the body and skull, three species of rodents were identified, i.e., *M. musculus*, *R. rattus*, and *R. norvegicus*. *R. norvegicus* comprised 81.1% ($n = 120$) of the total captured rodents, whereas *R. rattus* ($n = 24$) and *M. musculus* ($n = 4$) showed low density. Most of the collected rodents ($n = 138$, 93.2%) were adults. A major portion of the captured rodents was collected from Al Rayan municipality ($n = 92$, 62%). This municipality harbors all the three commensal species (*M. musculus* and *R. rattus*, and *R. norvegicus*), showing ($\chi^2 = 21.02$, $p < 0.05$) the highest density for *R. norvegicus* ($n = 64$). The majority of the rodents ($n = 79$, 49%) ($\chi^2 = 35.29$, $p < 0.05$) were collected from the livestock farms.

3.2. Morphometric Assessments of Rodents

The overall means of body weight, external morphometry, and cranio-mandibular variables per species are presented in Tables 2–4. Out of the 148 rodents, 108 rodents were dissected, comprised of 86 *R. norvegicus*, 18 *R. rattus*, and 4 *M. musculus*. The average body weight was variable among three rodent species (18.8 ± 2.2 gm, 264.3 ± 87.5 gm, and 130 ± 71.3 gm for *M. musculus*, *R. norvegicus*, and *R. rattus*, respectively). The skewness and kurtosis statistics of all the studied external body measurements of *R. norvegicus* and *R. rattus* were within −2 and +2. This indicated that the observed values were normally distributed. In general, the tail is longer than the length of the body and head of *M. musculus* and *R. rattus*, which is the opposite in *R. norvegicus*. Compared to the general length of a rodent, the ears and legs of *R. rattus* are longer than that of *R. norvegicus*. As the captured number of *M. musculus* was small, no further statistical comparative analysis could be considered on their body or cranio-mandibular measurements.

Table 1. Demographic characteristics of the trapped rodents.

Characters	*n* (% of Total Capture, 95% CI)
Trapping location (*n* = 148)	
Agriculture farm	31 (20.9, 14.69–28.39)
Bachelor residence	18 (12.2, 7.36–18.53)
Commercial area	11 (7.4, 3.76–12.91)
Family residence	11 (7.4, 3.76–12.91)
Industrial area	4 (2.7, 0.74–6.78)
Livestock farms	73 (49.3, 41.02–57.65)
Municipalities (*n* = 148)	
Al Khore	17 (11.5, 6.84–17.75)
Daayan	1 (0.7, 0.002–0.37)
Doha	10 (6.8, 3.29–12.07)
Rayyan	92 (62.2, 58.83–69.70)
Shamal	7 (4.7, 1.92–9.50)
Um Salal	8 (5.4, 2.36–10.37)
Wakrah	13 (8.8, 41.02–57.65)
Species (*n* = 148)	
Mus musculus	4 (2.7, 0.74–6.78)
Rattus norvegicus	120 (81.1, 73.83–87.05)
Rattus rattus	24 (16.2, 10.68–23.16)
Sex (*n* = 148)	
Female	75 (50.7, 42.34–58.98)
Male	73 (49.3, 41.02–57.65)
Pregnancy (*n* = 75)	
Pregnant	20 (26.7, 17.11–38.14)
Non-pregnant	55 (73.3, 61.86–82.89)
Age (*n* = 148)	
Adult	138 (93.2, 87.92–96.71)
Young	10 (6.8, 3.29–12.07)

Table 2. The external body linear measurements (mean ± SD) of the commensal rodents of Qatar.

Sl. No.	Parameters *	*Mus musculus* (*n* = 4)	*Rattus norvegicus* (*n* = 120)	*Rattus rattus* (*n* = 24)
1	Body weight	18.8 ± 2.2	264.3 ± 87.5	130.0 ± 71.3
2	General length	163.8 ± 4.8	398.5 ± 45.1	324.4 ± 80.0
3	Tail length	85.3 ± 4.1	191.4 ± 22.9	181.3 ± 39.0
4	Body length	78.5 ± 2.4	207.1 ± 23.0	143.1 ± 44.4
5	Right ear length	13.3 ± 1.7	18.9 ± 1.7	18.6 ± 2.1
6	Right hind leg length	16.5 ± 1.3	39.2 ± 3.6	32.4 ± 3.9

* The body weight was measured in grams and the rest of the parameters were measured in millimeters; *n*: Total observation, and SD: Standard deviation of mean.

Table 3. Cranial morphometric linear measurements (mean ± SD) of the commensal rodents of Qatar.

Sl. No.	Parameters *	*Mus musculus* (*n* = 4)	*Rattus norvegicus* (*n* = 86)	*Rattus rattus* (*n* = 18)
1	General cranial length	21.9 ± 0.4	46.8 ± 4.1	37.2 ± 2.7
2	Condylobasal length	21.3 ± 0.1	45.2 ± 4.1	35.5 ± 2.9
3	Henselion-basion length	18.7 ± 0.4	39.1 ± 3.6	29.4 ± 2.9
4	Henselion-palpation length	11.2 ± 1.3	22.4 ± 2.3	16.9 ± 1.7
5	Length of upper incisor	3.3 ± 0.6	7.5 ± 1.6	5.6 ± 1.0
6	Width of upper incisors, basal	2.1 ± 0.2	4.8 ± 0.6	3.5 ± 0.5
7	Width of upper incisors, apex	1.3 ± 0.1	3.3 ± 0.5	2.2 ± 0.4
8	Upper incisor to alveolus molar tooth 1	6.3 ± 0.4	14.4 ± 1.9	10.1 ± 1.4
9	Length of diastema	5.9 ± 0.4	13.4 ± 1.5	9.6 ± 1.2
10	Nasal bone length	7.5 ± 0.6	17.2 ± 1.9	12.6 ± 1.4
11	Breath of nasal bones	2.2 ± 0.4	5.2 ± 0.6	3.9 ± 0.3
12	Frontal bone length	7.1 ± 0.4	14.7 ± 1.3	12.2 ± 1.4
13	Frontal bone width	5.7 ± 1.1	10.9 ± 0.6	10.3 ± 1.1
14	Parietal bone length	7.3 ± 0.5	13.0 ± 1.1	11.2 ± 1.0
15	Breath of brain cage	9.8 ± 0.4	16.4 ± 2.1	16.2 ± 0.6
16	Interparietal bone length	3.2 ± 0.2	6.5 ± 0.7	5.5 ± 0.6
17	Interparietal bone width	6.7 ± 1.5	11.5 ± 1.0	10.7 ± 0.8
18	Occipital bone length	4.5 ± 0.4	6.0 ± 0.8	4.5 ± 0.4
19	General cranial height	7.4 ± 0.1	16.6 ± 1.5	13.7 ± 0.8
20	Rostrum height	6.3 ± 0.3	13.8 ± 1.3	10.8 ± 0.9
21	Rostrum breathe	3.5 ± 0.1	9.0 ± 1.0	6.5 ± 0.7
22	Smallest interorbital breadth	3.4 ± 0.3	6.8 ± 0.5	5.8 ± 0.4
23	Breath of Inferior ramus of the zygomatic process of maxillary	0.9 ± 0.2	1.9 ± 0.3	1.5 ± 0.2
24	Breath of base zygomatic process of squamosal	1.5 ± 0.2	3.0 ± 0.4	2.2 ± 0.4
25	Breadth of zygomatic plate	2.5 ± 0.2	5.1 ± 0.6	3.7 ± 0.6
26	Zygomatic breath	11.0 ± 0.5	22.4 ± 2.3	18.2 ± 1.0
27	Length of palatal foramen	4.1 ± 0.6	7.8 ± 0.8	6.1 ± 0.9
28	Smallest palatal breadth	2.1 ± 0.3	4.7 ± 0.6	3.6 ± 0.4
29	Upper cheek-teeth alveoli	3.4 ± 0.4	7.4 ± 0.4	6.7 ± 0.4
30	Breadth of upper dental arch	4.4 ± 0.2	9.4 ± 0.7	7.6 ± 0.4
31	Breadth of molar tooth 1	1.1 ± 0.1	2.8 ± 1.0	2.0 ± 0.2
32	Tympanic bulla length	2.4 ± 0.3	8.1 ± 0.6	7.1 ± 0.5
33	Tympanic bulla width	3.2 ± 0.1	6.0 ± 1.0	5.2 ± 0.6
34	Foramen magnum width	3.6 ± 0.3	6.9 ± 0.4	5.9 ± 0.3

* The parameters were measured in millimeters, *n*: Total observation, SD: Standard deviation of mean.

Table 4. Mandibular morphometric linear measurements (mean ± SD) of the commensal rodents of Qatar.

Sl. No.	Parameters *	*Mus musculus* (*n* = 4)	*Rattus norvegicus* (*n* = 86)	*Rattus rattus* (*n* = 18)
1	Length of lower incisors	3.8 ± 0.5	9.5 ± 2.0	6.9 ± 1.2
2	Lower incisors to coronoid process	10.8 ± 0.1	25.4 ± 2.6	19.2 ± 2.2
3	Lower incisors to condylar process	13.4 ± 0.2	30.2 ± 2.9	23.4 ± 2.2
4	Lower incisors to angular process	13.5 ± 0.3	30.5 ± 3.1	23.7 ± 2.3
5	Greatest jaw height	6.6 ± 0.2	14.3 ± 1.6	11.1 ± 1.0
6	Ramus to molar tooth 1	3.8 ± 0.1	8.8 ± 1.0	6.6 ± 0.7
7	Lower molar tooth 1- molar tooth 3	3.3 ± 0.3	7.3 ± 0.3	6.3 ± 0.5
8	Lower incisors to molar tooth 1	5.0 ± 0.3	11.4 ± 1.4	8.6 ± 1.0

* The parameters were measured in millimeters; *n*: Total observation, SD: Standard deviation of mean.

The *t*-test showed that there is no sexual or pregnancy-related dimorphism ($p > 0.05$) in any of the presented characteristics in the case of *R. norvegicus* (Tables 5–10). However, the right ear length measurements showed that females have longer ears than males in *R. rattus*. Moreover, the mandibular characters, such as the length of lower incisors and the distance between lower incisor to coronoid process, lower incisor to condyloid process, lower incisor to angular process, ramus to molar tooth 1, and lower incisor to molar tooth 1 of *R. rattus*, were significantly higher in females than males ($p < 0.05$). In addition, the value of lower molar tooth 1 to molar tooth 3 was higher in the case of males than females in *R. rattus* (Table 7). Furthermore, the right hind leg was longer ($p > 0.05$) in non-pregnant than pregnant *R. rattus* (Table 8).

Table 5. Sexual dimorphism of external body measurements (Mean ± SD) of *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Female (*n* = 62)	Male (*n* = 58)	*p*	Female (*n* = 10)	Male (*n* = 14)	*p*
1	Body weight	260.6 ± 76.1	268.2 ± 98.8	0.64	128.5 ± 65.7	131.0 ± 77.6	0.93
2	General length	396.5 ± 37.8	400.5 ± 52.0	0.63	342.5 ± 72.8	311.4 ± 85.0	0.36
3	Tail length	190.2 ± 18.8	192.7 ± 26.8	0.55	192.0 ± 42.0	173.6 ± 36.3	0.26
4	Body length	206.4 ± 20.1	207.8 ± 25.9	0.73	150.3 ± 33.1	137.9 ± 51.6	0.50
5	Right ear length	18.7 ± 1.7	19.0 ± 1.7	0.39	19.6 ± 1.8	17.9 ± 2.0	0.04
6	Right hind leg length	38.7 ± 2.9	39.8 ± 4.2	0.09	32.0 ± 2.0	32.6 ± 4.9	0.70

* The body weight was measured in grams and the rest of the parameters were measured in millimeters; *n*: Total observation, SD: Standard deviation of mean, and *p*: Probability at 95% confidence level.

Table 6. Sexual dimorphism of cranial morphometric measurements (mean ± SD) of *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Female (*n* = 38)	Male (*n* = 48)	*p*	Female (*n* = 9)	Male (*n* = 9)	*p*
1	General cranial length	46.3 ± 3.7	47.1 ± 4.3	0.38	38.2 ± 2.8	36.2 ± 2.2	0.11
2	Condylobasal length	44.8 ± 3.6	45.5 ± 4.4	0.48	35.3 ± 3.5	35.6 ± 2.3	0.83
3	Henselion-basion length	39.3 ± 3.5	38.9 ± 3.8	0.65	29.5 ± 3.8	29.2 ± 1.8	0.82
4	Henselion-palpation length	22.6 ± 1.9	22.2 ± 2.6	0.51	17.3 ± 1.4	16.4 ± 2.0	0.25
5	Length of upper incisor	7.5 ± 1.6	7.5 ± 1.6	0.95	5.8 ± 1.1	5.4 ± 0.9	0.38
6	Width of upper incisors, basal	4.8 ± 0.6	4.8 ± 0.6	0.77	3.6 ± 0.3	3.4 ± 0.7	0.40
7	Width of upper incisors, apex	3.2 ± 0.5	3.3 ± 0.4	0.31	2.4 ± 0.2	2.1 ± 0.4	0.08

Table 6. *Cont.*

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Female (n = 38)	**Male (n = 48)**	p	**Female (n = 9)**	**Male (n = 9)**	p
8	Upper incisor to alveolus molar tooth 1	14.4 ± 1.8	14.4 ± 2.0	0.99	10.8 ± 1.3	9.5 ± 1.4	0.06
9	Length of diastema	13.3 ± 1.5	13.4 ± 1.5	0.77	10.2 ± 1.1	9.1 ± 1.2	0.06
10	Nasal bone length	17.2 ± 1.8	17.2 ± 2.0	0.89	13.0 ± 1.3	12.2 ± 1.4	0.24
11	Breath of nasal bones	5.1 ± 0.5	5.2 ± 0.6	0.30	4.0 ± 0.1	3.8 ± 0.4	0.38
12	Frontal bone length	14.6 ± 1.1	14.7 ± 1.5	0.72	12.8 ± 1.5	11.7 ± 1.1	0.13
13	Frontal bone width	10.8 ± 0.6	10.9 ± 0.6	0.55	10.4 ± 1.2	10.2 ± 0.9	0.63
14	Parietal bone length	13.0 ± 0.9	13.1 ± 1.2	0.75	11.6 ± 0.6	10.9 ± 1.2	0.16
15	Breath of brain cage	16.1 ± 2.0	16.6 ± 2.3	0.33	16.1 ± 0.6	16.3 ± 0.7	0.48
16	Interparietal bone length	6.6 ± 0.9	6.4 ± 0.6	0.24	5.6 ± 0.5	5.4 ± 0.7	0.51
17	Interparietal bone width	11.4 ± 1.0	11.6 ± 1.0	0.20	10.8 ± 0.8	10.6 ± 0.9	0.79
18	Occipital bone length	6.0 ± 0.7	6.0 ± 0.9	0.75	4.5 ± 0.5	4.5 ± 0.2	0.86
19	General cranial height	16.6 ± 1.6	16.6 ± 1.5	0.97	14.1 ± 0.7	13.2 ± 0.8	0.03
20	Rostrum height	13.8 ± 1.1	13.7 ± 1.4	0.72	11.2 ± 0.7	10.4 ± 1.0	0.07
21	Rostrum breathe	9.1 ± 0.9	9.0 ± 1.1	0.74	6.7 ± 0.6	6.4 ± 0.8	0.41
22	Smallest interorbital breadth	6.7 ± 0.4	6.9 ± 0.6	0.32	6.0 ± 0.4	5.6 ± 0.3	0.04
23	Breath of inferior ramus of the zygomatic process of maxillary	1.8 ± 0.3	1.9 ± 0.3	0.11	1.6 ± 0.2	1.4 ± 0.1	0.09
24	Breath of base zygomatic process of squamosal	2.9 ± 0.4	3.0 ± 0.4	0.70	2.3 ± 0.4	2.1 ± 0.5	0.40
25	Breadth of zygomatic plate	5.2 ± 0.5	5.0 ± 0.6	0.34	4.0 ± 0.3	3.5 ± 0.8	0.08
26	Zygomatic breath	22.4 ± 2.0	22.3 ± 2.5	0.82	18.5 ± 0.8	17.9 ± 1.2	0.25
27	Length of palatal foramen	7.9 ± 0.7	7.8 ± 0.9	0.60	6.0 ± 1.0	6.1 ± 0.8	0.69
28	Smallest palatal breadth	4.8 ± 0.6	4.6 ± 0.5	0.29	3.8 ± 0.4	3.4 ± 0.4	0.06
29	Upper cheek-teeth alveoli	7.3 ± 0.4	7.4 ± 0.4	0.16	6.6 ± 0.4	6.7 ± 0.4	0.55
30	Breadth of upper dental arch	9.4 ± 0.7	9.4 ± 0.7	0.57	7.8 ± 0.3	7.5 ± 0.5	0.19
31	Breadth of molar tooth 1	2.8 ± 1.0	2.7 ± 1.0	0.84	2.0 ± 0.3	2.0 ± 0.2	0.65
32	Tympanic bulla length	8.1 ± 0.5	8.1 ± 0.7	0.76	7.1 ± 0.6	7.1 ± 0.5	0.91
33	Tympanic bulla width	6.1 ± 1.1	6.0 ± 0.9	0.78	5.2 ± 0.7	5.2 ± 0.6	0.99
34	Foramen magnum width	6.8 ± 0.4	6.9 ± 0.4	0.08	6.0 ± 0.3	5.8 ± 0.2	0.39

* The parameters were measured in millimeters; n: Total observation, SD: Standard deviation of mean, and p: Probability at 95% confidence level.

Table 7. Sexual dimorphism of mandibular morphometric measurements (mean ± SD) of *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Female (n = 38)	**Male (n = 48)**	p	**Female (n = 9)**	**Male (n = 9)**	p
1	Length of lower incisors	9.4 ± 1.9	9.6 ± 2.2	0.73	7.6 ± 1.1	6.3 ± 1.1	0.02
2	Lower incisors to coronoid process	25.1 ± 2.1	25.6 ± 2.9	0.34	20.6 ± 1.3	17.7 ± 1.9	0.01
3	Lower incisors to condylar process	30.4 ± 3.0	30.0 ± 2.9	0.57	24.8 ± 1.3	22.1 ± 2.1	0.01

Table 7. *Cont.*

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Female (n = 38)	Male (n = 48)	p	Female (n = 9)	Male (n = 9)	p
4	Lower incisors to angular process	30.6 ± 3.0	30.4 ± 3.2	0.69	25.0 ± 1.4	22.3 ± 2.3	0.01
5	Greatest jaw height	14.4 ± 1.6	14.3 ± 1.6	0.71	11.6 ± 1.0	10.7 ± 0.8	0.06
6	Ramus to molar tooth 1	8.8 ± 1.1	8.7 ± 0.9	0.70	7.1 ± 0.5	6.2 ± 0.6	0.01
7	Lower molar tooth 1- molar tooth 3	7.3 ± 0.3	7.3 ± 0.3	0.84	6.3 ± 0.4	6.4 ± 0.7	0.80
8	Lower incisors to molar tooth 1	11.3 ± 1.2	11.4 ± 1.5	0.63	9.3 ± 0.8	8.0 ± 0.8	0.01

* The parameters were measured in millimeters; n: Total observation, SD: Standard deviation of mean, and p: Probability at 95% confidence level.

Table 8. Pregnancy-related external body morphometric dimorphism (mean ± SD) in *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Pregnant (n = 16)	Non-Pregnant (n = 45)	p	Pregnant (n = 8)	Non-Pregnant (n = 2)	p
1	Body weight	275.3 ± 88.0	260.0 ± 65.6	0.47	111.5 ± 28.9	196.5 ± 146.4	0.10
2	General length	400.6 ± 31.1	398.3 ± 33.9	0.81	348.8 ± 68.1	317.5 ± 116.7	0.62
3	Tail length	190.6 ± 15.5	191.6 ± 17.1	0.85	196.9 ± 42.8	172.5 ± 46.0	0.50
4	Body length	210.0 ± 17.6	206.8 ± 17.7	0.53	151.9 ± 26.2	145.0 ± 70.1	0.81
5	Right ear length	18.9 ± 1.9	18.7 ± 1.7	0.78	19.8 ± 2.0	19.0 ± 1.4	0.63
6	Right hind leg length	38.3 ± 3.6	39.0 ± 2.3	0.37	31.4 ± 1.1	34.5 ± 3.5	0.04

* Body weight was measured in grams and rest of the parameters were measured in millimeters; n: Total observation, SD: Standard deviation of mean, and p: Probability at 95% confidence level.

Table 9. Pregnancy-related cranial morphometric dimorphism (mean ± SD) in *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Pregnant (n = 11)	Non-Pregnant (n = 27)	p	Pregnant (n = 7)	Non-Pregnant (n = 2)	p
1	General cranial length	46.0 ± 3.8	46.5 ± 3.8	0.74	38.7 ± 3.1	36.7 ± 0.3	0.41
2	Condylobasal length	44.6 ± 3.8	45.0 ± 3.6	0.77	36.0 ± 3.8	33.0 ± 1.4	0.34
3	Henselion-basion length	39.4 ± 3.4	39.2 ± 3.6	0.88	30.2 ± 3.8	27.2 ± 4.2	0.36
4	Henselion-palpation length	22.7 ± 2.1	22.5 ± 1.9	0.76	17.4 ± 1.6	17.0 ± 0.8	0.73
5	Length of upper incisor	7.8 ± 1.0	7.4 ± 1.9	0.53	5.8 ± 1.3	5.8 ± 0.1	0.99
6	Width of upper incisors, basal	4.7 ± 0.7	4.8 ± 0.6	0.75	3.6 ± 0.2	3.6 ± 0.5	0.66
7	Width of upper incisors, apex	3.1 ± 0.5	3.2 ± 0.5	0.47	2.4 ± 0.2	2.2 ± 0.1	0.19
8	Upper incisor to alveolus molar tooth 1	14.7 ± 1.1	14.2 ± 2.0	0.43	11.0 ± 1.2	9.8 ± 1.2	0.26
9	Length of diastema	13.3 ± 1.6	13.3 ± 1.4	0.94	10.4 ± 1.1	9.4 ± 0.8	0.29
10	Nasal bone length	17.2 ± 2.0	17.2 ± 1.8	0.97	13.3 ± 1.4	12.2 ± 0.3	0.32
11	Breath of nasal bones	5.1 ± 0.5	5.1 ± 0.6	0.90	4.0 ± 0.2	4.1 ± 0.1	0.32
12	Frontal bone length	14.3 ± 1.0	14.7 ± 1.2	0.27	12.9 ± 1.7	12.2 ± 0.7	0.61
13	Frontal bone width	10.9 ± 0.6	10.8 ± 0.6	0.87	10.7 ± 1.3	9.4 ± 0.1	0.19
14	Parietal bone length	12.9 ± 0.3	13.1 ± 1.1	0.61	11.6 ± 0.7	11.5 ± 0.3	0.83
15	Breath of brain cage	16.5 ± 0.9	16.0 ± 2.3	0.49	16.1 ± 0.7	16.0 ± 0.4	0.81
16	Interparietal bone length	6.6 ± 1.0	6.6 ± 0.8	0.84	5.6 ± 0.5	5.8 ± 0.6	0.59
17	Interparietal bone width	11.0 ± 0.8	11.5 ± 1.0	0.19	10.8 ± 0.8	10.5 ± 1.3	0.59
18	Occipital bone length	5.8 ± 0.8	6.1 ± 0.6	0.20	4.4 ± 0.5	4.9 ± 0.3	0.21
19	General cranial height	16.3 ± 1.6	16.7 ± 1.7	0.49	14.0 ± 0.7	14.3 ± 0.9	0.67

Table 9. *Cont.*

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Pregnant (n = 11)	Non-Pregnant (n = 27)	p	Pregnant (n = 7)	Non-Pregnant (n = 2)	p
20	Rostrum height	13.6 ± 1.3	13.9 ± 1.1	0.41	11.2 ± 0.8	11.0 ± 0.2	0.77
21	Rostrum breathe	9.0 ± 0.9	9.1 ± 0.9	0.68	6.8 ± 0.7	6.5 ± 0.2	0.61
22	Smallest interorbital breadth	6.6 ± 0.5	6.8 ± 0.4	0.21	6.1 ± 0.5	5.8 ± 0.1	0.44
23	Breath of inferior ramus of the zygomatic process of maxillary	1.8 ± 0.3	1.9 ± 0.3	0.26	1.6 ± 0.3	1.5 ± 0.1	0.63
24	Breath of base zygomatic process of squamosal	3.0 ± 0.5	2.9 ± 0.4	0.63	2.4 ± 0.4	2.0 ± 0.2	0.21
25	Breadth of zygomatic plate	5.2 ± 0.4	5.2 ± 0.5	0.89	4.0 ± 0.4	4.1 ± 0.2	0.63
26	Zygomatic breath	22.5 ± 1.7	22.4 ± 2.2	0.91	18.6 ± 0.8	17.9 ± 0.6	0.34
27	Length of palatal foramen	7.9 ± 0.7	7.9 ± 0.6	0.82	5.9 ± 1.2	6.1 ± 0.1	0.88
28	Smallest palatal breadth	4.7 ± 0.6	4.8 ± 0.5	0.54	3.9 ± 0.4	3.3 ± 0.2	0.06
29	Upper cheek-teeth alveoli	7.3 ± 0.5	7.4 ± 0.3	0.41	6.5 ± 0.4	6.9 ± 0.4	0.21
30	Breadth of upper dental arch	9.3 ± 0.8	9.5 ± 0.7	0.53	7.8 ± 0.3	7.8 ± 0.4	0.78
31	Breadth of molar tooth 1	2.8 ± 1.1	2.8 ± 1.0	0.98	2.0 ± 0.3	2.2 ± 0.2	0.26
32	Tympanic bulla length	8.1 ± 0.4	8.1 ± 0.5	0.99	7.2 ± 0.7	6.6 ± 0.1	0.25
33	Tympanic bulla width	6.1 ± 1.3	6.0 ± 1.0	0.77	5.4 ± 0.6	4.4 ± 0.2	0.05
34	Foramen magnum width	6.5 ± 0.4	6.9 ± 0.4	0.05	38.7 ± 3.1	6.1 ± 0.5	0.47

* The parameters were measured in millimeters; n: Total observation, SD: Standard deviation of mean, and p: Probability at 95% confidence level.

Table 10. Pregnancy-related mandibular morphometric dimorphism (mean ± SD) in *Rattus norvegicus* and *Rattus rattus*.

Sl. No.	Parameters *	*Rattus norvegicus*			*Rattus rattus*		
		Pregnant (n = 11)	Non-Pregnant (n = 27)	p	Pregnant (n = 7)	Non-Pregnant (n = 2)	p
1	Length of lower incisors	9.5 ± 1.1	9.4 ± 2.2	0.90	7.7 ± 1.2	7.2 ± 0.4	0.64
2	Lower incisors to coronoid process	24.9 ± 2.2	25.1 ± 2.1	0.75	20.9 ± 1.3	19.6 ± 0.5	0.19
3	Lower incisors to condylar process	30.1 ± 2.6	30.5 ± 3.1	0.70	25.1 ± 1.2	23.4 ± 0.3	0.10
4	Lower incisors to angular process	30.3 ± 2.8	30.8 ± 3.1	0.63	25.5 ± 1.2	23.4 ± 0.1	0.05
5	Greatest jaw height	14.0 ± 1.5	14.6 ± 1.6	0.35	11.8 ± 1.0	10.8 ± 0.8	0.23
6	Ramus to molar tooth M1	8.5 ± 1.2	9.0 ± 1.0	0.28	7.2 ± 0.5	6.7 ± 0.3	0.24
7	Lower molar tooth M1- molar tooth 3	7.2 ± 0.3	7.4 ± 0.3	0.13	6.2 ± 0.4	6.6 ± 0.1	0.19
8	Lower incisors to molar tooth 1	11.1 ± 1.1	11.4 ± 1.3	0.57	9.5 ± 0.7	8.4 ± 0.8	0.12

* The parameters were measured in millimeters; n: Total observation, SD: Standard deviation of mean, and p: Probability at 95% confidence level.

4. Discussion

The study of rodent demography is essential from ecological and public health perspective [32]. The present study identified three commensal rodent species in Qatar captured during routine pest control activities. These rodents have a cosmopolitan distribution and are mainly facilitated by anthropic activities [2]. Four species of rodents were reported previously in Qatar, viz., Arabian Jerboa (*Jaculus loftusi*, previously included in *Jaculus jaculus*), house mouse (*M. musculus*), brown rat (*R. norvegicus*), and black rat (*R. rattus*) [13,19,20,33]. *Jaculus loftusi* is a wild dipodid rodent that lives in the desert ecosystem, like the sandy and rocky places [34], so this species is not in the scope of the present study. However, the current study found that a significant component of commensal rodents in Qatar is *R. norvegicus*. This is supported by the previous reports [19,20], which captured only *R. norvegicus* during their studies in Qatar.

Our study revealed that most of the rodents were from livestock farms. The livestock farms are mostly made up of mixed livestock species with poor management and biosecurity [35], making an ideal place for rodents to colonize and why we captured a major part of rodents from these places. A previous study reported that over 75% of the livestock farms were infested with rodents, mainly by *R. norvegicus*, and the incidence of house mouse *M. musculus* was detected less in Qatar [13], which is congruent with the present study. Out of the 148 captured rodents, only four were *M. musculus*.

Traditional morphometry is a valuable tool for species identification in small mammals, including rodents [28,36]. The present study found the body weight and general body length of *R. norvegicus* as 264.3 gm and 398.5 mm, respectively, which were 259 ± 85.2 gm and 405 ± 54.7 mm, respectively, for the same species in Turkey [37]. In the case of cranial morphometry, the condylobasal length and the zygomatic breadth of *R. norvegicus* in the current study were 45.2 mm and 22.4 mm, which were 45.52 mm and 23.75 mm in the case of Turkey [37] and 46.84 mm and 21.64 mm in the case of Iran [38], respectively, for the same species and measurements. The overall body length of *R. rattus* in Turkey was 378.43, which was 324.4 mm for the same species of Qatar. The cranial length and zygomatic width of *R. rattus* in the current study were 37.2 mm and 18.2 mm, which were 39.15 mm and 19.86 mm, respectively, for Turkey [37] and 39.08 mm and 19.97 mm, respectively, for Tunisia, respectively for the same species and measurements [39].

Similarly, the body length of *M. musculus* in Qatar was 78.5 mm, which was 85.41 mm [24] and 88.0 mm [40] for the same species from different parts of Iran. Due to the small sample size (n = 4), we do not have strong support in the results of *M. musculus* morphometry. However, the overall body and cranial size indicate that the three studied rodent species in Qatar are comparatively smaller than the same species from the countries like Turkey, Tunisia, and Iran. This variation may be due to Qatar harsh environmental effects [6–8], which is supported by Bergmann's rule [41]. Rodents of the colder environment are bigger in body size than the wormer environment [42,43]. This further highlights the necessity of performing traditional morphometry on the geographic population of rodents, specifically cosmopolitan species.

Based on the average general body and skull morphometric measurements, males were slightly larger than females, although there is no significant sexual dimorphism. This finding is supported by a previous study by Ventura and Lopez-Fuster [7]. However, the present study showed that the body and cranio-mandibular linear measurements of commensal rodents in Qatar were normally distributed for the two species, *R. norvegicus*, and *R. rattus*. Bodyweight and body and skull linear measurements distribution shape were approximately symmetric since the statistic of skewness measures were between −0.2 and 0.2 [30,31]. Normality analysis of the biometric traits can be considered typical characteristics of the two rodent species, *R. norvegicus* and *R. rattus*, in this country. To the best of the authors' knowledge, such work is the first time in Qatar. Therefore, the current study can be used as a reference for morphometric measurements of the commensal rodents in this country, especially for *R. norvegicus* and *R. rattus*.

5. Conclusions

The current study estimated, identified, and characterized the morphometric variables of three commensal rodents in Qatar. The research identified that the commensal rodents of Qatar are comparatively smaller than the same species of some other countries, such as Iran, Tunisia, and Turkey. The is the first study on rodent morphometry in Qatar and even in the Arabian Peninsula. Due to geo-ecological similarities, the present study can be a reference study to rodent or small mammal identification in Qatar and other countries of the Arabian Peninsula.

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Chapter 4: Diversity of Rodent-Borne Pathogens in Qatar

Using standard laboratory techniques, we investigated rodent-borne pathogens diversity and identified different species of helminths, protozoa, and bacteria among commensal rodents in Qatar. Some of the pathogens that were detected in this study have zoonotic potential. We analyzed the prevalence of the pathogens among rodents, risk factors of their prevalence, and reported our findings as articles. To the best of our knowledge, this type of study is novel for Qatar.

Chapter 4.1: Detection of rodent-borne parasites in different ecosystem of Qatar: a possible risk for public health

Rodents carry several ectoparasites, cestodes, nematodes, trematodes, and protozoa that are of public health importance. The current study aimed to explore the rodent-borne parasites, zoonotic potentiality, and their related risk factors in Qatar.

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Detection of rodent-borne parasites in different ecosystem of Qatar: a possible risk for public health

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Abstract: Rodents are known reservoirs for a diverse group of zoonotic pathogens that pose a serious threat to humans health. The availability of the commensal rodents among the human population and the high risk of spillover for the pathogens they carry, it is essential to study such pathogens to institute prevention and control measures accordingly. Therefore, the current study was undertaken to investigate the incidence of different parasites among the commensal rodents in different ecosystem of Qatar. A total of 148 rodents, including *Mus musculus* (n=4), *Rattus norvegicus* (n=120), and *Rattus rattus* (n=24), were captured using traps across different ecosystems, incuding agricultural farms, livestock farms, and other areas. Blood, fecal, ectoparasite, and visceral organs were collected for gross, microscopic, immunological, and molecular examination. The study identified ten species of parasites, viz. *Capillaria annulosa, Eimeria* spp., *Giardia* spp., *Hymenolepis diminuta, Mastophorus muris, Ornithonyssus bacoti, Taenia taeniaeformis, Toxoplasma gondii, Trypanosoma lewisi*, and *Xenopsylla astia*. About 62.2% of the rodents were positive for at least one parasitic species. Helminths were found to be most prevalent (46.0%), followed by ectoparasites (31.8%), and protozoa (10.1%). However, individually *X. astia* ranked the highest (31.8%), where the lowest prevalent parasite was *C. annulosa* (0.7%). *X. astia* and *H. diminuta* prevalence has significantly differed between ecosystems ($p < 0.05$). The prevalence of *H. diminuta* was positively correlated (OR=4.13; $p = 0.00$) with the prevalence of *X. astia*. The phylogenetic pattern of *H. diminuta* suggested that the sequences detected in rodents of Qatar were very similar to each other and were closely related to the previously reported *H. diminuta* in Canary Island, South Africa, Australia, Iran, Spain, China, and Mexico. The majority of the reported parasites has public health importance. Aside from *X. astia* and *H. diminuta*, all other parasites are first recorded occurrences among commensal rodents in the history of Qatar. Further studies should be conducted to understand the biology, epidemiology, and transmission dynamics of these parasites to combat possible parasite-associated future epidemics in Qatar.

Keywords: ectoparasite; helminth; protozoa; commensal rodents; Qatar

Introduction

The majority of the emerging and re-emerging infectious diseases are of zoonotic origin, especially from wild lives (Jones et al., 2008). Albeit most of these emerging diseases are viral in nature (Mostafavi et al., 2021), many countries are facing a rising number of parasitic infections as well (Alasil and Abdullah, 2019). The spillover of zoonotic parasites to the human population occurs from different sources, including livestock, pets, poultry, fishes, and wild animals, including rodents (Meerburg et al., 2009; Thompson et al., 2009). Rodents are the largest territorial mammalian group capable of surviving in different telluric ecosystems, including deserts. Their small-medium-sized body, robust shape, high prolificacy, and short gestation period afford them morphological and

biological adaptability with different lifestyles (Macpherson and Craig, 1991; Rabiee et al., 2018). As a part of the ecosystem, they provide different bennifites such as soil structure modification, soil aeration and hydration, seed and spore distribution (Rabiee et al., 2018). However, about 10% of the rodents act as pests (Han et al., 2015). These animals carry several ectoparasites, such as fleas, lice, mites, and ticks, which act as vectors for zoonotic pathogens, such as *Yersinia pestis*, *Coxiella burnetii*, *Bartonella* spp., *Rickettsia felis*, and Crimean-Congo hemorrhagic fever (Islam et al., 2021a). In the Middle Eastern countries, around 100 helminth species were reported in rodents, of which 22 are considerable public health concerns (Islam et al., 2020). Rodent-borne protozoa, including *Toxoplasma gondii*, and *Leishmania* spp. have global health importance (Bigna et al., 2020; Galeh et al., 2020; Mohebali et al., 2018). Some rodent-borne diseases, such as leishmaniosis, schistosomosis, and helminthosis, are called neglected tropical diseases, and thus they do not get enough attention when it comes to developing their prevention and control measures. As a result, they are detrimental to human and animal health and cause great economic loss by increasing morbidity, mortality, medical cost, and damaging food (Atehmengo and Nnagbo, 2014; Engels and Zhou, 2020).

Qatar is a small desert country located in the Arabian Peninsula, with three predominant species of commensal rodents: *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* (Islam et al., 2021b; Noureldin and Farrag, 2010). As such rodents live close to humans, they can transfer zoonotic pathogens from one host to another more readily (Dahmana et al., 2020; Rabiee et al., 2018). *Xenopsylla astia*, a rodent flea, is widely distributed in the Middle Eastern countries (Islam et al., 2021a), including Qatar (Abu-Madi et al., 2005), and is a carrier of *Y. pestis* (Dennis, 1999). The zoonotic cestode, *Hymenolepis diminuta* was identified in *R. norvegicus* of this country (Abu-Madi et al., 2005; Abu-Madi et al., 2001). Many rodent-borne parasitic diseases, including echinococcosis, hymenolepiosis, taeniosis, toxocariosis, trichuriosis, schistosomosis, amoebic dysentery, babesiosis, cryptosporidiosis, giardiosis, leishmaniosis, toxoplasmosis, have been reported in pet animals (Abu-Madi et al., 2010b; Dubey et al., 2010; Lima et al., 2019) and humans (Abu-Madi et al., 2008a; Abu-Madi et al., 2011; Abu-Madi et al., 2016b; Al Ani et al., 2014; Al Soub et al., 2016; Boughattas et al., 2017b). As it stands, there is a considerable knowledge gap concerning zoonotic transmissions and the dynamics of these parasites in Qatar (Islam et al., 2021c). Factors such as population demographics, rapid urbanization, agricultural and livestock projects can facilitate these parasites to jump between different species, resulting in future spillovers with new dynamics (Alasil and Abdullah, 2019; Atehmengo and Nnagbo, 2014; Petersen et al., 2018). Rodents can facilitate these parasite transmissions at the human-animal-environment interface in Qatar (Islam et al., 2021c). Understanding a pathogen, its possible hosts, risk factors, and transmission dynamics is essential for early preparedness, prevention, and control (Rahmann and Seip, 2007). Therefore, the primary aim of this study was to determine the incidence of parasites among commensal rodents in Qatar and to understand the associated factors of their occurrence. The secondary objective was to identify the zoonotic rodent-borne parasites, which may have potential risk for public health in this country.

Materials and Methods

Rodent collection and identification

A total of 148 rodents, including *Mus musculus* (n=4), *Rattus norvegicus* (n=120), and *Rattus rattus* (n=24), were captured using baited traps set across different ecosystems, such as agricultural farms, livestock farms, and other areas (residential, commercial, and industrial areas) in eight municipalities of Qatar (Figure 1). The present study was carried out from August 2019 to February 2020. Details of the rodents have been described previously (Islam et al., 2021b). The related information of the trapped rodents, such as the municipality, ecosystem facilities, species, age, sex, and pregnancy, were recorded accordingly.

Blood microscopic examination and ELISA

The rodents were anesthetized using 5% isoflurane inhalation for 3-5 minutes, and 3-5 ml of blood was collected through cardiac puncture using a 5 ml vacutainer EDTA tube (Parasuraman et al., 2010). All the blood samples were screened for parasites by microscopy using Giemsa staining (Thrall, 2005). The anti *T. gondii* and *Leishmania* spp. IgG was analyzed using commercial ELISA kits (kit multi-species ID Screen® Toxoplasmosis IgG Indirect, IDVET, Montpellier; *Leishmania* IgG, Cat No. IB0510, IBL, Minneapolis), according to the manufacturers' instructions.

Ectoparasite collection and identification

Ectoparasites were collected using a hairdryer as described elsewhere (Herrero-Cófreces et al., 2021). The ear, face, and perineal areas were examined for the presence of mites and ticks (Stekolnikov et al., 2019). All the ectoparasites were counted and recorded for each rodent and confirmed by direct microscopy based on standard external identification criteria (Centers for Disease Control and Prevention, 1967; Royal Entomological Society of London, 1954).

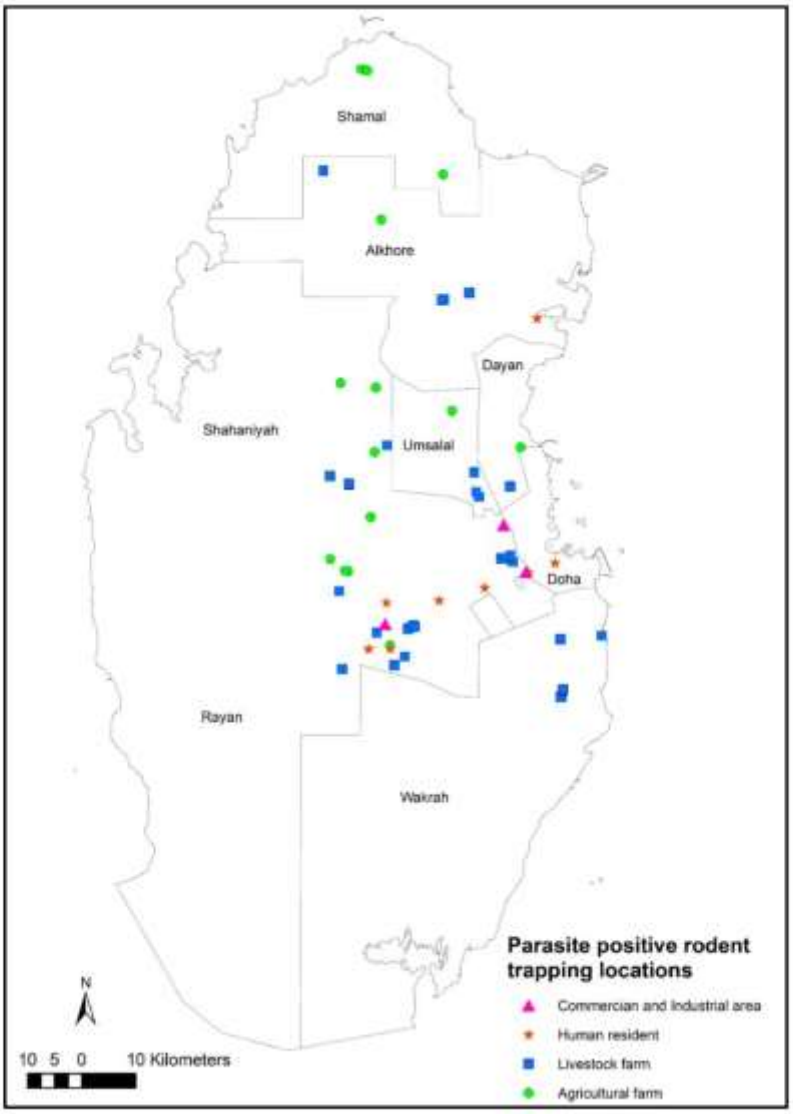

Figure 1. Location of the trapped rodents positive with different parasites

Necropsy, feces examination, and histopathology

After euthanasia, The rodents were necropsied, and their liver, stomach, and intestine were examined for the presence of parasitic cyst and helminth, based on standard identification criteria (Baker, 2007; Taylor et al., 2016; Viney and Kikuchi, 2017). Six visceral samples, such as liver, lungs, spleen, kidney, intestine, and diaphragm, were collected from each rodent in an aseptic condition and stored at -40°C for further study. Fecal samples from the rectum were collected, and parasitic egg or ova were examined by direct smear method using normal saline and a microscope (Taylor et al., 2016; Zajac and Conboy, 2012). In addition, a small piece of liver of each of the rodents was fixed with 10% neutral buffered formalin and subjected to paraffin-blocked histological processing. The liver blocks were sectioned with a 5µm diameter and stained with routine hematoxylin and eosin stains (Sheehan, 1987). The stained slides were examined under a microscope in search of *Capillaria hepatica*.

Molecular assessment

Sample preparation and DNA extraction

All the visceral specimens of a rodent were grouped as a single tissue pool and homogenized, which have been detailed previously (Islam et al., 2022). Genomic DNA was extracted from feces by QIAamp DNA stool mini kit and from tissue pools and five randomly selected cestodes by tissue mini kit, according to the manufacturer's instructions (Qiagen, CA, USA), and stored at -80^{0}C for further assay.

Molecular detection of parasites

Conventional and nested PCR were used to detect *Hymenolepis* spp. and *Giardia lamblia,* respectively, whereas the real-time PCR was used to detect *Leishmania* spp. and *T. gondii*. Commercial master mixes were used for each method. The samples used for pathogen detection, primers/probes, and PCR conditions used in this study are shown in Table 1. Positive DNA comprising ITS 1 and 5.8s rRNA gene was used for *Hymenolepis* spp. PCR validation. Similarly, gdh, aap3, and b1 genes were targeted for the detection of *Giardia lamblia*, *Leishmania* spp., and *Toxoplasma gondii* , respectively. The conventional and nested PCR amplicons were loaded on the 1% agarose gel for the verification of the amplification. The electrophoresis was performed at 80V for one hour for the visualization of the PCR products.

Table 1. Primers, probes, and the PCR conditions for detecting Hymenolepis spp. Giardia lamblia, Leishmania spp., and Toxoplasma gondii the current study

Pathogen and sample	Primer name	Primer (5′-3′)	PCR conditions	Reference
Hymenolepis spp.; stool and cestode	Hym spF	GCGGAAGGATCATTACACGTTC	95°C for 10 min, 35 cycles of 95°C for 30 sec, 60°C for 30 sec and 72°C for 30 sec, 72°C for 5 min, and 12°C hold	(Makki et al., 2017)
	Hym spR	GCTGCACTCTTCATCGATCCACG		
Giardia lamblia; stool	GDHeF	TCAACGTYAAYCGYGGYTTC CGT	95°C for 10 min, 35 cycles of 95°C for 30 sec, 60°C for 30 sec and 72°C for 30 sec, 72°C for 5 min, and 12°C hold	(Rafiei et al., 2020)
	GDHiF	CAGTACAACTCYGCTCTCGG		
	GDHiR	GTTRTCCTTGCACATCTCC		
Leishmania spp.; tissue	LeishF	GGCGGC-GGTATTATCTCGAT	50°C for 2 min, 95°C for 10 min, 40 cycles of 95°C for 15 sec, 60°C for 1 min, and 10°C hold	(Vidal et al., 2017)
	LeishR	ACCACGAGGTAGATGACAGA-CA		
	Leish (Probe)	FAM-ATGTCGGGCATCATC-NFQ		
Toxoplasma gondii; tissue	ToxoF	TCCCCTCTGCTGGCGAAAAGT	45°C for 10 min, 95°C for 10 min, 45 cycles of 95°C for 15 sec, 60°C for 45 sec and 10°C hold	(Lin et al., 2000)
	ToxoR	AGCGTTCGTGGTCAACTATCG ATTG		
	Toxo (Probe)	FAM-TCTGTGCAACTTTGGTGT ATTCGCAG-TAMRA		

Sequencing and phylogenetic analysis

The PCR products of cestode samples were purified using AddPrep PCR purification kit according to the manufacturer's instructions (www.addbioinc.com). Purified products were sequenced using the Sanger sequencing (SolGent Co. Ltd., Daejeon, 34014, Korea; http://www.solgent.com). The obtained DNA sequences were analyzed using BioEdit software. The BLAST searches were performed for each generated DNA sequence to identify the species. In addition, all the sequences that were generated in the present study were compared within the relevant groups, with each other, to assess the percent pairwise identities. Further, all the available ITS1 and 5.8s ribosomal RNA sequences of *H. diminuta* (n = 24) were downloaded from the NCBI-GenBank for the phylogenetic analysis, including the sequences (n = 2) generated in the present study. The DNA sequences (n = 26) were used to identify the best model for the phylogenetic analysis using MEGA-11 software (https://www.megasoftware.net/). We used Hasegawa-Kishono-Yano (HKY) model with 1,000 bootstrap replications for constructing a Neighbour-Joining tree in Geneious Prime 2022.0.2 software.

Statistical Analysis:

The field and laboratory data were entered in a Microsoft Excel 2016 spreadsheet, and statistical analyses were performed using STATA/IC- 13 (STATA Corp LLC, Lakeway Drive, TX, USA). Descriptive analysis was performed to determine the overall prevalence of parasites expressed as a percentage, frequency number, and 95% confidence interval (CI). Ectoparasite indices were calculated for each type of ectoparasite (fleas or mites) by dividing the total numbers detected for the specific ectoparasite by the total number of sampled rodents (Dennis, 1999). Univariate analysis was done for different factors related to the demographic (rodent species, age, sex), and ecosystem facilities by the Fisher exact test in identifying the association between parasitic prevalence and the factors. Univariate logistic regression was performed to check the strength of association between the two

specific parasites and the fleas assumed as the intermediate host for those parasites. In comparison, the outputs of the univariate logistic regression were expressed in Odds Ratio (OR), p-value, and 95% CI.

Results

Description and general prevalence of parasites

The present study identified ten parasite species among commensal rodents in Qatar (Table 2). Helminths were found to be the highest (45.9%) prevalent, followed by ectoparasites (31.8%) and protozoa (10.1%). Going by individual species prevalence, *X. astia* was the maximum prevalent (31.76%) parasite, whereas the lowest prevalent parasite was *Capillaria annulosa* (0.68%).

Table 2. Commensal rodent-borne parasitic prevalence in Qatar

Parasites	*Mus musculus* (n=4)	*Rattus norvegicus* (n=120)	*Rattus rattus* (n=24)	*Overall* (N=148)
Ectoparasites	1, 25.0 (0.6-80.6)	42, 35.0 (26.5-44.2)	4, 16.7 (4.8-37.4	47, 31.8 (24.4-39.9)
Ornithonyssus bacoti	-	4, 3.3 (0.9-8.3)	-	4, 2.7 (0.7-6.8)
Xenopsylla astia	1, 25.0 (0.6-80.6)	42, 35.0 (26.5-44.2)	4, 16.7 (4.8-37.4)	47, 31.8 (24.4-39.9)
Helminths	1, 25.0 (0.6-80.6)	61, 50.8 (42.0-59.6)	6, 25.0 (9.8-46.7)	68, 45.9 (38.1-54.0)
Capillaria annulosa	-	1, 0.8 (0.12-4.6)	-	1, 0.7 (0.1-3.7)
Hymenolepis diminuta	-	36, 30.0 (21.9-39.1)	6, 25.0 (9.8-46.7)	42, 28.4 (21.3-36.4)
Mastophorus muris.	1, 25.0 (0.6-80.6)	23, 19.2 (12.6-27.4)	-	24, 16.2 (10.7-23.2)
Taenia taeniaeformis	-	25, 29.1 (19.8-39.1)	-	25, 16.9 (11.7-23.7)
Protozoa	-	9, 7.5 (4.0-13.6)	6, 25 (12.0-44.9)	15, 10.1 (6.2-16.0)
Eimeria spp.	-	4, 3.3 (1.3-8.3)	1, 4.1 (0.7-20.2)	5, 2.7 (1.1-6.7)
Giardia spp.	-	4, 3.3 (0.9-8.3)	2, 8.3 (1.1-26.3)	6, 4.1 (1.5-8.6)
Toxoplasma gondii	-	2, 2.3 (0.3-8.2)	-	2, 1.4 (1.3-5.3)
Trypanosoma lewisi	-	1, 0.8 (0.12-4.6)	3, 12.5 (2.7-32.3)	4, 2.7 (0.7-6.8)
Overall	2, 50.0 (15.0-85.0)	77, 64.2 (55.3-72.2)	13, 54.2 (35.1-72.1)	92, 62.2 (54.1-69.6)

Result presented as total number of positive rodents, prevalence (95% Confidence Interval)

Overall, 31.8% of the rodents were positive for one parasite species, and 30.4% carried two or more parasite species. In the present study, the parasitic intensity was highest (up to 6) in *R. norvegicus* (Table 3). As the capture number of *M. musculus* (n=4) and *R. rattus* (n=24) were small, no further statistical analysis could be considered for these two species.

Table 3. Parasite species load among different rodent species in Qatar

Rodent species	No of parasite species	Total rodent positive, % (95%CI)
Mus musculus (n=4)	1	2, 50.0 (15.0-85.0)
Rattus norvegicus (n=120)	1	35, 29.2 (21.8-37.8)
	2	27, 22.5 (15.9-30.8)
	3	10, 8.3 (4.6-14.7)
	4	3, 2.5 (0.9-7.1)
	5	1, 0.9, (0.1-4.6)
	6	1, 0.9, (0.1-4.6)
Rattus rattus (n=24)	1	10, 41.7 (24.5-61.2)
	2	3, 12.5 (4.3-31.0)

Rodent-borne ectoparasites

The study identified 249 fleas (*X. astia)* (79% were females and 21% were males), and 4 mites (*Ornithonyssus bacoti*) from the captured rodents. *X. astia* were detected on all three species of rodents, where *O. bacoti* was identified only from *R. norvegicus*. Overall flea prevalence on *M. musculus, R. norvegicus,* and *R. rattus* were 25.0%, 35.0%, and 16.7%, where the flea indices were 0.8, 1.9, 0.6, respectively. *O. bacoti* was detected only on *R. norvegicus,* and the mite prevalence and index were 3.3% and 0.03, respectively. The Fisher exact test showed that rodent-borne flea prevalence was significantly (p = 0.01) higher on *R. norvegicus* from agricultural farms (48.3%), followed by the rodents from livestock farms (39.7%) and other sources (15.2%) (Table 4).

Table 4. Univariate association between different categories and ectoparasite prevalence in *Rattus norvegicus* in Qatar

Categories	*Xenopsylla astia*		*Ornithonyssus bacoti*	
	Positive (%)	*p*-value	Positive (%)	*p*-value
Age				
Adult (n=115)	41 (35.7)	0.47	4 (3.5)	0.67
Young (n=5)	1 (20.0)		0 (0.0)	
Sex				
Female (n=62)	21 (33.9)	0.79	3 (4.8)	0.34
Male (n=58)	25 (36.2)		1 (1.7)	
Pregnancy				
Pregnant (n=16)	4 (25.0)	0.38	1 (6.3)	0.76
Non-pregnant (n=46)	17 (37.0)		2 (4.4)	
Ecosystem				
Agricultural farm (n=29)	14 (48.3)		1 (3.5)	
Livestock farm (n=58)	23 (39.7)	0.01	3 (8.2)	0.42
Other areas (n=44)	5 (15.2)		0 (0.0)	

Rodent-borne helminths

H. diminuta was the most prevalent helminth (28.4%) (Table 2), found in both rodent intestine and the feces (Figure 2), by cestode morphological and eggs examination, respectively. Presence of *H. diminuta* was confirmed by PCR, followed by Sanger sequencing and the phylogenetic analysis. Phylogenetic analysis showed that the five cestodes were from two identical gene sequences, which got NCBI GenBank accession number: OM778284 and OM773635. The NCBI BLAST search identified that the DNA sequences generated in the present study were *H. diminuta* which shared 97-100 % nucleotide sequence identities with the reference genome of *H. diminuta*. The Neighbour-Joining phylogenetic tree of *H. diminuta* ITR1 and 5.8s ribosomal RNA gene sequenes generated in the present study confirmed that the Qatar isolates belonged to the same clade and were related to the other sequences reported from Canary Island, South Africa, Australia, Iran, Spain, China, and Mexico (Fig 3). In addition, we found 24 (16.2%) *Mastophorus muris* by detecting nematodes in the rodent stomach or eggs by fecal examination (Figure 2). No *R. rattus* was positive for *M. muris*. Out of 25 *Cysticercus fasciolaris* (Cysticerci of *Taenia taeniaeformis*) positive livers, about 70% contained a single cyst, and the rest had two-three cysts. *T. taeniaeformis* and *C. annulosa* (only one positive) were reported only in *R. norvegicus*. Gross or histological examination did not identify any *C. hepatica* in the livers of the rodents.

The Fisher exact test revealed that the prevalence of *H. diminuta* was significantly higher ($p = 0.00$) in the livestock farms (39.7%), followed by agriculture farms (37.9%) and other sources (6.1%) (Table 5). Moreover, the logistic regression showed that the prevalence of *H. diminuta* has a positive correlation (OR=4.13; $p = 0.00$) with the increased prevalence of fleas *X. astia* on rodents (Table 6).

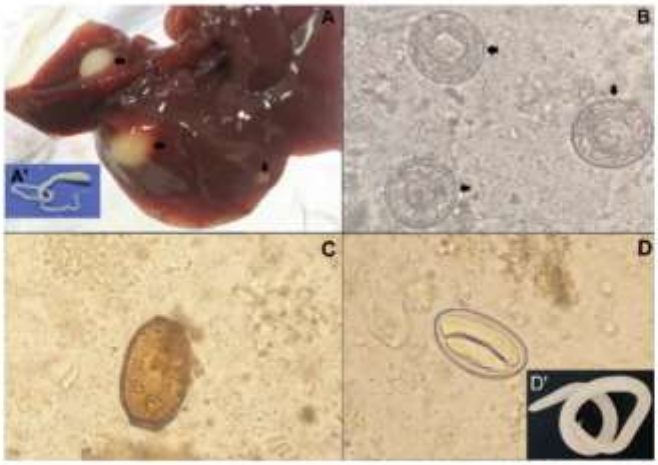

Figure 2. Helminths detected in the commensal rodents in different ecosystem of Qatar. Cysts of *Cysticercus fasciolaris* (A' is the larva from a cyst) in a liver (A), Egg of *Hymenolepis diminuta* (B), *Capillaria annulosa* (C), and *Mastophorus muris* (D' is a *M. muris* found in rodent stomach) (D) in rodent feces.

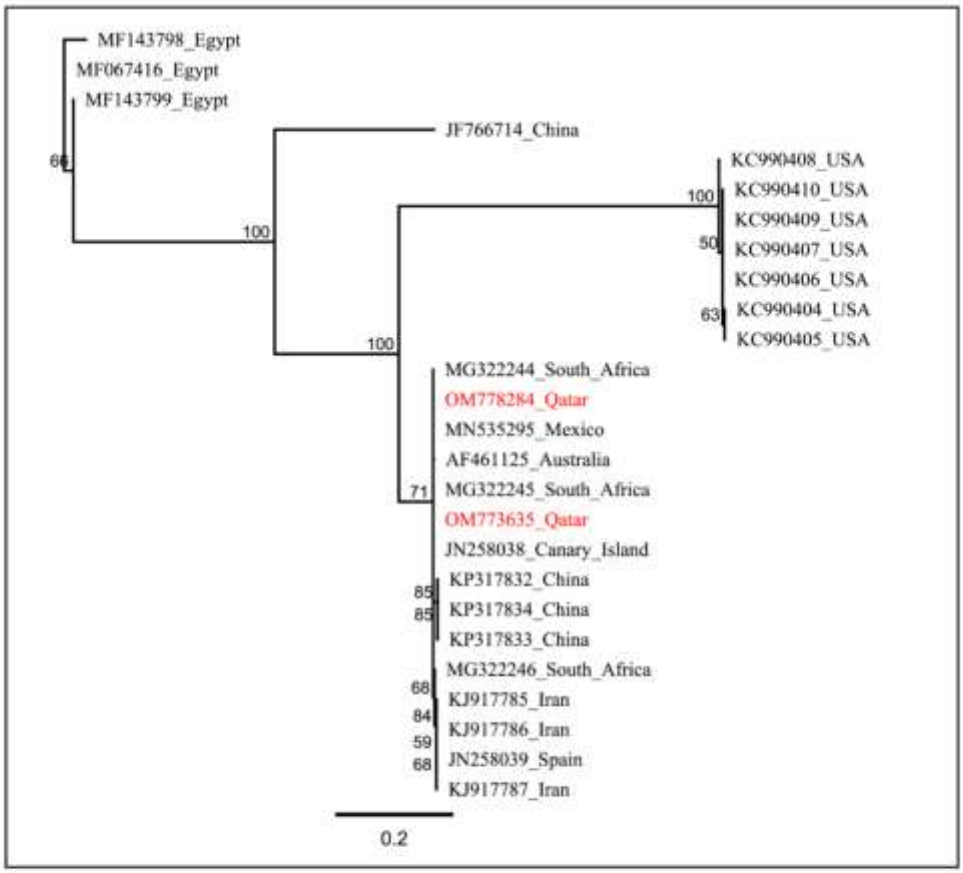

Figure 3. The Neighbour-Joining phylogenetic tree of the *Hymenolepis diminuta* ITS1 and 5.8s ribosomal RNA partial gene sequences generated in the present study from rodents in Qatar (n = 2) and related sequences downloaded from NCBI-GenBank reported during 2003 - 2022 worldwide. The *H. diminuta* sequences generated from rodents in Qatar clustered with the sequences reported from several countries, including South Africa, Mexico, Australia, Canary Island etc which suggested a broad circulation of *H. diminuta* in rodents.

Table 5. Univariate association between different categories and helminth prevalence in *Rattus norvegicus* in Qatar

Categories	*Hymenolepis diminuta*		*Mastophorus muris*		*Taenia taeniaeformis*	
	n (Positive) %	*p*-value	n (Positive) %	*p*-value	n (Positive) %	*p*-value
Age						
Adult	115 (36) 31.3	0.14	115 (23) 20.0		82 (25) 30.5	
Young	5 (0) 0.0		5 (0) 0.00	0.27	4 (0) 0.00	0.19
Sex						
Female	62 (18) 29.0	0.81	62 (14) 22.6	0.33	38 (8) 21.1	
Male	58 (20) 31.0		58 (9) 15.5		48 (17) 35.4	0.15
Pregnancy						
Pregnant	16 (6) 37.5	0.39	16 (2) 12.5		11 (2) 18.2	
Non-pregnant	46 (12) 16.1		46 (12) 26.1	0.26	27 (6) 22.2	0.78
Ecosystems						
Agricultural farm	29 (11) 37.9		29 (5) 17.2		24 (9) 37.5.	
Livestock farm	58 (23) 39.7	0.00	58 (13) 22.4	0.67	46 (14) 30.4	0.22
Other areas	33 (2) 6.1		33 (5) 15.1		16 (2) 12.5	

Table 6. Univariate logistic regression of the effect of fleas on the prevalence of parasites in rodents

Parasites	**Odds Ratio**	***p*-value**	**95%CI**
Hymenolepis diminua	4.13	0.00	1.93-8.83
Trypanosoma lewisi	0.73	0.79	0.06-7.98

Rodent-borne protozoa

A total of five fecal samples were positive for *Eimeria* spp. (Figure 4). Although six feces were positive for *Giardia* spp. by microscopy (Figure 4), all feces were negative by PCR for *Giardia lamblia*. None of the samples was positive for *Leishmania* spp. by ELISA or PCR. However, two (1.4%) samples were IgG positive against *T. gondii* by ELISA, but none of the tissue samples was positive by PCR. It is noteworthy that *Eimeria* spp. was more prevalent among females (4.8%) than male rodents (1.7%) ($p = 0.03$) in *R. norvegicus* (Table 7). *Giardia* spp. was found to be more prevalent ($p = 0.01$) among young rodents (40.0%) compared with adults (1.7%).

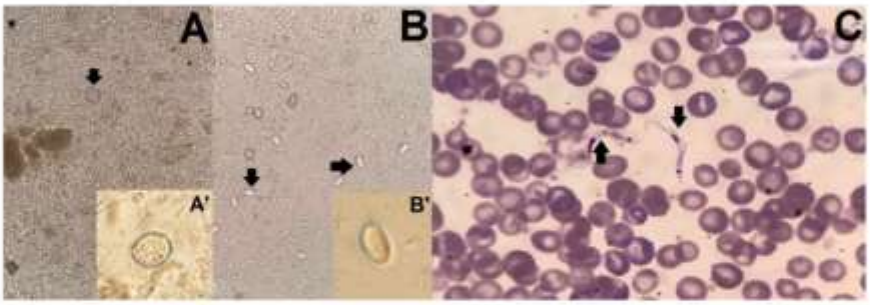

Figure 4. *Eimeria* spp. oocyst (A) and *Giardia* spp. oocyst in the feces (B) and *Trypanosoma lewisi* worm in the blood (C) (indicated by arrows) of rodents in Qatar. A' and B' are the large size figure of the respective parasite oocysts.

Table 7. Univariate association between different categories and protozoa prevalence in Rattus norvegicus in Qatar

Categories (n)	*Eimeria* spp.		*Giardia* spp.		*Toxoplasma gondii*	
	Positive (%)	*p*-value	Positive (%)	*p*-value	Positive (%)	*p*-value
Age						
Adult (115)	4 (3.5)	1.00	2 (1.7)	0.00	2 (1.7)	0.77
Young (5)	0 (0.0)		2 (40.0)		0 (0.0)	
Sex						
Female (62)	3 (4.8)	0.03	1 (1.6)	0.28	0 (0.0)	0.14
Male (58)	1 (1.7)		3 (5.2)		2 (3.45)	
Pregnancy						
Pregnant (16)	3 (18.8)	1.00	0 (0.0)	0.55	0 (0.0)	-
Non-pregnant (46)	0 (0.0)		1 (2.2)		0 (0.0)	
Ecosystems						
Agricultural farm (29)	2 (6.7)	1.00	1 (3.5)	1.00	0 (0.0)	0.34
Livestock farm (58)	0 (0.0)		2 (3.5)		2 (3.45)	
Other areas (22)	2 (9.1)		1 (3.0)		0 (0.0)	

Discussion

Rodents are the importnat wildlife in the ecosystem but involved with several epidemics in the last few decades in the history of the Middle East (World Health Organization, 2021). The present study was aimed to investigate the risk of rodent-borne parasitic zoonoses with public health significance and pattern of incidence in different ecosystem of Qatar. The study identified a total of ten parasite species , of which *X. astia* and *H. diminuta* had been previously reported in Qatar (Abu-Madi et al., 2005; Abu-Madi et al., 2001; Armed Forces Pest Management Board, 1999). Hoever, we detected eight new species of parasites. In addition, we identified *X. astia* and *H. diminuta* across different ecosystems of Qatar, suggesting that these parasites are widely distributed within the country.

In the Middle Eastern region, a total of 104 species of rodent fleas and 134 species of rodent mites have been reported (Islam et al., 2021a). In addition to *X. astia*, an earlier report had identified *Xenopsylla cheopis* in Qatar (Armed Forces Pest Management Board, 1999). *X. astia* prevalence on *R. norvegicus* was lower than in the previous studies (45.6% and 35.8%, respectively) (Abu-Madi et al., 2005; Abu-Madi et al., 2001). In our study,

the flea prevalence on *R. norvegisus* was higher, followed by *M. musculus* and *R. rattus*, which is inconsistent with a previous report in the Middle East, where the overall prevalence of flea was 44.4% on *R. norvegisus*, followed by 33.9% on *R. rattus*, and 21.6% on *M. musculus*. Nevertheless, the rodent flea index in the current study was higher than the overall rodent flea index in Iran (13%) (Islam et al., 2021a). It was stated previously that the prevalence of rodent fleas depends on geographical location and the type of ecosystems (Antoniou et al., 2010; Hanafi-Bojd et al., 2007). This is the first study identifying *O. bacoti* in Qatar to the best of our knowledge. We have recently reported that rodent-borne fleas and mites of Qatar are carriers of *Rickettsia* spp. (Islam et al., 2022), suggesting that *X. astia* and *O. bacoti* can mediate transmission of Rickettsial pathogens at the human, animal, and envioronmental interface through rodents in this country (Islam et al., 2021c).

The study identified two species of cestodes, namely: *H. diminuta*, *T. taeniaeformis*, and two species of nematodes, namely: *C. annulosa* and *Mastophorus muris*, out of which *H. diminuta* and *T. taeniaeformis* were the most prevalent. *H. diminuta* is an intestinal parasite commonly found in small rodents worldwide (Islam et al., 2020; Kapczuk et al., 2020), including in Qatar (Abu-Madi et al., 2005; Abu-Madi et al., 2001). Arthropod vectors, namely beetles, caterpillars, cockroaches, and fleas, can act as intermediate hosts of *H. diminuta* (Kapczuk et al., 2020). Humans, especially children, can acquire an infection with *H. diminuta* by accidentally ingesting the intermediate host carrying the cysticerci of the cestode (Chatterjee, 2012; Kapczuk et al., 2020). Previous studies have identified cysticerci of *H. diminuta* in *X. cheopis* (Gárate et al., 2011). In the present study, we observed a positive correlation between the prevalence of *H. diminuta* and *X. astia*, which corroborates with the previous studies (Abu-Madi et al., 2005; Abu-Madi et al., 2001). *Cysticercus fasciolaris* is the cystic form of *T. taeniaeformis*, for which cats are the primary host and rodents act as intermediate hosts (Taylor et al., 2016). Previous studies identified eggs of *T. taeniaeformis* among cats in Qatar (Abu-Madi et al., 2010b; Abu-Madi et al., 2008c). This indicates that *T. taeniaeformis* is a common dweller at the cat-rodent interface in this country. *T. taeniaeformis* is zoonotic with little significance (Little, 2012). There is a human reports of *T. taeniaeformis* infection in Sri Lanka (Ekanayake et al., 1999), which shows that this cestode is zoonotic in nature. *M. muris* and *C. annulosa* parasitize in the stomach and small intestine of rodents, respectively (McGarry et al., 2015). These parasites are not important for public health (Islam et al., 2020). Previous studies have detected *M. muris* in rodents of neighboring countries such as Egypt and Iran (Behnke et al., 2000; Behnke et al., 2004; Fasihi Harandi et al., 2016), whereas *C. annulosa* has been reported from Iran (Meshkekar et al., 2014).

Four species of protozoa are infested in the Qatari rodents, namely *Eimeria* spp., *Giardia* spp., *T. gondii*, and *T. lewisi*. Several species of *Eimeria* were reported in rodents of the Middle Eastern countries, such as *Eimeria alorani, Eimeria anzanensis, Eimeria cahirinensis, Eimeria carmelensis, Eimeria elliptica, Eimeria lancasterensis, Eimeria serbica, Eimeria spalacensis, Eimeria uptani*, and *Eimeria zuhairamri* (Couch et al., 1997; Couch et al., 1993; Hůrková et al., 2005; Ozmen et al., 2009). *Eimeria* parasites are not zoonotic, but are economically important as they infect livestock and poultry (Burrell et al., 2020), though the degree of host specificity of rodent eimeriosis still not clearly known (Kvičerová and Hypša, 2013). Giardiosis is an important parasitic disease affecting the gastrointestinal tract of humans and other mammals. *G. lamblia* is a zoonotic parasite that can infect humans, pets, livestock, and other mammals, including rodents (Heyworth, 2016). *G. muris* and *G. microti* are commonly reported among rodents and do not have any zoonotic importance (Thompson and Monis, 2012). *G. lamblia* and *Giardia muris* were reported from rodents of some Middle Eastern countries, such as Iran, Egypt, and Palestine (Abd el-Wahed et al., 1999; Al Hindi and Abu-Haddaf, 2013; Mohebali et al., 2017). *Giardia microti* was found in rodents of Germany and Italy (De Liberato et al., 2021; Helmy et al., 2018). In Qatar, Giardia lamblia is a common cause of enteritis among humans and animals (Abu-Madi et al., 2016a; Abu-Madi et al., 2016b; Boughattas et al., 2017b; Veterinary laboratory, 2020). *Giradia* spp. detected in this study are not *G. lamblia*, maybe some other species, like *G. microti* or *G. muris*, which needs further confirmation. However, human giardiasis is more common among females than males in Qatar (Abu-Madi et al., 2010a; Abu-Madi et al., 2008b), which observed similar trends in the present study.

A single study reported that toxoplasmosis is endemic among humans in Qatar (Abu-Madi et al., 2008a). Toxoplasmosis has been reported to cause abortion among livestock animals of this country (Veterinary laboratory, 2020). Cats were considered as a source of transmission of this pathogen at the human-animal interface (Boughattas et al., 2017a; Dubey et al., 2010). In the present study, we observed a low seroprevalence of *T. gondii* in rodents. *T. lewisi* causes murine trypanosomiasis in domestic rodents worldwide (Durden and Hinkle, 2019) and infects humans occasionally (Truc et al., 2013; Verma et al., 2011). Previous studies reported that *Ceratophyllus fasciatus*, *Nosopsyllus fasciatus, X. cheopis*, and *Xenopsylla nubica* act as the biological carrier of *T. lewisi* (Lee and Armstrong, 2008; Schwan et al., 2016). There is a lack of reports about the pathophysiology and epidemiology of *T. lewisi* in Qatar.

The current trend in the emerging and re-emerging infectious diseases has raised public health concerns for health practitioners and policymakers for their severity, dynamics and source of origin (Atehmengo and Nnagbo, 2014; Mostafavi et al., 2021). We identified ten species of parasites that infest rodents of Qatar, some of which

have the potentiality to infect directly or indirectly to humans and other animals and can act as reservoirs or carriers of zoonotic pathogens. Rodent control, more specifically, integrated pest management practice, is essential to prevent these rodent-borne hazards. However, our study had some limitations, the first of which is that we used the direct smear method to detect fecal parasites, which may mislead parasitic prevalence due to false-negative results. Second, we only collected limited samples of *M. musculus* and *R. rattus*.

Conclusions

The current study has identified a diverse range of rodent-borne ectoparasites, helminths, and protozoa. Out of the ten species of rodent-borne parasites, *X. astia, O. bacoti, H. diminuta, T. gondii, T. lewisi,* and *T. taeniaeformis* are important for public health. Commensal rodents can mediate in transmission of these parasites at the human-animal-environment interface. Apart from *X. astia* and *H. diminuta*, all other parasites are first recorded among commensal rodents in the different ecosystems of the history in Qatar. Further studies are required to identify the biology and transmission dynamics of these parasites in different ecosystems to combat future epidemics.

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Conflicts of Interest The authors declare no conflict of interest.

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Chapter 4.2: Diversity of Bacterial Pathogens and Antimicrobial Resistance Profile among Commensal Rodents in Qatar

Antimicrobial resistance is the current threat for humans and animals. We identified diversity of rodent-borne bacterial pathogens and their antimicrobial resistance status in our current study.

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ORIGINAL ARTICLE

Diversity of bacterial pathogens and their antimicrobial resistance profile among commensal rodents in Qatar

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Abstract

Rodents are sources of many zoonotic pathogens that are of public health concern. This study investigated bacterial pathogens and assessed their antimicrobial resistance (AMR) patterns in commensal rodents in Qatar. A total of 148 rodents were captured between August 2019 and February 2020, and blood, ectoparasites, and visceral samples were collected. Gram-negative bacteria were isolated from the intestines, and blood plasma samples were used to detect antibodies against *Brucella* spp., *Chlamydophila abortus*, and *Coxiella burnetii*. PCR assays were performed to detect *C. burnetii*, *Leptospira* spp., *Rickettsia* spp., and *Yersinia pestis* in rodent tissues and ectoparasite samples. Antimicrobial resistance by the isolated intestinal bacteria was performed using an automated VITEK analyzer. A total of 13 bacterial species were isolated from the intestine samples, namely *Acinetobacter baumannii, Aeromonas salmonicida, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Hafnia alvei, Klebsiella pneumoniae, Providencia stuartii, Proteus mirabilis, Pseudomonas aeruginosa,* and *Salmonella enterica.* The majority of them were *E. coli* (54.63%), followed by *P. mirabilis* (17.59%) and *K. pneumoniae* (8.33%). Most of the pathogens were isolated from rodents obtained from livestock farms (50.46%), followed by agricultural farms (26.61%) and other sources (22.94%). No antibodies (0/148) were detected against *Brucella* spp., *C. abortus,* or *C. burnetii.* In addition, 31.58% (6/19) of the flea pools and one (1/1) mite pool was positive for *Rickettsia* spp., and no sample was positive for *C. burnetii, Leptospira* spp., and *Y. pestis* by PCR. A total of 43 (38%) bacterial isolates were identified as multidrug resistant (MDR), whereas *A. salmonicida* ($n = 1$) did not show resistance to any tested antimicrobials. Over 50% of bacterial MDR isolates were resistant to ampicillin, cefalotin, doxycycline, nitrofurantoin, and tetracycline. The presence of MDR pathogens was not correlated with rodent species or the location of rodent trapping. Seven (11.86%) *E. coli* and 2 (22.2%) *K. pneumoniae* were extended-spectrum beta-lactamases (ESBL) producers. These findings suggest that rodents can be a source of opportunistic bacteria for human and animal transmission in Qatar. Further studies are needed for the molecular characterization of the identified bacteria in this study.

Keywords Commensal rodents · Gram-negative bacteria · Rickettsia · Antimicrobial resistance · Qatar

Introduction

The global importance of emerging and reemerging infectious diseases has increased immensely in the last few decades, with over 60% of them are of zoonotic origin (Jones et al. 2008; Mostafavi et al. 2021). Rodents are potential sources of more than 88 zoonotic pathogens and are historically linked to multiple epidemics (Bessat 2015; Hashemi Shahraki et al. 2016; Islam et al. 2021a; Rosenthal and Michaeli 1977). Commensal rodents, that live close to humans and share human food, water, and shelter for living, are common causes of damage to crops, destruction of resources, and disease transmission (Meerburg et al. 2009; Pinto 1993; Rabiee et al. 2018). Typical pathways for pathogen transmission from rodents to humans by direct contact; food and water contaminated with rodent urine, feces, or fur; or through their ectoparasites and other animals, such as livestock and pets (Hamidi 2018; Rabiee et al. 2018).

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Qatar is a small country located in the Arabian Peninsula (World Travel Guide 2019) with a diverse population (Planning and Statistics Authority 2020). Recently, three commensal rodent species have been reported in Qatar: *Mus musculus*, *Rattus norvegicus*, and *Rattus rattus* (Islam et al. 2021b; Noureldin and Farrag 2010). The cestode, *Hymenolepis diminuta*, was found in *R. norvegicus* (Abu-Madi et al. 2005), which is of public health importance (Torgerson and Macpherson 2011). Several rodent-borne bacterial diseases, such as campylobacteriosis (Abu-Madi et al. 2016; Ghunaim et al. 2015; Humphrey et al. 2016; Mohammed et al. 2015), non-diphtheritic corynobacteriosis (El-Nemr et al. 2019), *Escherichia coli* enteritis (Ghunaim et al. 2015; Humphrey et al. 2016; Mohammed et al. 2015), listeriosis (Khan et al. 2017), Q-fever (Royal et al. 2013), salmonellosis (Ghunaim et al. 2015; Humphrey et al. 2016), tuberculosis (Al Marri 2012), and non-plague yersiniosis (Ghunaim et al. 2015) have been reported in humans and animals in Qatar. Q-fever, brucellosis, and chlamydiosis are major causes of livestock abortion in Qatar (Department of Animal Resource 2019).

The majority of Qatari residents originate from the Indian subcontinent, which is endemic for many rodent-borne zoonotic diseases, such as typhoid fever (Centers for Disease Control and Prevention 2020; World Health Organization 2018). Hence, frequent travel between Qatar and these countries poses a risk of transboundary transmission of rodent-borne diseases in Qatar (Islam et al. 2021a; Mangili and Gendreau 2005). Qatar has antimicrobial stewardship programs (ASPs) in the medical field (Helen et al. 2018), although no legislation and guidelines are available for its use in the veterinary field. Several studies have been performed to determine the antimicrobial sensitivity (AST) and Antimicrobial resistance (AMR) profiles of bacterial isolates from humans and animals (Alhababi et al. 2020; Sid Ahmed et al. 2020). Previous reports showed that urban rodents could be potential carriers of AMR bacteria (Gwenzi et al. 2021; Huy et al. 2020). However, presently there is insufficient scientific data on the zoonotic bacteria and their AMR profile from wildlife, such as rodents in Qatar. Therefore, this study investigated the diversity of rodent-borne bacterial pathogens and their AMR patterns to assess the public health risk in Qatar.

Methods

The sample collection

A total of 148 rodents were captured between August 2019 and February 2020 from different municipalities and environments (Fig. 1). A detail of these rodents was described previously (Islam et al. 2021b). They included three commensal species; *M. musculus* (n = 4), *R. norvegicus* (n = 86), and *R. rattus* (n = 18). After administering general anesthesia using 5% isoflurane inhalation (Marquardt et al. 2018), cardiac blood was collected (Parasuraman et al. 2010), and fleas and mites were captured from rodents skin (Herrero-Cófreces et al. 2021; Stekolnikov et al. 2019). In addition, 108 rodents were necropsied, and six visceral samples were collected from each rodent, including the diaphragm, intestine, kidney, liver, lung, and spleen. Information related to each rodent, such as species, age, sex, pregnancy, ectoparasite type, ecosystem facility, and municipality, was recorded.

Isolation, identification, and antimicrobial resistance testing

All rodent intestines were processed under a laminar airflow cabinet with a BSL 2 facility (Labconco, Cat: 3620924, Sl: 060757988) for the gram-negative gut bacterial isolation. Using sterilized swabs, the intestinal contents were inoculated on MacConkey agar (MCA), Hektoen enteric agar (HEA), eosin methylene blue agar (EMBA), and selenite cystine broth (SCB) and incubated overnight at 37 °C. Growth on SCB was subcultured on MCA, HEA, and EMBA. The colony characteristics were studied on each culture medium, and the isolates were primarily identified (Vandepitte 2003; Washington et al. 1985). Subsequent sub-cultures from the MCA, HEA, and EMBA were performed to obtain a single colony. An identical single colony of each primarily identified bacterial species from a single rodent sample was transferred to the automated VITEK system (VITEK®2, Version 07.01 compact system, Ref: 27630, SL: VK2C9944) for confirmatory identification and AST following the VITEK protocol (VITEK 2008). A gram-negative identification kit (VITEK® 2 GN kit, Ref: 21341) was used to confirm the identification of the isolates. The minimum inhibitory concentration (MIC) of an antimicrobial is the lowest concentration of the antimicrobial that inhibits the growth of a microorganism after overnight incubation (Andrews 2001). Using MIC, we checked the antimicrobial resistance of the isolates using two cards: VITEK® 2 AST-GN 38 for samples number 1–65, and because of the production of AST-GN 38 being halted by the manufacturer, we alternated to VITEK® 2 AST-GN 85 for the rest of the samples (samples number 66–108). These two cards tested AMR against 20 antimicrobials: amikacin, amoxicillin/clavulanic acid, ampicillin, cefalotin, cefovecin, cefpodoxime, ceftiofur, chloramphenicol, doxycycline, enrofloxacin, gentamicin, imipenem, marbofloxacin, neomycin, nitrofurantoin, piperacillin, pradofloxacin, tetracycline, tobramycin, trimethoprim/sulfamethoxazole.

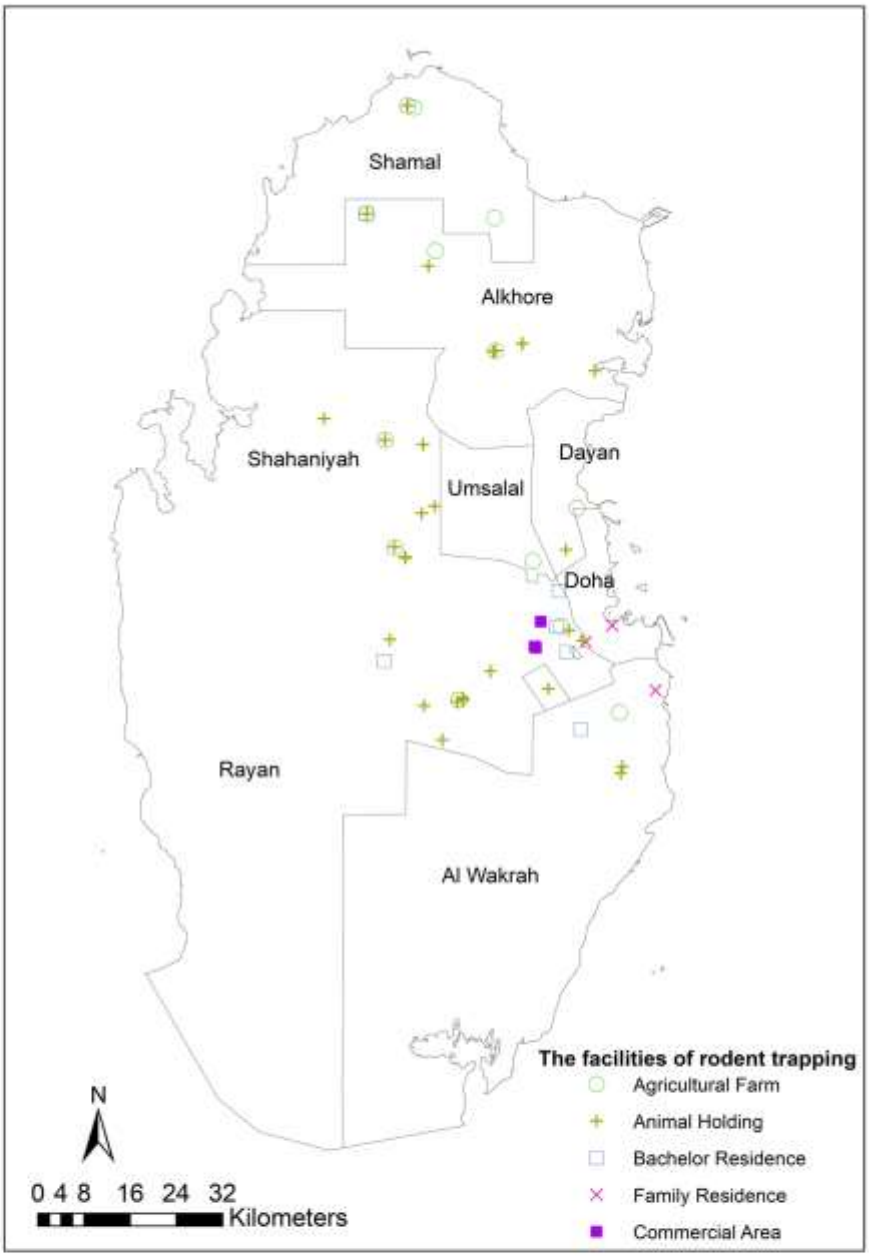

Fig. 1 Location of the different municipalities of Qatar and the facilities for trapping of commensal rodents for isolating bacterial pathogens in the current study

If an isolate was resistant to three or more antimicrobials, it was considered MDR (Magiorakos et al. 2012). The VITEK 2 AST-GN cards also tested the extended-spectrum beta-lactamase (ESBL) producing ability of the isolated *E. coli* and *Klebsiella pneumoniae*.

ELISA

Antibodies against *Brucella* spp., *Chlamydophila abortus*, and *Coxiella burnetii* were quantified in plasma by indirect IgG ELISA kits (IDVet, 310 rue Louis Pasteur – 34,790 Grabels, France), following the manufacturer's protocol.

Molecular assays

Sample processing and DNA extraction

Genomic DNA was extracted from homogenized materials of rodent tissues and ectoparasite samples using DNeasy DNA blood and tissue (QIAGEN GmbH, Germany) as per the manufacturer's instructions. The visceral samples of each rodent were grouped as a single tissue pool. The fleas (n = 250) were collected into 19 pools (9–25 fleas per pool) based on the flea sex and origin of the rodent host. All mites (n = 4) were combined as a single pool. The tissue and ectoparasite pools were homogenized in a 2 ml microtube (Sarstedt, 72.694.006) using a speed mill for two minutes with 1 mm, 4 mm, and 30 mm ceramic beads in 500 µL DMEM, 5% Gln, 1% Penstrep, 3% FKS. The microtube was centrifuged for five minutes at 13000 rpm, and the supernatant was transferred to a new 1.5 ml tube and centrifuged at 13000 rpm for 15 min.

Molecular detection of bacteria

Real-time PCR was carried out to detect DNA of *Leptospira* spp., *Rickettsia* spp., and *Yersinia pestis* using 2X master mix (5x Hot FIREPol Probe Universal qPCR Mix, Solis BioDyne, Estonia) by Gentier 96E Real-time PCR System (Tianlong Science and Technology, China). Conventional PCR using AddStart Taq Master (2X concentration, South Korea) was used to identify genomic DNA of *C. burnetii* by SimpliAmp Thermal cycler and GDS-200C Gel documentation system. The PCR reaction conditions and primer/probe used are listed in Table 1. The positive DNA of *C. burnetii* was used from our internal positive control stock in the Department of Animal Resources, Qatar. However, positive DNA of *Rickettsia* spp., *Listeria* spp., and *Y. pestis* was collected from the Central Laboratory of the Ministry of Higher Education and Scientific Research, Sudan. Distilled water was used as the negative control.

Data analysis

All analyses were performed using the STATA/IC-13 (STATA Corp LLC, Lakeway Drive, TX, USA). Descriptive statistics were expressed as frequency number, percentage (%), and 95% confidence intervals (CI). The relationship between bacterial isolation and MDR isolates with rodent species and trapping locations were analyzed. The p value (<0.05) was considered as a significant variation among the variables.

Table 1 Primers, probes, and the annealing temperature for detecting *Leptospira* spp. and *Rickettsia* spp. used in rodent and ectoparasite samples the current study

Pathogen and sample	Primer name	Primer (5'-3')	Annealing temperature	Reference
Coxiella burnetii; Tissue and flea	*C. burnetii*(F)	CGGGTTAAGCGTGCTCAGTATGTA	95 °C for 10 min, 35 cycles of 95 °C 20 s, 60 °C for 30 s, 72 °C for 45 s, and 72 °C for 5 min	(Bruin et al. 2011)
	C. burnetii(R)	TGCCACCGCTTTTAATTCCTCCTC		
Leptospira spp.; Tissue	LipL32(F)	AGAGGTCTTTACAGAATTTCT TTCACTACCT	50 °C for 2 min, 95 °C for 10 min, 40 cycles of 95 °C for 15 s, 60 °C for 1 min	(Tellevik et al. 2014)
	LipL32(R)	TGGGAAAAGCAGACCAACAGA		
	LipL32 (Probe)	FAM-AAGTGAAAGGATCTTTCGT TGC-MGB		
Rickettsia spp.; Tissue flea, and mite	PanR8(F)	AGCTTGCTTTTGGATCATTTGG	94 °C for 2 min, 45 cycles of 94 °C for 15 s, 60 °C for 30 s	(Kato et al. 2013)
	PanR8(R)	TTCCTTGCCTTTTCATACATCTA GT		
	PanR8(Probe)	FAM-CCTGCTTCTATTTGTCTTGC AGTAACACGCCA-BHQ1		
Yersinia pestis; Tissue and flea	Yp-F132(F)	CTGCAAGCACCACTGCAAC	95 °C for 10 min, 35 cycles of 95 °C 20 s, 60 °C for 30 s, 72 °C for 45 s, and 72 °C for 5 min	(Hinnebusch and Schwan 1993)
	Yp-R560(R)	TACGGTTACGGTTACAGCATCAGTG		

Table 2 Overall prevalence of rodent intestinal gram-negative bacteria from Qatar

Bacteria	Total number of isolates, % (95% CI)
Family: Moraxellaceae	
Acinetobacter baumannii	2, 1.85 (0.22–6.53)
Family: Aeromonadaceae	
Aeromonas salmonicida	1, 0.93 (0.02–5.05)
Family: Enterobacteriaceae	
Citrobacter freundii	2, 1.85 (0.22–6.53)
Citrobacter koseri	2, 1.85 (0.22–6.53)
Enterobacter aerogenes	3, 2.73 (0.58–7.90)
Enterobacter cloacae	3, 2.73 (0.58–7.90)
Escherichia coli	59, 54.63 (44.76–64.24)
Klebsiella pneumoniae	9, 8.33 (3.88–15.23)
Salmonella enterica	3, 2.73 (0.58–7.90)
Family: Hafniaceae	
Hafnia alvei	1, 0.93 (0.02–5.05)
Family: Morganellaceae	
Proteus mirabilis	19, 17.59 (10.94–26.10)
Providencia stuartii	2, 1.85 (0.22–6.53)
Family: Pseudomonadaceae	
Pseudomonas aeruginosa	4, 3.70 (1.02–9.21)

Results

Demography of identified bacteria

Among the 108 rodent intestine samples, 95 (87.95%, 95%CI: 80.30–93.43) were positive for gram-negative bacteria. Of these, 14.74% (n = 13, 95%CI: 8.30–23.49) of the rodents carried two or more bacterial species. Most of the positive rodents were collected from livestock farms (n = 54, 50.46%, 95%CI: 40.72–60.18), followed by agricultural farms (n = 30, 26.61%, 95%CI: 18.60–35.93) and other areas (n = 26, 22.94%, 95%CI: 15.43–31.97). The study detected 110 isolates from 13 bacterial species (Table 2). The majority of the isolates were *E. coli* (54.763%, 95%CI: 44.76–64.24), followed by *Proteus mirabilis* (17.59%, 95%CI: 10.94–26.10), and *Klebsiella pneumoniae* (8.33%, 95%CI: 3.88–15.23).

Furthermore, *E. coli* were found to be prevalent in all species of rodents: *M. musculus* (100%), *R. norvegicus* (54.12%), and *R. rattus* (47.37%) (Table 3). On the other hand, *P. mirabilis* was detected only in *R. norvegicus* (20.00%) and *R. rattus* (10.53%). The majority of *E. coli* were isolated from the rodents of agricultural farms (61.54%), followed by the livestock farms (53.33%), and

Table 3 Univariate association of rodent intestinal gram-negative bacteria with rodent host species and trapping location in Qatar

Bacteria (N = 110)	Species wise positive; n (%)				Trapping location wise positive; n (%)			
	Mus musculus (n = 4)	*Rattus norvegicus* (n = 91)	*Rattus rattus* (n = 15)	*p* value*	Agricultural farm (n = 30)	Livestock farm (n = 54)	Other areas (n = 26)	*p* value*
Acinetobacter baumannii	0 (0.00)	1 (1.18)	1 (5.26)	0.47	0 (0.00)	0 (0.00)	2 (9.09)	0.02
Aeromonas salmonicida	0 (0.00)	0 (0.00)	1 (5.26)	0.09	0 (0.00)	1 (1.67)	0 (0.00)	0.67
Citrobacter freundii	0 (0.00)	2 (2.35)	0 (0.00)	0.76	1 (3.85)	1 (1.67)	0 (0.00)	0.61
Citrobacter koseri	0 (0.00)	0 (0.00)	2 (10.53)	0.01	0 (0.00)	1 (1.67)	1 (1.85)	0.50
Enterobacter aerogenes	0 (0.00)	3 (3.53)	0 (0.00)	0.66	2 (7.69)	1 (1.67)	0 (0.00)	0.20
Enterobacter cloacae	0 (0.00)	3 (3.53)	0 (0.00)	0.66	0 (0.00)	2 (3.33)	1 (4.55)	0.59
Escherichia coli	4 (100.00)	46 (54.12)	9 (47.37)	0.15	16 (61.54)	32 (53.33)	11 (50.00)	0.69
Hafnia alvei	0 (0.00)	1 (1.18)	0 (0.00)	0.87	0 (0.00)	0 (0.00)	1 (4.55)	0.14
Klebsiella pneumoniae	0 (0.00)	9 (10.59)	0 (0.00)	0.27	2 (7.69)	5 (8.33)	2 (9.09)	0.99
Providencia stuartii	0 (0.00)	2 (2.35)	0 (0.00)	0.76	1 (3.85)	0 (0.00)	1 (4.55)	0.28
Proteus mirabilis	0 (0.00)	17 (20.00)	2 (10.53)	0.40	6 (23.08)	9 (15.00)	4 (18.18)	0.66
Pseudomonas aeruginosa	0 (0.00)	4 (4.71)	0 (0.00)	0.57	1 (3.85)	0 (0.00)	3 (13.64)	0.02
Salmonella enterica	0 (0.00)	3 (3.53)	0 (0.00)	0.65	1 (3.85)	2 (3.33)	0 (0.00)	0.67

*$p < 0.05$ was considered as significant variation among the variables

other areas (50.00%), and in the case of *P. mirabilis,* it was 23.08%, 15.00%, and 18.18%, respectively.

ELISA and molecular assessment of bacterial pathogens

We assessed the specific antibodies in the plasma of rodents by ELISA and no IgG antibodies were detected against *Brucella* spp. *C. abortus* and *C. burnetii* (0%, N = 148, 95%CI: 0–0.024). The visceral samples were negative for *C. burnetii, Leptospira* spp., *Rickettsia* spp., and *Y. pestis* (0%, N = 108, 95%CI: 0–0.03) by PCR. The fleas were also negative for *C. burnetii* and *Y.* (0%, N = 18, 95%CI: 0–0.18). Furthermore, six flea pools (31.58%, N = 19, 95%CI: 12.58–56.55) and one mite pool (1/1) were positive for *Rickettsia* spp.

Antimicrobial resistance profile

AMR patterns were varied among the isolates. Out of the 110 bacterial isolates, 31 isolates (28.18%, 95%CI: 20.02–37.56), which were *E. coli* only, did not show resistance to any of the tested antimicrobials. Thirty-six isolates (32.73%, 95%CI: 24.08–42.33) were resistant to 1–2 antimicrobials, which includes *E. coli* (n = 14), *P mirabilis* (n = 9), and *K. pneumoniae* (n = 6). The rest 43 (39.09%, 95%CI: 29.93–48.86) isolates, which were from 12 (n = 13, 92.31%, 95%CI: 63.97–99.8) bacterial species, were identified as MDR (Table 4). The MDR bacteria were resistant to 17 antimicrobials (85%, n = 20, 95%CI: 62.11–96.79), whereas all bacterial isolates were sensitive to neomycin, and pradofloxacin. Over 50% of the MDR isolates were resistant to ampicillin, cefalotin, doxycycline, nitrofurantoin, and tetracycline. The resistance pattern among the MDR bacteria varied between three to nine antimicrobials. The highest resistance were by *P. stuarti* (n = 1), *E. coli* (n = 3), and *P. merabilis* (n = 1), which were resistant to 9 antimicrobials; followed by *P. aeruginosa* (n = 1), *Salmonella enterica* (n = 2), resistant to 8 antimicrobials; and *P. stuarti* (n = 1), resistant to 7 antimicrobials. Although the majority of the MDR pathogens were isolated from agricultural facilities (n = 28), there was no significant correlation ($p = 0.14$) among MDR pathogens isolated from different facilities. Similarly, the majority of the MDR isolates were from *R. norvegicus*, and there was no significant difference ($p = 0.92$) among MDR pathogens isolated from different rodent hosts. Two (22.2%, 95%CI: 2.81–60.01) *K. pneumoniae* and seven (11.86%, 95%CI: 4.91–22.93) *E. coli* were ESBL producers. All ESBL producing bacteria were isolated from *R. norvegicus*, although there was no significant correlation ($p = 0.33$) between the ESBL producing pathogens and the location of rodent trapping.

Discussion

The presence or absence of a disease, pathogen, or a vector plays a major role in the success of any disease surveillance program (Mohammed et al. 2015). Rodents are sources of various pathogens in humans and animals (Han et al. 2015; Meerburg et al. 2009). To the best of our knowledge, this is the first study to identify and characterize bacterial species from rodents in Qatar. We have reported 13 bacterial species, the majority of which were isolated from rodents captured in livestock farms. The livestock farms in Qatar are usually managed with insufficient biosecurity measures. Different domestic and exotic animals and birds are kept together in the same enclosures, where the shepherds also live on the farm premises. There are resting places (*majlis*) in the farms, where the owners visit during their leisure time (Farag et al. 2018). A previous report from Qatar revealed that around 80% of livestock farms were infested with rodents (Noureldin and Farrag 2010). Infectious bacteria can infect humans and other animals by direct or indirect exposure (Taylor et al. 2001). As such, keeping multi-species along with human dwellers within the same enclosures can increase the risk of cross-species transmission of infectious diseases (Rogdo et al. 2012).

As the majority of the rodents were *R. norvegicus* and were captured from the livestock farms, the relationship with the isolated bacteria, AMR pattern, or ESBL production with the rodent host or location of trapping may not give an accurate picture of Qatar in our study. Among the 13 bacterial species, the prevalence of *E. coli* was high (54.63%), which was substantially lower than that reported in a previous study on livestock animals (88.7%) in Qatar (Alhababi et al. 2020). In Saudi Arabia, the recovery rate of *E. coli* from chicken was 31.1% (Altalhi et al. 2009). Rodent fecal samples showed 75% and 4.8% positivity for *E. coli* in Cyprus [46] and Singapore [47], respectively. *E. coli* is a commensal bacterium in the animal intestine, and we did not identify the pathogenic strains of *E. coli* in our study. Methodological differences can also result in variations in bacterial recovery rates (Ong et al. 2020). Therefore, *E. coli* recovery in this study may be less important as pathogenic strains of *E. coli* were not identified (Ramos et al. 2020).

Rodents are overlooked reservoirs of *Brucella abortus, Brucella melitensis,* and *C. burnetii,* which has both human and animal health importance (Abdel-Moein and Hamza 2018; Doosti and Moshkelani 2011; Psaroulaki et al. 2014; Tiller et al. 2010). *Rickettsia* spp. are the causal agents of spotted fever and typhus fever. Several vectors of *Rickettsia* spp. have been reported in Qatar, such as *Xenopsylla cheopis, Ctenocephalides felis*, and *Ornithynyssus bacoti* (Armed Forces Pest Management Board 1999). Rodents and their ectoparasites can act as reservoirs for *Rickettsia* spp. (Han

Table 4 Multidrug resistant gram-negative bacteria isolated from rodent intestine and their resistant pattern

Bacterial Isolates	*Acinetobacter baumannii* ($n=2$)	*Citrobacter freundii* ($n=2$)	*Citrobacter koseri* (n = 1)	*Enterobacter aerogenes* ($n=1$)	*Enterobacter cloacae* ($n=1$)	*Escherichia coli* ($n=14$)	*Hafnia alvei* ($n=1$)	*Klebsiella pneumoniae* ($n=3$)	*Proteus mirabilis* ($n=10$)	*Providencia stuartii* ($n=2$)	*Pseudomonas aeruginosa* ($n=3$)	*Salmonella enterica* ($n=3$)	Total MDR species ($n=43$)
Antimicrobials													
Amikacin												3	1
Amoxicillin/ Clavulanic Acid	1	2		1	1	5	1	2	1		3		9
Ampicillin	1					11	1	3	1	2	3	2	8
Cefalotin		2	1	1		3			1			2	6
Cefovecin	1		1										2
Cefpodoxime	2	1	1	1		7		2	1		3		8
Ceftiofur	2	1	1	1		6			1		3		7
Chloramphenicol	1				1	1	1		2	1	1		7
Doxycycline						2			6			2	3
Enrofloxacin						5	1	1	4	1	2	1	7
Gentamicin						1				2		3	3
Imipenem						3		2	5			2	4
Nitrofurantoin	1			1	1	2	1	3	10	2	2	3	10
Piperacillin						3		3					2
Tetracycline						10	1		10	2	3	3	6
Tobramycin										2		1	2
Trimethoprim/ Sulfamethoxazole						10			2		3		3
Total antimicrobials	7	4	4	5	3	14	6	7	12	7	9	10	

et al. 2015; Meerburg et al. 2009; Rabiee et al. 2018). In the current study, we found *Rickettsia* spp. in rodent-borne fleas and mites, which is reported for the first time among humans and animals in Qatar. Although there is no previous report of rickettsial disease in humans or animals in Qatar, the country is at risk of this pathogen when considering the close interaction between humans and animals. Leptospirosis is also a rodent-borne disease, which is commonly seen in flood-prone areas and among those people who are in constant contact with animals (Naing et al. 2019). In Qatar, the majority of residents and animal shepherds are from the Indian subcontinent (Priya D'Souza Communations 2019; Social & Economic Survey Research Institute 2021), where leptospirosis is commonly seen (Victoriano et al. 2009). Hence, we tested for the presence of this disease in the Qatari rodents. Plague is a reemerging disease in the WHO Eastern Mediterranean region (Mostafavi et al. 2021). There were three outbreaks of bubonic plague in this region; two in Lebanon and one in Afghanistan in the last two decades. Rodents and rat flea (*Xenopsylla astia)* act as reservoir of *Y. pestis* (Dennis 1999; Mahmoudi et al. 2020). Our study revealed that *Brucella* spp., *C. abortus, C. burnetii*, *Leptospira* spp. and *Y. pestis* were not present in our sample of rodents in Qatar.

The bacterial pathogens that we identified are primarily found in soil and water, and sometimes as normal flora of the animal intestine (Brown et al. 2012). They have opportunistic pathogenic dynamics in humans and animals (Brown et al. 2012; Done and Radostits 2007), causing infections associated with community-based and healthcare settings, especially in pediatric, elderly, and immunocompromised patients, resulting in gastroenteritis, urinary tract infection (UTI), pneumonia, and sepsis (Choi et al. 2015; Gillespie 1994; Levinson 2018; Tomas 2012; Wie 2015). Some of these pathogens have been identified in patients of different hospital settings in Qatar. *E. coli* and *Salmonella* spp. are common causes of human gastroenteritis in Qatar (Ghunaim et al. 2015; Humphrey et al. 2016; Mohammed et al. 2015). *Acinetobacter baumannii* was isolated from hospitalized adult patients and caused pneumonia (Al Samawi et al. 2016). *C. fruendii, Enterobacter aerogenes, Enterobacter cloacae, E. coli,* and *K. pneumoniae* were detected in the intensive care unit patients. Pediatric patients with UTI were positive for *Citrobacter koseri* and *E. cloacae*. Similarly, *P. aeruginosa* was isolated from hospitalized patients in Qatar (Sid Ahmed et al. 2020). Moreover, *Escherichia, Klebsiella, Pseudomonas*, and *Salmonella* cause enteritis, pneumonia, mastitis, and septicemia in livestock animals (Done and Radostits 2007). *Acinetobacter*, *Aeromonas*, and *Proteus* are also pathogenic to animals (Askari et al. 2019; Schukken et al. 2012). It is possible to transmit these pathogens from animals to humans through tainted animal products for human consumption (Guerra et al. 2014).

AMR occurs when a pathogen changes over time and does not respond to antimicrobials. It makes an infection difficult to treat, thereby increasing the risk of spreading disease, severe illness, and death. AMR organisms are found in nature, which usually occur through genetic changes and spread at the human-animal-environment interface (Khan et al. 2020). The major drivers of AMR are the misuse and overuse of antimicrobials; inadequate access to clean water; lack of proper sanitation and hygiene for humans and animals; poor infection and disease prevention and control (IP&C) in healthcare and farm settings; poor access to medical services; lack of awareness, knowledge, and related legislation (Hassan et al. 2021; Kalam et al. 2021; World Health Organization 2015). This study examined the antimicrobial resistance to 20 antimicrobials agents to reveal the drug resistance patterns of gram-negative gut bacteria in commensal rodents of Qatar. Many microbes in the environment can have natural resistance to some of these antibiotics (Nair et al. 2011). Of the isolated bacteria in this study, six were from the ESCAPE group. ESCAPE, stands for *Enterococcus faecium, Staphylococcus aureus, Clostridium difficile, A. baumannii, P. aeruginosa*, and *E refers to Enterobacteriaceae* including *E. coli, K. pneumoniae, Proteus* spp., and *Enterobacter* spp., are generally MDR pathogens (Akova 2016). Our study found that several *K. pneumoniae* and *E. coli* were ESBL producers, which affirming a previous finding that mentioned that CTX-M-1 gene in *E. coli* and *K. pneumoniae* is responsible for ESBL production in Qatar (Sid Ahmed et al. 2016). ESBL can make a pathogen resistant to cephalosporins, carbapenems, and aminoglycosides (Ghafourian et al. 2015; Paterson and Bonomo 2005; Sawa et al. 2020). In this study, the majority of MDR *E. coli* strains were resistant to ampicillin, tetracycline, and trimethoprim/sulfamethoxazole. More than 50% of *E. coli* from chickens in Saudi Arabia showed resistant to ampicillin, chloramphenicol, gentamycin, tetracycline, and trimethoprim/Sulfamethoxazole (Altalhi et al. 2009). Over 50% resistance to ampicillin, cefalotin, and tetracyclin was reported for *E. coli* isolated from chicken in Qatar (Johar et al. 2021). Over 50% of *P. mirabilis* in this study were resistant to doxycycline and tetracycline, which is in accordance with the statement by Stock (Stock 2003), who indicated that *P. mirabilis* can be naturally resistant to these antimicrobials. However, Stock showed that *P. mirabilis* could be naturally sensitive to nitrofurantoin, whereas in our study, there was major resistance (89%) against this antimicrobial. Due to the lack of guidelines and ambiguous regulations regarding antibiotic use among animals in veterinary practice, there are chances of increased antimicrobial resistance among animals (Gillings 2013). As most livestock farms keep mixed species animals with poor biosecurity management, there is a chance to cross

the species barrier by MDR pathogens between rodents and other animals, including humans.

Our study suggests that rodents can serve as a source of zoonotic bacteria at the human-animal-environmental interface. Raising caution within the community and implementing appropriate preventive measures can help to alleviate the burden of vector-borne diseases (Desoky 2018; Núñez et al. 2014). These measures can include maintaining proper hygiene, enhancing biosecurity and farm management in the animal and agricultural farmsteads, and appropriate IP&C in hospital settings. The limitations of the current study were that we did not determine the pathogenic potential of the isolates and concentrated only on gram-negative bacteria; therefore, the gram-positive enteric bacteria, such as *Fusobacterium* or *Bacteroides*, were not analyzed. Additionally, we only used aerobic culture methods, which is why we did not detect any anaerobic bacteria, such as *Clostridium* spp.

Conclusions

This study constitutes the first report of rodent-borne bacterial investigation in commensal rodents in Qatar. These isolates include *A. baumannii, A. salmonicida, Citrobacter freundii, C. koseri, E. aerogenes, E. cloacae, Hafnia alvei, K. pneumoniae, P. stuartii, P. mirabilis*, and *P. aeruginosa*, which were first time reported in rodents. Our study shows that rodents are potential sources of zoonotic and opportunistic bacterial pathogens at the human-animal-environmental interface in Qatar. The risk increases if MDR pathogens cross the species barriers and infect humans and other animals. Particularly in the latter case, animal and agricultural farms can serve as sources of such pathogens. Therefore, farm biosecurity measures must be implemented in animal and agricultural settings to avoid such pathogenic transmission. We recommend conducting further studies for molecular characterization of these pathogens.

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Author contributions Conceptualization, MMI, EF, and ZM-K; methodology, MMI, KAE, MSK, MA, MKS, AMA-M; formal analysis, MMI and MMH; writing—original draft preparation, MMI, MMH, DB, and ZM-K; writing—review and editing, MMI, MMH, EF, DB, KAE, HMY, and ZM-K; visualization, AAS, EF, and ZM-K; supervision, EF and ZM-K; project administration, HA-R, AMA-M, AAA-Z, and EF; funding acquisition, EF AAS, and HA-R. All authors have read and agreed to the published version of the manuscript.

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Declarations

Ethical permission The current study is a part of the "Risk assessment of rodent-borne zoonotic diseases in Qatar" project. Ethical approval was obtained from the Institutional Animal Care and Use Committee of the Ministry of Municipality and Environment, the State of Qatar (IACUC-A-MME-4) to conduct the study.

Conflict of interest The authors declare no conflict of interest.

Consent to participate and consent for publication All authors attended in the work and accepted the manuscript to publish.

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Chapter 4.3: Rodent-borne viruses in commensal rodents of Qatar

Besides ectoparasites, helminths, protozoa, and bacteria, rodents carry several viruses with zoonotic importance. We tested our rodent samples by using standard laboratory techniques for detection of hantavirus and Rift Valley fever virus. None of our samples were positive for those viruses. We reported our findings in the statement below.

Rodent-borne viruses in commensal rodents of Qatar

Abstract

Rodents are known to be potential sources for over 60 zoonotic viruses. Commensal rodents have a higher importance in transmitting zoonotic viruses as they live close to humans. Several rodent-borne viral diseases, including Rabies, Chikungunya, and Hepatitis E virus, have been reported at the human-animal interface in Qatar. There are reports of Hantavirus (HV), Rift Valley Fever virus (RVFV) in some other countries of the Arabian Peninsula. The current study investigated HV and RVFV in rodents of Qatar. The study tested 108 rodents tissue samples using the RT-PCR method to check nucleic acids of HV and RVFV. However, all the samples were negative by RT-PCR. A further longitudinal study is required to investigate the diversity of rodent-borne zoonotic viruses at the human-animal interface in Qatar.

Keywords: *Mus musculus, Rattus norvegicus, Mus musculus,* Rift Valley fever virus, Hantavirus, Qatar

Introduction

Spillover of zoonotic pathogens from animals to humans in the last decades indicates that every animal in close proximity to humans should be investigated for zoonotic pathogens [1]. Rodents are the largest mammalian order in the terrestrial ecosystem [2, 3]. Although these animals have several benefits in the landscape ecosystem, including soil aeration and hydration, they are known as potential sources of resource damage and zoonotic pathogens. Commensal rodents have a higher importance in transmitting zoonotic viruses as they live close to humans. Bats are known as the highest per species zoonotic virus carrier. However, rodents are potential sources for around 68 zoonotic viruses [4].

Qatar is a small country in the Arabian Peninsula, where the risk of zoonotic viruses increased due to climate change, rapid urbanization, higher population growth, and desert ecosystem damage in the recent years [5, 6]. Several rodent-borne viral diseases have been reported among the humans and animals in the country, including Rabies, Chikungunya, and Hepatitis E, which were mainly considered as imported diseases [7-11]. Many rodent-borne viruses have been reported in the neighboring countries of Qatar. For example, hantavirus (HV) specific antibodies were reported among humans and rodents in Kuwait [12]. Crimean-Congo hemorrhagic fever (CCHF) was detected among humans in Oman [13]. Hepatitis E virus, rabies virus, CCHF virus, and hantaan virus were detected in humans and rodents in Iran [14]. West Nile fever virus was reported among humans and animals in Saudi Arabia and Yemen [15, 16]. Yemen and Saudi Arabia experienced outbreaks of Rift Valley fever virus (RVFV). Rift Valley fever (RVF) is one of the most important viral diseases in Africa [17]. Qatar imports livestock animals from the countries of the Arabian Peninsula and Africa, such as Saudi Arabia, Kuwait, Oman, Sudan, and Somalia. There is a chance of importing RVFV and HV to Qatar while importing livestock animals. Recent studies showed several rodent-borne parasitic and bacterial pathogens in Qatar [18, 19]. However, no virological investigation has ever been done in rodents of the country. Therefore, the current study was undertaken to explore the rodent-borne zoonotic viruses, specifically HV and RVFV among commensal rodents of Qatar.

Methods

Ethical approval

Ethical permission was obtained to conduct the research from the *Institutional Animal Care and use Committee* of the Ministry of Municipality and Environment, Qatar (IACUC-A-MME-4, Date: 10 February 2019).

Rodent trapping

A cross-sectional study was conducted from November 2019 to February 2020 in Qatar, which was detailed previously [20]. The study trapped rodents from different municipalities of the country. Six types of locations were considered for the rodent trapping, viz. livestock farms, agricultural farms, bachelor accommodations, family accommodations, commercial areas, and industrial areas. After trapping, the rodents were transferred to the rodent research laboratory in the Central Veterinary Laboratory of the Department of Animal Resources, Qatar, which is equipped to work with rodents possibly carrying zoonotic pathogens.

Virological sample collection

Following anesthesia by inhalation of 5% isoflurane for 3-5 minutes in a desiccator, the rodents were used to identify species, sex, and age. Then whole blood was collected from each rodent by cardiac venipuncture using a 5 ml vacutainer EDTA tube. Afterward, the rodents were returned to the desiccator for euthanasia and necropsied to collect visceral samples viz. diaphragm, intestine, kidney, liver, lung, and spleen. Each of the visceral sample was collected in a 2 ml cryotube and stored at -80°C for further study.

Molecular assessment

The visceral samples were transferred to the biosafety level 3 laboratory in the Biomedical Research Complex of Qatar University. The visceral samples of each rodent were grouped in a single tissue pool and homogenized using ceramic beads in a speed mill. Viral RNA was extracted from homogenized materials of rodent tissue using commercial kits (QIAGEN GmbH, Germany), following the manufacturer's protocol. Real-time RT–PCR was carried out to detect the nucleotides of RVFV using QuantStudio7 Pro Real-time PCR system (Thermofisher, USA). A nested PCR was used to detect RNA of HV using SimpliAmp Thermal cycler and GDS-200C gel documentation system. The PCR reaction conditions and primer/probe used have been shown in Table 1. The PCR protocols were previously developed in the Virology Unit of the Central Veterinary Laboratory of the Department of Animal Resources, Qatar. We used the positive control RNA of HV and RVFV collected from the Central Laboratory of the Ministry of Higher Education and Scientific Research, Sudan. Distilled water was used as the negative control.

Table 1 Primers, probes, and annealing temperature for detecting hantavirus and Rift Valley fever virus used in rodent samples of the current study

Pathogen	Primer name	Primers	Annealing temperature	Reference
Hantavirus	HAN-L-F1	5′- ATGTAYGTBAGTGCWGATGC -3′	94°C for 2 minutes, 45 cycles of 94°C for 15 seconds, 60°C for 30 seconds	[21, 22]
	HAN-L-R1	5′- AACCADTCWGTYCCRTCATC -3′		
	HAN-L-F2	5´-TGCWGATGCHACIAARTGGTC-3´		
	HAN-L-R2	5´-GCRTCRTCWGARTGRTGDGCAA-3´		
Rift Valley Fever virus	RVFV-S-F	5′- TGATGGTCCTCCCAGGATAC -3′	45°C for 10 minutes, 95°C for 10 minutes, 40 cycles of 95°C for 10 seconds, and 60°C for 1 minute.	[23]
	RVFV-S-R	5′- ACTAGGACGATGGTGCATGA -3′		
	RVFV-probe	5′- FAM-AAAGCTTTGATATCTCTCA GTGCCCCAA-BHQ1-3′		

Statistical analysis

Descriptive statistics of the trapped rodents were conducted using STATA/IC-13 (Stata Corp, 4905 Lakeway Drive, College Station, Texas 77845, USA), and the results were expressed as percentage (%) and 95% Confidence intervals (CI).

Results

The current study used 108 rodents, belonging to three species; *Mus musculus* (n=4), *Rattus norvegicus* (n=86), and *Rattus rattus* (n=8). Descriptive statistics of the rodents have been presented in table 2. The majority of the rodents were trapped from the livestock farms (55.6%), followed by agricultural areas (26%) and other areas (14%). The rodents were mainly from the Rayyan municipality (48%), followed by Alkhore (16%) and other municipalities (37%). In addition, all the *Mus musculus* and *Rattus rattus* were captured from the Rayyan municipality. The rodents mainly were adult (92%) and males (54%). A total of 46.3% of the rodents were females, of which 30% were pregnant.

The study aimed to detect the HV and RVFV in the visceral organs of the rodents using the RT-PCR method. All the tested samples were negative for HV and RVFV.

Table 2 Demographic characteristics of the rodents used for virological investigation in the current study

Characters	n (% of total capture, 95% CI)
Trapping location (N=108)	
Agriculture Farm	26 (24.1, 16.4-33.3)
Bachelor residence	12 (11.1, 5.9-18.6)
Commercial area	6 (5.6, 2.1-11.7)
Family residence	3 (2.8, 0.6-7.9)
Industrial area	1 (0.9, 0.1-5.1)
Livestock farms	60 (55.6, 45.7-65.2)
Municipalities (N=108)	
Al Khore	17 (15.7, 9.5-24.1)
Daayan	1 (0.9, 0.1-5.1)
Doha	10 (9.3,4.5-16.4)
Rayyan	52 (48.1, 38.5-56.9)
Shamal	7 (6.5, 2.7-12.9)
Um Salal	8 (7.4, 3.3-14.1)
Wakrah	13 (12.1, 6.6-19.7)
Species (N=108)	
Mus musculus	4 (3.7, 1.1-9.2)
Rattus norvegicus	86 (79.6, 70.8-86.8)
Rattus rattus	18 (16.7, 10.2-25.1)
Sex (N=108)	
Female	50 (46.3, 36.7-56.2)
Male	58 (53.7, 43.9-63.4)
Pregnancy (N=50)	
Pregnant	15 (30.0, 17.9-44.6)
Non-pregnant	35 (70.0, 55.4-82.2)
Age (N=108)	
Adult	99 (91.7, 84.8-96.2)
Young	9 (8.4, 3.9-15.3)

Discussion

Due to the global importance of emerging and reemerging viral diseases, it is immensely important to investigate the zoonotic viruses, their sources, prevalence, and transmission dynamics. RVF is a disease of domestic animals and humans, transmitted by mosquitoes, characterized by fever, headache and muscle pains, hemorrhagic fever, and meningoencephalitis. RVF was first discovered in 1934 in Kenya [24]. Rodents are considered as a reservoir host for maintenance of the virus [25]. HV causes pulmonary syndrome and hemorrhagic fever with renal syndrome in humans [26]. Rodents are considered as the major reservoirs of HV. Out of 80 known hantavirus reservoirs in nature, 51 are rodent species. *Mus musculus* and *Rattus* spp. have been identified to carry hantavirus [27, 28]. There is a chance of migrating these viruses through human travelers, livestock and agricultural trades from the partner and neighbor countries in Asia and Africa to Qatar. However, our study shows that the sampled commensal rodents of Qatar did not carry HV and RVFV. There may no such zoonotic viral existence among the commensal rodents in Qatar or the pathogens were not detected due to several limitations in the current study, such as small sample size, short period of study, and investigation of only two zoonotic viruses. A further longitudinal study is required with more samples using serology and molecular methods to investigate the zoonotic viral diversity among rodents in Qatar.

Conclusion and recommendation

The current study tested the presence of HV and RVFV among commensal rodents in Qatar and found that the commensal rodents trapped in this study were not important for these two zoonotic viruses. Further study is necessary by serologic and molecular methods to investigate the rodents role in zoonotic virus diversity in this country.

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Chapter 5: Mandibular Tumor in *Rattus norvegicus* from Qatar: A Case Report

Tumors in wild animals are rarely reported. While working with the rodents in the current study, we detected a mandible of a *Rattus norvegicus* with abnormal growth. Primarily we diagnosed the case as ameloblastoma. A short report of the case has been presented here.

Ameloblastoma in the mandible of *Rattus norvegicus* from Qatar: a case report

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Abstract

An adult male rat, *Rattus norvegicus*, was captured from a livestock farm of the Rayan area in Qatar as a part of the survey of rodent-borne zoonotic pathogens. The rat had swelling on the right side of its mouth. We conducted a morphologic and morphometric study of the rodent, complete blood count, plasma biochemistry to understand its physical status. The rodent was also subjected to fecal and blood film parasitic examination, gram-negative gut bacterial isolation and identification, ELISA, and PCR to detect zoonotic pathogens. However, the rodent had neutrophilia and regenerative macrocytic normochromic anemia. It was positive for *Cesticercus fascioliaris* and *Hemenolepis diminuta*. *Escherichia coli* and *Salmonella enterica* spp. *diarizonae* were isolated from its intestine. The rat was negative for the antibodies against *Coxiella burnetii*, *Chlamydophila abortus, Brucella* spp., *Toxoplasma gondii*, *Leishmania* spp., and West Nile Virus by ELISA. The rat was negative for the DNA of *Coxiella burnetii, Rickettsia* spp., *Leptospira* spp., *Yersinia pestis, Leishmania* spp., and *Toxoplasma gondii* by PCR method. Moreover, the rodent was negative for RNA of Rift Valley fever virus and Hantavirus by RT-PCR. In addition, we conducted histopathology of the rat thyroid, prescapular, and the inter-jugular lymph nodes, lung, liver, kidney, and intestine. Only hemosiderin pigment at the prescapular lymph node was identified. While processing the skull as a part of the morphometric study, we found a swelling mass on the right mandible. There was extensive development throughout the body and ramus of the mandible. The length of the right abnormal mandible was longer than the same of the left healthy mandible (29.43 mm vs. 28.09 mm). The length, width, and height of the mass of the right mandible were 26.92, 21.5, and 19.67 mm, respectively. All the incisors except the lower right one were longer than the standard size. We diagnosed the case as solid ameloblastoma. Based on a systematic search on PubMed, Scopus, Science Direct, and Web of Science, the current case is considered a unique case of mandibular ameloblastoma in wild rodents.

Keywords: ameloblastoma, mandible, *Rattus norvegicus,* wild rodent

Introduction

Odontogenic tumors are the tumors of the oral and maxillofacial area, which can be benign or malignant. Ameloblastoma is a type of odontogenic tumor, defined as "A benign but locally invasive polymorphic neoplasm consisting of proliferating odontogenic epithelium, which usually has a follicular or plexiform pattern, lying in a fibrous stroma" [1]. This type of tumor is rare in both humans and animals [1-3]. Overall, 1% of human oral tumors are ameloblastoma, whereas it is the second most prevalent (9-11%) among human odontogenic tumors [4, 5]. Previous reports diagnosed ameloblastoma in buffalo [6], cat

[7], cattle [8], dog [9], fish [10], horse [11], mouse [3], sheep [12], and snake [13]. Among rodents, ameloblastoma was found in amargosa vole (*Microtus californicus*), domestic brown rat (*Rattus norvegicus*), and Syrian hamster (*Mesocricetus auratus*) [14], and Wistar rat [15]. Like human cases [1], animals also get the tumor mostly at the mandible [14z].

Ameloblastoma is classified into four types: conventional/solid/multicystic, Extraosseous/peripheral, desmoplastic, and unicystic [1, 5]. Ameloblasts arise from odontogenic epithelial or mesenchymal, especially from the rests of the dental lamina, surface epithelium, or the radius of the dental lamina. Sometimes ameloblast can arise due to neoplastic change. The cause is described as alteration or mutation in the genetic material of the cells that are embryogenically programmed for the tooth, such as odontogenic epithelium, including bone membrane protein, fibroblast growth factors, sonic hedgehogs, and wingless [16]. Arenavirus may be a potential causal agent of odontogenic tumors [17]. Different treatment methods, including enucleation, curettage, and enblock resection, were described in humans [4, 18], but no ameloblastoma treatment cases were reported among veterinary species. We presented a case of ameloblastoma in the right mandible raised from the ramus of the mandible of wild rodents. The tumor and pathobiology of the rodent have been illustrated here.

The Case description

The research team of the case was working with the rodents of Qatar to find rodent-borne zoonotic pathogens. While trapping, a brown rat was captured on 29 January 2020 from a livestock farm located in the Al Rayan area.

As a routine research process, we anesthetized the rodent with 5% isoflurane and conducted a morphologic examination. We collected its blood through cardiac venipuncture using a 5ml vacutainer EDTA tube and conducted a complete blood count (CBC) (ABX Micros ESV 60, SL#207EVOH04392) and plasma biochemistry (UniCel DxC 600, Backman Coulter, SL#962). Then the rodent was examined for ectoparasites, such as flea, louse, mite, and tick. We euthanized the rodent, necropsied it, examined its visceral organs for gross abnormality, and collected the skull and visceral organs, viz lung, liver, diaphragm, kidney, spleen, and intestine for further study. The rodent feces and blood were used to conduct parasitologic examination by direct microscopy. The intestinal content was subjected to detect Gram-negative gut bacterial isolation and identification (VITEK®2, Version 07.01 compact system, SL#14EFDOFF, using the kit: VITEK® 2 GN Ref#21341). We conducted histopathology of the rodent thyroid, prescapular, and inter-jugular lymph nodes, lung, liver, kidney, and intestine. The blood plasma was examined by ELISA for detection of antibodies against some zoonotic pathogens, such as *Coxiella burnetii* (Ref: FQS-MS-2P, IDvet, France), *Toxoplasma gondii* (Ref: TOXOS-MS-2P, IDvet, France), West Nile virus (Ref: WNC-2P, IDvet, France), *Chlamydophila abortus* (Ref: CHLMS-MS-2P, IDvet, France), *Brucella* spp. (Ref: BRUS-MS-5P, IDvet, France), and *Leishmania* spp. (Ref: IB0510, IBL, Minneapolis). We tested the rodent visceral organs by PCR method to detect DNA of *Coxiella burnetii, Rickettsia* spp., *Leptospira* spp., *Yersinia pestis, Leishmania* spp., and *Toxoplasma gondii*. The rodent visceral organs were also tested to detect RNA of Rift Valley fever virus and Hantavirus by RT-PCR method.

The subject case was an adult male *Rattus norvegicus* weighing 440gm and a total length of 47cm. The rodent had a swelling on the right side of its mouth (Figure 1). As a part of the morphometric study [18], the rodent head was subjected to prepare skull skeleton by hot water treatment [19]. While processing the skull of the rodent, we identified a swelling mass on its right mandible (Figure 2). There was extensive development of the right mandible throughout the body and ramus. The abnormal expansion was more at the lateral posterior side. The three processes of the mandible, such as the coronoid process, condyloid process, and angular process, as well as the alveolar part of the molar teeth, were free from that growth. The length (base of incisor to condyloid process) of the right abnormal mandible became slightly longer than the left healthy mandible (29.43 mm vs. 28.09 mm). The length, width, and height of the mass of the right mandible were 26.92, 21.5, and 19.67 mm, respectively. The right and left lower incisors were 8.56 mm and 11.57 mm, respectively. The left lower incisor was broader than the right lower one. Except for the upper incisors, the cranium did not have any abnormality. The right and left upper incisors were 12.9 mm and 11.56 mm long, respectively. Both the upper and lower incisors were blunt, not sharp as typical rodent incisors.

Figure 1: The ventral and right lateral view of the rodent. The rodent had swelling on the right side of its head.

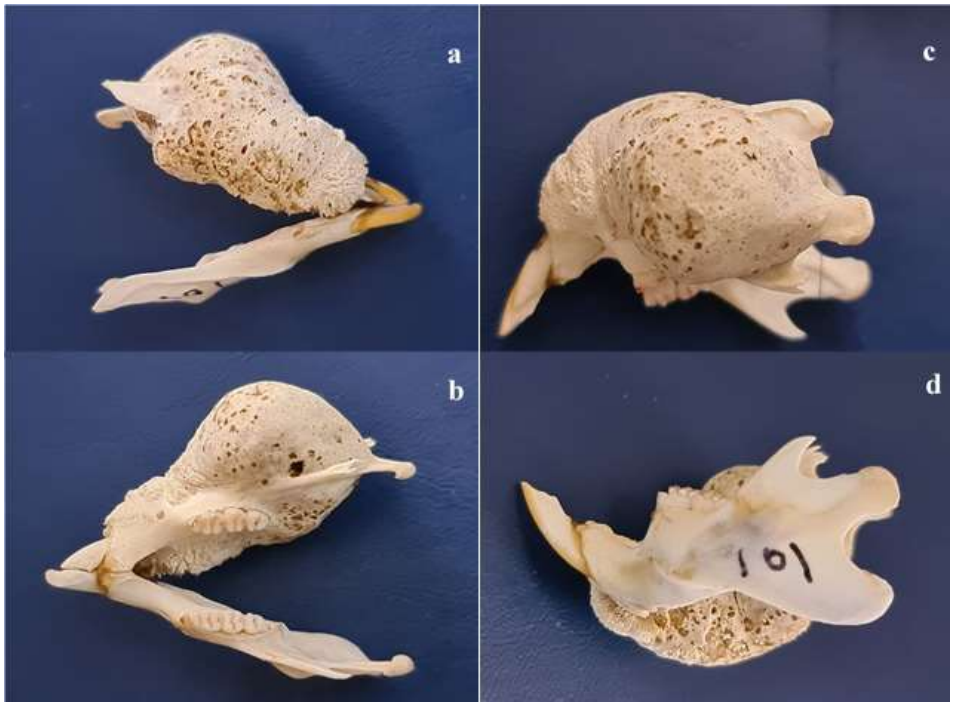

Figure 2: The four-sided (ventral [a], dorsal [b], right lateral [c], and left lateral [d]) view of the mandible suffering from ameloblastoma. There was soap-foamy development at the right mandible.

The detailed result of CBC and plasma biochemistry have been presented in Table 1. There was lymphocytosis, more appropriately neutrophilia. The blood film examination showed that there were reticulocytes (5%) and anisocytosis (>90%). We confirmed that the rodent had regenerative macrocytic normochromic anemia. There were hypoproteinemia, hypoglycemia, and abnormality on some of the enzymes and metabolites.

Table 1 The complete blood count and plasma chemistry of the case

Parameters	Results	Reference range	Parameters	Results	Reference range
Hematology					
White blood cell, WBC ($\times 10^3$/µl)	22.3	7.3-12.7	Red blood cell, RBC (10^6/µl)	5.795	6.6-9.0
Lymphocyte (%)	33.6	13-15	Hemoglobin, Hbg (g/dl)	12.6	13.2-16.4
Monocyte (%)	3.9	3-5	Hematocrit, Hct (%)	39	41.1-51.1
Neutrophil (%)	62.5	79-81	Mean corpuscular volume, MCV (μm^3)	72.15	52.6-65.4
Eosinophil (%)	4.2	1-2	Mean corpuscular hemoglobin, MCH (pg)	23.25	16.5-21.3
Lymphocyte (10^3/µl)	7.5	5.1-9.1	mean corpuscular hemoglobin concentration, MCHC (g/dl)	32.31	30.2-34.6
Monocyte (10^3/µl)	0.8	0.1-0.4	Red cell distribution width, RDW (%)	20.6	28.0-38.2
Neutrophil (10^3/µl)	14.1	1.3-3.7	Platelet, Plt ($\times 10^3$/µl)	1.03	0.8-1.2
Basophil (10^3/µl)	0	0-0.1	Mean platelet volume, MPV (µm)	7.7	5.7-9.0
Eosinophil (10^3/µl)	0.94	0.1-0.3	Reticulocyte, RT (%)	5	0-4.6
Plasma biochemistry					
Albumin, Alb (g/dL)	2	4.1-5.4	High density lipoprotein, HDL (mg/dL)	11.3	19.1-57.1
Alanine aminotransferase, ALT (IU/L)	16	26-37	Iran, Fe (mg/dL)	2.5	7.2-7.7
Aspartate Aminotransferase, AST (IU/L)	414	40-53	Gamma-Glutamyl Transferase, GGT (IU/L)	4	2.5-3.9
Cholesterol, Chol (mg/dL)	27	36-100	Lactate dehydrogenase, LDH (IU/L)	2650	63-573
Creatinine, Cr (mg/dL)	0.94	0.5-1.5	Phosphorus, P	10.5	5.3-7.5
Creatinine kinase, CK (IU/L)	3339	6-309	Total bilirubin, TB (mg/dL)	0.3	0.1-0.6
Glucose, Glu (mg/dL)	2	114-143	Urea, U (mg/dL)	59.5	54.1-71.7
References: [20-25]					

At necropsy, we found two cysts of *Cesticercus fascioliaris* (the cystic form of *Taenia taeniaeformis*) on the liver. There were no visible pathological lesions on the other visceral organs. We found eggs of *Hemenolepis diminuta* in feces. We also isolated *Escherichia coli* and *Salmonella enterica* ssp. *diarizonae* from the intestine. The histopathology showed normal histology of the organs except for hemosiderin pigments in the prescapular lymph node and mild congestion in the liver. Furthermore, the rodent was negative for the antibodies against *Coxiella burnetii*, *Chlamydophila abortus, Brucella* spp., *Toxoplasma gondi, Leishmania* spp., and *West Nile Virus.* The PCR method did not identify the DNA of *Coxiella burnetii*, *Rickettsia* spp., *Leptospira* spp., *Yersinia pestis, Leishmania* spp., and *Toxoplasma gondii* by PCR method. The rat also was negative for RNA of Rift Valley fever virus and hantavirus by RT-PCR. Finally, we diagnosed the mandibular mass as ameloblastoma.

Discussion

We conducted a systematic search on PubMed, Scopus, Science Direct, and Web of Science to check reports on rodent ameloblastoma. The search detected three articles [14, 15, 26] that reported ameloblastoma in three laboratory rodents (one Sprague-Dawley rat, one Fischer rat, and one female Wistar rat), one domestic brown rat (*Rattus norvegicus*), one Syrian hamster (*Mesocricetus auratus*) from a hamster breeding farm, and one client owned Amargosa vole (*Microtus californicus*). As per our knowledge, the current report is the first report of ameloblastoma among wild rodents. We favor the

current diagnosis as ameloblastoma, a benign bone tumor of the mandible. There are reports of malignant ameloblastoma in humans, which usually metastases to the lung, although, it is rare [27, 28]. The CBC, plasma biochemistry, and histopathologic figure of different organs did not show any indication to consider the case as a malignant tumor.

Rodent enamel grows throughout its life. The upper and lower teeth grind down on one another, which helps the rodent to maintain a regular teeth length. The lower incisors are generally longer than the upper ones [29]. The asymmetric size of two mandibles and the giant ameloblastoma caused loss of occlusion and the inability of the incisors to grind each other. As a result, the incisors increased in length and lost their sharpness. Therefore, upper incisors became longer than the lower ones. The tumor may be behind the reduction of growth of the right lower incisor; as a result, it was shorter and narrower than the left lower one.

There is a relation between ameloblastoma with anemia and decreased albumin. In extensive ameloblastoma, protein (mainly albumin) leaks to the oral cavity through the tumor mass [30]. Giant ameloblastoma, asymmetric mandibles, loss of occlusion, and blunt incisors can result in malnutrition [5], thereby producing anemia. Moreover, the rodent was coinfected with *T. taeniaeformis* and *H. diminuta*. There is no previous report of *C. fasciolaris* in rodents of Qatar, but the parasitic form of the cestode *T. taeniaeformis* is common among stray cats in the country [31]. *C. fasciolaris* causes damages to hepatic cells near the parasitic cyst [32], which may result in hepatic congestion. *T. taeniaeformis* infected rodent shows reduced ALT and Urea and increased GGT [25]. Similarly, our current case had low ALT and urea, along with high (upper level) GGT. Rodents infected with *H. diminuta* can have a liver function and hematological disorder. Anemia, leucocytosis, eosinophilia, and neutrophilia has also been described with cysticercosis and hymenolopeasis [33-35]. Ameloblastoma is associated with extensive tissue destruction and deformity [16]. It may be the cause of the higher CK of the rodent [20]. LDH can be increased if an animal has bony or muscular disorder [20]. The animal was hypoglycemic and maybe diabetic too. Diabetes can lead to hypoglycemia as well as a lowering of HDL [36].

Conclusion and way forward

Ameloblastoma is a rare tumor for both human & veterinary species. Its detail is that veterinary practice is not well known yet due to rarity & lack of economic interest. We described this incidentally found case in the rat at skull processing. Antemortem analysis of this condition in veterinary species is required for further evaluation & management planning.

The sample was not subject to routine histological examination because the tumorous mandible was incidentally identified, and the mandibular skeleton was already prepared. ‘Dry bone histology’ by epoxy embedding method is a suggested technique of dry bone histology. This method of dry bone histology is rarely used in routine histology laboratories [37, 38]. The Fgfr2 gene can be behind this type of bony development. We got the primer to detect the gene Fgfr2: F: 5'-CACGACCAAGAAGCCAGACT-3', R: 5'-CTCGGCCGAAACTGTTACCT-3' and extracted DNA from the tumorous mandible to identify the mutant gene [39]. It is noteworthy that this incidental finding was not a part of the thesis objectives. Nonetheless, we are adopting the dry bone histology and PCR methods to confirm the mandibular tumor diagnosis for scientific interest.

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Chapter 6: Synthesis and Conclusion

Rodents act as vectors of several zoonotic pathogens, although there is a knowledge gap on such zoonoses in many countries of the Middle East, including Qatar (Chapter 2.1 and Chapter 2.2) [1,2]. The current study is the first in-depth study on commensal rodents and rodent-borne pathogens in Qatar. Our study listed 88 rodent-borne zoonotic diseases, which pathogens can be transmitted by rodents to humans globally (Chapter 2.3). Recent histories of zoonotic spillover of pathogens from animals to humans suggest that zoonoses through rodents is not a neglected issue. The rodent can be a source of future epidemics in Qatar, as the region has several histories of rodent-borne zoonotic disease epidemics [3-7], and Qatar has interconnections with several countries, which are endemic with rodent-borne zoonotic diseases, from which pathogens can be imported. Therefore, intervention on rodent-borne zoonoses needs to be emphasized. liaison

Rodents as a source of zoonotic pathogens

Our review identified 85 species of rodents in the Middle Eastern region, of which three commensal species (*Mus musculus, Rattus norvegicus, and Rattus rattus*) are widely distributed in this region (Chapter 2.1 and Chapter 2.2) [1,2], including Qatar [8-11]. The current study (Chapter 3) is the first to describe the rodent morphometric pattern of these three commensal rodents in Qatar and the Arabian Peninsula [12]. We found that these rodents are relatively smaller than the same species in Iran, Turkey, and Tunisia, which supports Bergmann's rule of ecology that animals of the colder environment are bigger in body size than the same animals of warmer environments (Chapter 3) [12]. It had been recorded that the average annual temperature of Qatar, Iran, Tunisia, and Turkey is 28.02°C, 17.99°C, 20.38°C, and 11.69°C, respectively [13]. *R. norvegicus* was found to be most prevalent, followed by *R. rattus* and *M. musculus* in Qatar. These commensal rodents have public health significance as they carry several pathogens that can transmit to humans and other animals through contact with rodent stool, urine, and skin/fur and through ectoparasites and other animals.

The systematic review [1] (Chapter 2.1) identified at least 104 species of fleas, followed by 134, 27, and 28 species of mites, ticks, and lice, respectively prevailing on rodents in the Middle East. *Xenopsylla astia* and *Xenopsylla cheopis* are two widely distributed rodent ectoparasites, which also have been reported previously in Qatar [10,14]. The most common rodent ectoparasite found in the present study was *X. astia* (Chapter 4.1), a finding supported by previous studies in Qatar [9,10]. Interestingly, *Ornithonyssus bacoti* was identified for the first time in Qatar in this study (Chapter 4.1) [12], which was previously reported in rodents of Egypt, Iran, Kuwait, Saudi Arabia, and Turkey [1]. In addition, a review (Chapter 2.2) was aimed to provide a baseline data on rodent-borne helminths to recognize the threats to public health in Qatar and in the region [15]. *Hymenolepis diminuta* was the most prevalent helminth (Chapter 4.1), and this is in accordance with the previous studies [9,10], where *H. diminuta* is highly prevalent in rodents and positively correlated with the prevalence of *Xenopsylla astia*. *Cysticercus fasciolaris* is the intermediate form of *Taenia taeniaeformis*, where cat is the primary host and a rat is an intermediate host. Our study found that 23% of *R. norvegicus* are carrying cysticerci of *T. taeniaeformis* in their liver. Presence of both intermediate and mature forms of this cestode [16] suggests that *T. taeniaeformis* is prevalent at the cat-rodent interface in Qatar. In addition, (Chapter 2.3) there are previous reports of *Echinococcus granulosus*, *Hymenolepis nana*, *Trichuris trichiura*, *Schistosoma mansoni*, non-specific *Taenia* reported in humans [17-19], and non-specific *Taenia* and *Toxascaris leonine* in cats [20] in this country. Three species of *Giardia* have been reported in rodents in the Middle Eastern countries; *Giardia lamblia*, *Giardia muris*, and *Giardia microti* [21-23], of which, only *G. lamblia* has zoonotic importance [24-26]. *G. lamblia* was found in rodents of Egypt [21] and Palestine [22], where *G. muris* was reported from rodents of Iran [23]. There are human and ruminant reports of Giardiasis in Qatar [27-30]. *Toxoplasma gondii* has importance for human and livestock abortion and is highly prevalent in humans and cats. Presence of antibodies (Chapter 4.1) of *T. gondii* in Qatari rodents indicates that this protozoon is disseminated at the Qatari ecosystem. Additionally, *Leishmania* spp. has also been reported in dogs and cats [31], and in fleas in the current study, which emphasize that this pathogen should not be neglected in Qatar, like in the other tropical countries [32,33]. Rodents could mediate in transmission of these pathogens at the human-animal-environment interface, which increases the public health risk of getting an infection by such pathogens in this country.

In the current study (Chapter 4.2), several bacterial spp. viz. *Acinetobacter baumannii, Aeromonas salmonicida, Citrobacter freundii, Citrobacter koseri, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Salmonella enterica, Hafnia alvei, Klebsiella pneumoniae, Proteus mirabilis, Providencia stuartii,* and *Pseudomonas aeruginosa* were detected in rodent intestines. These pathogens are commensal in mammalian intestines and in the environment and cause opportunistic infections in humans and other animals. Most of them were identified in our study for the first time among rodents in Qatar. Some of these bacteria are multi-drug-resistant (Chapter 4.2). Likewise, this study also detected *Rickettsia* spp. in rodent fleas and mites, which could be a public health risk in Qatar. Our review (Chapter 2.3) showed campylobacteriosis, corynobacteriosis/non-diphtheritic corynebacterium, listeriosis, Q-fever, and non-plague yersiniosis in humans. As rodents have access from kitchen to sewage and agricultural facility to human residence, rodents can mediate transmission of these disease pathogens at the human-animal-environment interface in Qatar (chapter 2.3) [15].

Based on life history and ecological factors, rodents are listed as top zoonotic virus carriers. In general, a total of 61 species of zoonotic viruses were identified in bats, where it was 68 species of viruses in case of rodents [34]. Several rodent-borne viral diseases (Chapter 2.3), such as chikungunya, hepatitis E, and rabies have been reported among humans and animals in Qatar [35-37]. Hantavirus-specific antibodies were reported in both rodents and humans in Kuwait [38]. Crimean-Congo hemorrhagic fever was detected in Oman [39], and West Nile fever was detected in Saudi Arabia and Yemen [40,41]. In this study (Chapter 4.3), Rift valley fever and hantavirus were not detected in rodent samples. However, a further large cohort study is required to investigate the rodent-borne viruses in Qatar.

Risk factors for rodent-borne zoonoses

Rodent abundance is an important factor for related pathogen availability [9,42-44]. The rodent population is variable in urban and semi-arid regions [45], and in the current study (Chapter 3), we found that the commensal rodents are mostly distributed in the livestock farms, followed by agricultural farms, residential areas, industrial areas, and commercial areas in Qatar. The current study showed that certain rodent-borne pathogens, such as *Giardia* spp., *H. diminuta*, and *X. astia* prevalence varied with rodent host, age, and trapping location. Hitherto, several studies have been performed to understand the rodent factors in relation to rodent-borne pathogens. Some studies reported that the prevalence of pathogens is dependent on rodent host (species, age, sex, body size), season, and location of trapping, whereas some others showed that such factors are not necessarily important [9,46-59]. Therefore, the prevalence of rodent-borne pathogen is a complex phenomenon and consequence of a combination of many factors together, mainly rodent population, availability of reservoir, vectors and intermediate, facilities in the trapping location (cleanliness, use of rodenticide, insecticide, and management), and changes of climate (temperature, humidity, and rainfall).

Possible drivers of rodent-borne zoonoses in Qatar

There have been massive changes over the past 70 years in Qatar, such as economics, population, landscape, agriculture, and urbanization. Based on these changes, some drivers could be considered as mediators in rodent population and rodent-borne disease emergence in Qatar: (1) Oil and gas revolution, (2) rapid increase of multicultural population, (3) rapid urbanization, (4) importation of food and agricultural products, (5) agricultural and livestock development, (6) farm biosecurity, and (7) stray animals. In the past, Qatar was a country of the Bedouin whose main business was fishing, pearl harvesting, and livestock farming. After the oil revolution in the 1950s, economic development and globalization [60-62] has attracted high numbers of skilled and semi-skilled workers [61,63]. This migration played an important role in determining population change and the dynamics of the socio-economic environment. In 1960s, the Qatar population was 47000, which was increased 12 folds in 21st century [64], and around 2.8 million in 2020 [65]. Over the period, the majority of urban infrastructural projects, such as residential facilities, markets, hospitals, and roads, were accomplished. The urban growth was increased at least 4 times between 1987 and 2013 [66]. The spatial range was also changed considerably for the development of highways, residents, coastline, and airport [66,67]. Therefore, the rodent ecosystem in the deserts could be damaged, and rodents could migrate toward the cities. Generally, rodents prefer to live in the cities as they get more food and less predation pressure [68]. The country imports food and agricultural products from different countries. The annual cost of food import

has been raised from around $100 million in 2000 to $1000 million in 2018 [71]. Some major partner countries for importation of manpower, live animals and food products are India, Bangladesh, Nepal, Srilanka, Pakistan, Philippines, Egypt, Turkey, and Sudan [71,72], which are endemic with many rodent-related diseases, such as rabies, typhoid fever, chikungunya, leishmaniasis, and Rift Valley fever [73-77]. Several studies reported that the newly immigrant workers are more prevalent with gastrointestinal parasites than the old residents and citizens in Qatar, such as *Giardia lamblia* and *Cryptosporidium* spp. [17,18,28], which can be transmitted by rodents [3]. There is a chance of importing rodent-borne pathogens by immigrant residents, live animal trade, and imported food and agricultural products to Qatar [14]. Being a decertified country, Qatar had minimal agricultural activities in the past [69,70], which trend has been changed in the recent years by increasing the effort to agricultural practices. The amount of vegetated area and arable land increased from 5.3% to 5.8% and 6.8% to 7.2%, respectively [71]. Rodent-borne pathogens can spread throughout the country by contaminated agricultural products. The number of livestock and livestock farms have also been increased by 3 times in the last 10 years [78]. In Qatar, livestock farms are mostly managed traditionally with insufficient biosecurity measures. These farms are generally keeping mixed livestock in the same housing facility. The majority of farmworkers are from Bangladesh, India, Nepal, and Sudan and live in the farm compound. The owners keep their resting place (majlis) inside the farms, where they spent their evening and holiday times. Our study demonstrates that livestock and agricultural farms are more prevalent with rodents than other areas [12]. Due to the close contact between human workers, owners, and multispecies animals with poor biosecurity management in the Qatari livestock farms, there is chance to cross the species barrier by the zoonotic pathogens at human and animal interface, which was observed in a MERS-CoV case. The owner, worker, and camels of a farm were found positive for MERS-CoV [60]. Although there is no documented report of stray dogs and cats in Qatar, according to the newspaper reports [79-81], there has been a rise in the population of stray animals, which can influence the transmission cycle of the rodent-borne pathogens [15].

Possible rodent control programs

Rodent control is considered to be a significant tool to prevent rodent-borne disturbances. The current study (Chapter 4.1 and Chapter 4.2) revealed that over 50% of the commensal rodents carry at least one pathogen of public health importance, highlighting the necessity of rodent control. Several steps, such as control of rodent population, rodent access, and rodent contact could be valuable for controlling rodents. In general, 90% of rodent populations are not pests. Therefore, it is not recommended to kill large populations of these animals. Infectious agents can remain even if 75% of the total population is controlled. Rodent-borne diseases can disappear after few years of continuous rodent control programs but can reemerge if the control program is either stopped or the population increases. Even after the entire rodent population has been eliminated, pathogens can still increase with new/adaptive ecological and evolutionary dynamics. A pathogen may establish a different transmission pathway, e.g., find different vector instead of rodents [68]. In some cases, the rodents are harmful, and in other cases, rodent-ectoparasites are more dangerous [68]. Moreover, the rodent is a part of an ecosystem [82]. Therefore, it is essential to find an eco-friendly and balanced way of managing rodent control in Qatar.

In Qatar, governmental and corporate services are managing pest control, including rodents. The service beneficiaries are mostly corporate offices, industries, residential areas, major public parks, and other public places. However, limited interventions are applied in livestock and agricultural farms, which may be one of the causes of high rodent and rodent-borne pathogen abundance in such areas. Due to the absence of clear rodent control guidelines, pest control service providers work on their own strategies. It is essential to develop a national guideline for rodent control. Additionally, ecological surveillance is needed to understand the rodent population demography, habitual distribution, and associated factors for rodent abundance and overload. An epidemiological study on rodent-borne pathogens is important to understand the rodents and other animals as vectors, pathogen prevalence at different host levels, and pathogen transmission dynamics. It might be helpful to prioritize rodent-borne pathogens, their transmission pathways, which may not necessarily need the understanding of the whole ecology but only the common drivers and understanding the common risks based on the context that will alleviate the control program.

Rodent control should be organized considering four major keywords: humanity, effectiveness, biosafety, and cost-efficiency. For this, it is essential to raise the activity of governmental authority, engage the lobbyists, and educate the citizens and residents to develop collective consciousness about rodents. Although animal ethics are intensely practiced for experimental cases, less attention is given when they are pests. Human social behavior and perception are a challenge in controlling rodents. People usually prefer to have a magic box to kill all the rodents, hence they like to use acute poison. Rodent control and prevention are a public-private joint work. As the inhabitant of the world, these animals deserve a moral value. A humane way should be favored in treating them. Integrated Pest Management (IPM) is an environmentally friendly and common-sense approach pest controlling program, which is considered as the best rodent control approach [83]. IPM should be implemented as a quality procedure of biosafety and management in the hospitals, residential complexes, business centers, airports, and seaports in Qatar. Categorizing control strategies, such as short-medium-long term rodent control in different facilities, can be applied. A short-term solution addresses the immediate rodent problem, whereas a long-term plan focuses on understanding rodent ecology and risk factors. In the residential, corporate, and industrial areas, short-term or emergency rodent control is applicable. Higher emphasis should be given to the livestock and agricultural areas. The development of biosecurity in the farming systems is a prime requirement in rodent and zoonoses control. Modifying the rodent habitat, such as hiding and nesting places, blocking rodent entrances, and reducing food and water access lead to significant prevention of rodent abundance. Trap barrier system/fencing is a well-known non-toxic rodent control method, where they can enter but is unable to exit, so it is easy to catch and eliminate. Such techniques can be applied in the Qatari livestock and agricultural farms. Poisoning, fumigation, chemo sterilant, glue-board, and trapping are also accepted methods of rodent control. Before selecting any of such methods, there is a need to evaluate the number of targets to kill, degree of pain, distress, or discomfort to the rodent; time length to kill the animal; effects on the rest of the population; and chances of secondary poisoning (e.g., children, livestock, and environment) [84].

One-Health movement

The One Health approach advocates for a holistic approach to tackling diseases at the human-animal-environment interface. The rodent-borne zoonoses are the classic example of where the One Health movement can play a key role. We propose a possible One Health framework for rodent-borne pathogen surveillance and control to combat future epidemics in Qatar (Table 1).

Working with wild or commensal rodents needs time, money, dedication, facilities, and expert involvement. Multidisciplinary involvement is needed to quantify the impacts of rodents, rodent control, and control of rodent-borne hazards. In rodent-borne pathogen surveillance, a single/specific pathogen surveillance is not practical. The individual sectoral movement will cause time and cost consumption, whereas joint-team work can enhance sharing of knowledge and views of one sector with the others, and increase the efficiency of each sectoral work. Therefore, the One Health movement is essential in the prevention and control of rodent and rodent-borne zoonoses. One Health approach in rodent control gives a complex connection between different sectors and levels (local, regional, national, and global), who need to join together and assess relationships between humans, animals, plants, shared environment, climate, economics, and society. Multisectoral engagement is needed, including stakeholders, such as rodentology, entomology, acarology, microbiology, parasitology, ecology, policy makers, lobby groups, and media; considering the local socio-economic, cultural and spiritual facets; capacity building for research, data collection, and control of rodent-borne disease outbreak; access of up-to-date technologies for pathogen surveillance and characterization; risk mapping, stratification, GIS, big data, and prediction model preparation; translating research findings to rodent control; and unified decision making. Such One Health team showed success in working together for emerging disease research, such as outbreak investigation, surveillance, early detection of pathogens in many countries [85,86], including Qatar [87]. The “National Outbreak Control Task Force” of Qatar can be strengthened by capacity-building, formulating supportive legislation, allocating budget, and engaging relevant international and national organizations and personals.

Table 1: Possible One Health framework for rodent-borne pathogen surveillance and control to combat future epidemics in Qatar

Risk assessment	One Health surveillance and pathogen control program		
Risks	**Goals**	**Surveillance**	**Intervention**
Rodents: • Four species of rodents. Three are commensal (*Mus musculus, Rattus norvegicus,* and *Rattus rattus*) and one is wild (*Jaculus jaculus*) species • *R. norvegicus* is the dominant species • Commensal rodents are highly prevalent in the livestock and agricultural farms • Over 50% of the commensal rodents carry zoonotic pathogens **Other animals:** • Livestock farms keep multispecies animals at a close proximity • Animals in the livestock farms are reared in a traditional way with inappropriate biosecurity management • There are many stray dogs and cats **Humans:** • Risk of transboundary rodent-borne zoonoses entry with live animal trade, food, and agricultural products from the partner countries **Environment:** • Vectors, such as *Xenopsylla cheopis, X. astia,* and *Ornithonyssus bacoti* are available **Pathogens:** • 45 rodent-borne zoonotic pathogens (18 parasites, 24 bacteria, and 3 virus) are available at the human-animal-environment interface • Epidemiology and transmission dynamics of the rodent-borne zoonoses are unknown **Health system:** • No national guideline for rodent and rodent-borne pathogen control • No national guideline for livestock and agricultural farm biosecurity practices	**Prevent:** • Reduce rodent-overload • Prevent rodent infestation in the farms, residential, commercial, and industrial areas • Combat rodent-borne zoonoses **Detect:** • Early detection of rodent-borne pathogen epidemics • Rodent population demography, habitat, abundance, and overload • Biology and epidemiology of the rodent-borne pathogens at the human-animal-environment interface • Risk factors of rodent and rodent-borne zoonoses, and risk mapping **Respond:** • Outbreak investigation and surveillance for rodent-borne zoonoses • Early preparedness of any outbreak or epidemic • Rodent-borne zoonoses management	**One Health team:** • Multisectoral involvement with medical, veterinary, and environmental specialists. • The specific stakeholders include rodentology, ecology, entomology, acarology, microbiology, parasitology, molecular biology, and epidemiology • The associated stakeholders are community members, lobby groups, media, and policy makers • Relevant national, regional and international organizations and personals **Local capacity building:** • Capacity building for surveillance and monitoring • Strengthen research collaboration • Disease modeling and translating research findings to field application **Support of One Health movement:** • Activate the "National Outbreak Control Task Force" of Qatar or strengthen it. • Approve supportive legislation, timeline, and budget	• Integrated Pest Management policy development to control rodent and rodent-borne vectors • Biosecurity policy development and implementation • Border control • Vaccination • Development of awareness • Rapid response • Consider the local socio-economic, cultural and spiritual facets in One health policy making

Conclusion and recommendation

In general, 5-10% of the rodents are pests or carriers of zoonotic pathogens. The current study reported that over 50% of the rodents in Qatar carry at least one pathogen, including ectoparasites, helminths, protozoa, and bacteria, which indicates that the commensal rodents of this country are indicators of the presence and dispersal of zoonotic pathogens. In our initial study, we reviewed the available data in the history and found the diversity of ectoparasites and helminths in the Middle East. Moreover, we estimated the pooled prevalence of rodent-borne parasites in the region. In addition, we reviewed available historical data of rodent-borne zoonotic pathogens in Qatar, estimated the pooled prevalence of the pathogens, and identified the major risk factors and diversity. In our study, livestock and agricultural farms are the hotspots for rodent abundance. We found different rodent-borne zoonotic pathogens, which have the potential to transmit to humans and other animals. Inappropriate farm

biosecurity may be behind the rodent abundance and rodent-borne pathogens in these facilities. Urgent action is needed to prevent future spillover of these pathogens at the human-animal-environment interface. A policy needs to be prepared for rodent, and rodent-borne zoonoses control in this country, which should go through three principles: (1) surveillance, monitoring, evaluation, and analysis; (2) set action thresholds; (3) prevention and control. It is essential to develop a surveillance system to explore rodent biology, including demography and population overload, and epidemiology of the rodent-borne zoonoses. Capacity development for pathogen detection by both medical and veterinary sectors, vaccination to both humans and animals (including rodent vaccination) are suggested. A multifactorial and multisectoral rodent and rodent-borne disease control program should be built on IMP models, in which local structure, environment-ecosystem between humans and rodents, socio-economic balance, and cost-benefit will be respected. Based on our study, we recommend the relevant authority and policymakers in Qatar to implement an appropriate intervention program. A roadmap identifying priorities for research and development, capacity building in rodent control programs should be developed. Furthermore, implementing the One Health approach to combat rodent-borne zoonoses and reduce the risk of the future epidemic with rodent-borne pathogens in Qatar is strongly recommended.

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Supplementary Materials

Detail of the supplementary materials	Online sources
Chapter 2.1 Figure S1: Funnel plots of overall rodent ectoparasite prevalence and subgroup analysis Table S1: Prisma 2009 checklist Table S2: Quality assessment of the 113 studied articles Table S3: Extracted data from the selected 113 studies Table S4: Rodents, fleas, lice, mites, and ticks on prevailing rodents in the Middle East	https://www.mdpi.com/2076-0817/10/2/139/s1
Chapter 2.2 Table S1: Prisma checklist Table S2: Extracted data from the selected 65 studies Table S3: Prevailing rodents and common cestodes, nematodes, and trematodes in the Middle East	http://www.mdpi.com/2076-2615/10/12/2342/s1
Chapter 2.3 Table S1: Prima checklist Table S2: List of the rodent-borne zoonotic diseases; mini-review Table S3: Extracted data from the selected 94 studies.	https://www.mdpi.com/article/10.3390/ijerph18115928/s1