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REVIEW ARTICLE

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Prevalence of influenza A infection in the Middle-East: A systematic review and meta-analysis

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Abstract

Objective: This systematic review and meta-analysis was performed to determine the prevalence rate of influenza virus from different parts of Middle East region, and present an overall relative frequency (RF) for this region.

Methods: The authors performed a systematic literature review from several reliable databases such as PubMed, ISI Web of Science and Scopus during 2000–2016. Furthermore, the keywords of this research were 'Influenza', 'Subtype', 'Seroprevalence', 'Incidence', 'Seroepidemiology', 'H1N1', 'H3N2', 'H5N1', 'H9N2', 'Middle-East' and 'Meta-analysis'. The reported data were selected according to inclusion and exclusion criteria.

Results: The authors selected 71 studies out of 1147 for the present review. The overall estimation of the prevalence of influenza virus was 10.2% [95% confidence interval (CI): 10.1%–10.3%]. However, based on our records, the evident heterogeneity of influenza virus was observed among the studies (Cochran Q test, P value $<.001$ and I-squared = 100%). It should be noted that influenza virus infection's RF varied from 0.5% in Qatar to 70% in Syria.

Conclusions: The results of this review are remarkable, they show that influenza infection RF is variable due to several factors. Thus, further researches should be taken to minimize the emergence and transmission of influenza virus.

KEYWORDS
influenza, Middle-East, meta-analysis, subtype

1 | INTRODUCTION AND OBJECTIVES

Respiratory tract infections are one of the most common acute illness which can be classified into two main types including upper and lower respiratory tract infection (URI, LRI), which caused by bacteria, viruses and mycobacteria.[1] Influenza virus is a major cause of acute respiratory disease in human and many animal species; so that approximately 20% of the world's population annually are infected by influenza, resulting in a significant growth in morbidity and mortality.[2] Influenza, a member of the *Orthomyxoviridae* family, is characterized by segmented negative-sense RNA genomes. Influenza is subdivided into three types (A, B and C) based on antigenic differences in the virion core proteins. In addition, as far as surface glycoprotein is concerned, the virus is classified in six genera.[3,4] Generally, influenza A viruses infect both humans and such animals as ducks, chickens, pigs, whales, horses, seals and cats; while, influenza B viruses circulate primarily in humans.[5] Based on hemagglutinin (HA) amino acid differences, influenza A is divided into 16 different HA subtypes (H1-H16), and also nine different NA subtypes (N1-N9).[6,7] The main subtypes of influenza based on pathogenesis and epidemiology aspects include H1N1, H5N1, H3N2, H7N7 and H9N2.[8] The most symptoms of influenza infection can be mild to severe include fever, sore throat, nasal discharge, myalgia, headache and cough.[9,10] Influenza has an epidemic outbreak (every 1–3 years) during the past 400 years.[11] This virus is spread from person to person mainly with respiratory droplets when infected person coughs or sneezes.[12] The documents show that at least one pandemic influenza has occurred during the century. Figure 1 presents the World Health Organization's (WHO) report about the status of the infection. It is worth noting that the epidemiologic pattern clearly shows that multiple factors are involved in the changing of nature of the antigenic properties of influenza viruses, and their spread accordingly. For example, influenza A viruses, have a considerable ability to undergo periodic changes in the antigenic characteristics of their envelope glycoproteins, the hemagglutinin and the neuraminidase over other types.[13]

Seasonal pattern of influenza is different based on temperate zones: June-September in the Southern Hemisphere, and December-April in the Northern Hemisphere. Moreover, this pattern in tropical regions has seasonal variations and mostly related to the rainy season.[14]

Although several studies have been performed on the prevalence of influenza in Middle-East countries, there is no overall estimation of the infection in such regions. With this in mind, the present study aimed to systematically review the published data about the prevalence rate of influenza from different parts of Middle-East countries, and also the epidemiological characteristics of influenza in this region by using Meta-analysis.

2 | DATA SOURCE AND STUDY SELECTION

2.1 | Search strategy

We selected several reliable databases including PubMed, ISI Web of Science, and Scopus (up to December 2016) by using the following keywords: 'Influenza', 'Subtype', 'Seroprevalence', 'Incidence', 'Seroepidemiology', 'H1N1', 'H3N2',

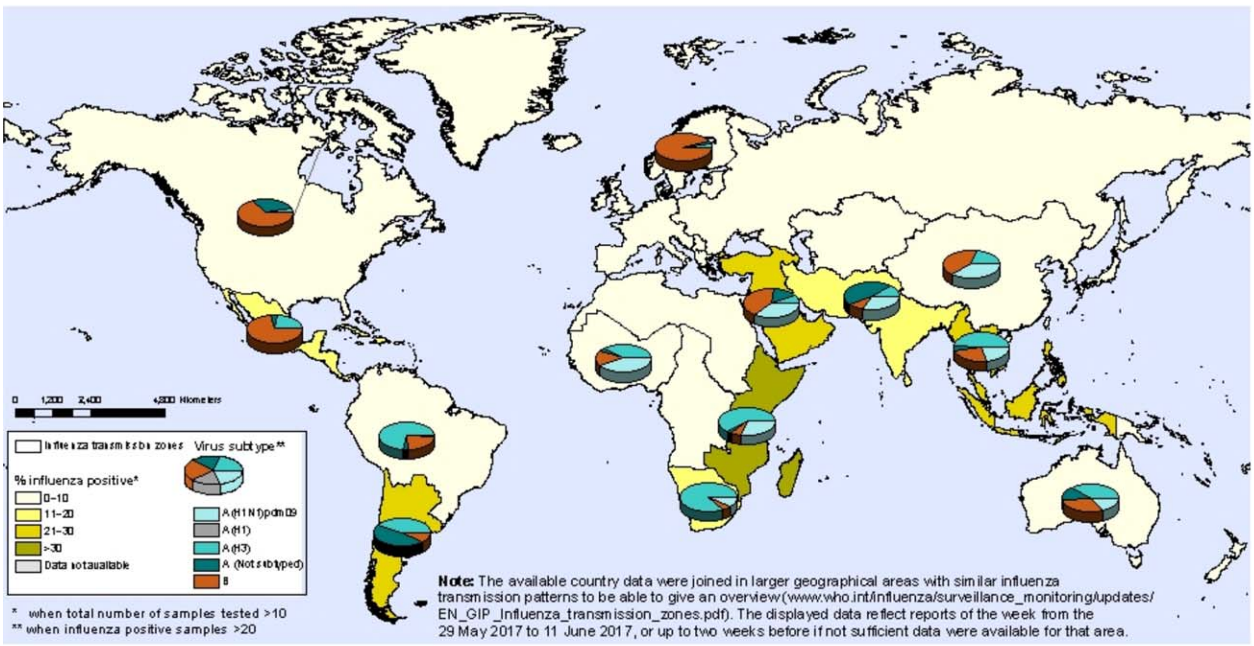

FIGURE 1 Percentage of influenza positive test based on the region in WHO report, 2016[9]

'H5N1', 'H9N2', 'Middle-East' and 'Meta-analysis'. In addition to English sources, the relevant articles in two Persian scientific search engines including 'The Iranian Scientific Information Database' (www.sid.ir), and 'Barakat Knowledge Network System' (www.barakatkns.com) were scrupulously searched. Furthermore, the search by mentioned keywords was restricted to the original articles, titles, abstract, keywords, published abstracts in English and Persian which reported the prevalence of influenza virus by Hemagglutination Inhibition (HI), and methods based on PCR such as RT-PCR and Multiplex RT-PCR in the Middle East.

2.2 | Inclusion criteria

The selected references (English and Persian) in this meta-analysis and systematic review should meet the following criteria:

- Published between 2000 and 2016.
- All studies included samples from blood, nasal swab, throat swab, bronchial wash, sputum and nasal or endotracheal aspirate from patients in the Middle East.
- The reported data is a relation to a group of individuals taken from the general population.
- Studies that used HI, ELISA, Microneutralization, Culture, Immunochromatographic assay, Immunofluorescent assay and PCR based methods.

2.3 | Exclusion criteria

The sources with the following criteria were removed:

- Studies published before 2000 and samples were taken from patients outside of the Middle East with other diagnostic methods.
- Congress abstracts, case report articles, review articles, studies reported in languages other than English or Persian.
- Meta-analysis or systematic reviews and duplicate publication of the same study (or published both in English and Persian) with the exception of duplicate studied in which most sample sizes and more detailed results were provided.

2.4 | Data collection

A complete information list was extracted from the documents, including the author's name, publication date, sample size, type of outbreak, type of subjects, study setting, the RF of influenza and research location. Such details were reviewed and confirmed by three researchers independently. Furthermore, for unclear data, the other authors were consulted and achieved consensus before recording an entry in the dataset. Cohen's kappa as the agreement coefficient between the researchers was acceptable and was equal to 0.81.

2.5 | Assessment of quality studies

Firstly, a checklist and a diagram of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) are prepared, then the critical appraisal was applied with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) form. Items related to study type, sample sizes, research objectives, population, inclusion/exclusion criteria for primary research, a method of analysis and appropriate presentation of results were determined; then, a score was assigned to each item. Each question is assigned by one score. Finally, the studies achieved at least eight quality scores were considered eligible for final Meta-analysis.

2.6 | Statistical methods

In this study, the number of total participants suffering influenza was used to estimate the RF. For the meta-analysis, RF was converted to log RF and its Standard Error (SE). Additionally, we use the Freeman-Tukey Double arcsine transformation of relative frequencies to calculate a pooled RF.[15] The heterogeneity and the variation in pooled estimations were assessed using the Cochran's Q test and I-squared, respectively.[16] The pooled RF of influenza was derived by a random effect model, while the I^2 index is more than to 50% and otherwise this pooled prevalence was derived by a fixed effect model. Meta-regression was used to examine the relationships between RF of influenza and year, country of publication, sample sizes and the cause of heterogeneity of results.[17] Finally, the sub-group analysis was used to avoid the confounding the relationships between research location/country, type of outbreak, type of subjects and the year of publication (before 2009 vs after of 2009) with the pooled prevalence. Moreover, a sensitivity analysis was done by successively removing a particular study or group of studies (if any) that had the highest impact on the heterogeneity test. Publication bias was checked by Egger's regression asymmetry test and Begg's adjusted rank correlation test[18]. All statistical analyses were performed using STATA 11.0 (STATA Corp, College Station, TX). A P-value less than .05 were considered statistically significant.

3 | RESULTS

The study selection process and flowchart of the literature search is shown in Figure 2. A total of 8983 articles reporting influenza infection and subtypes from Middle East countries

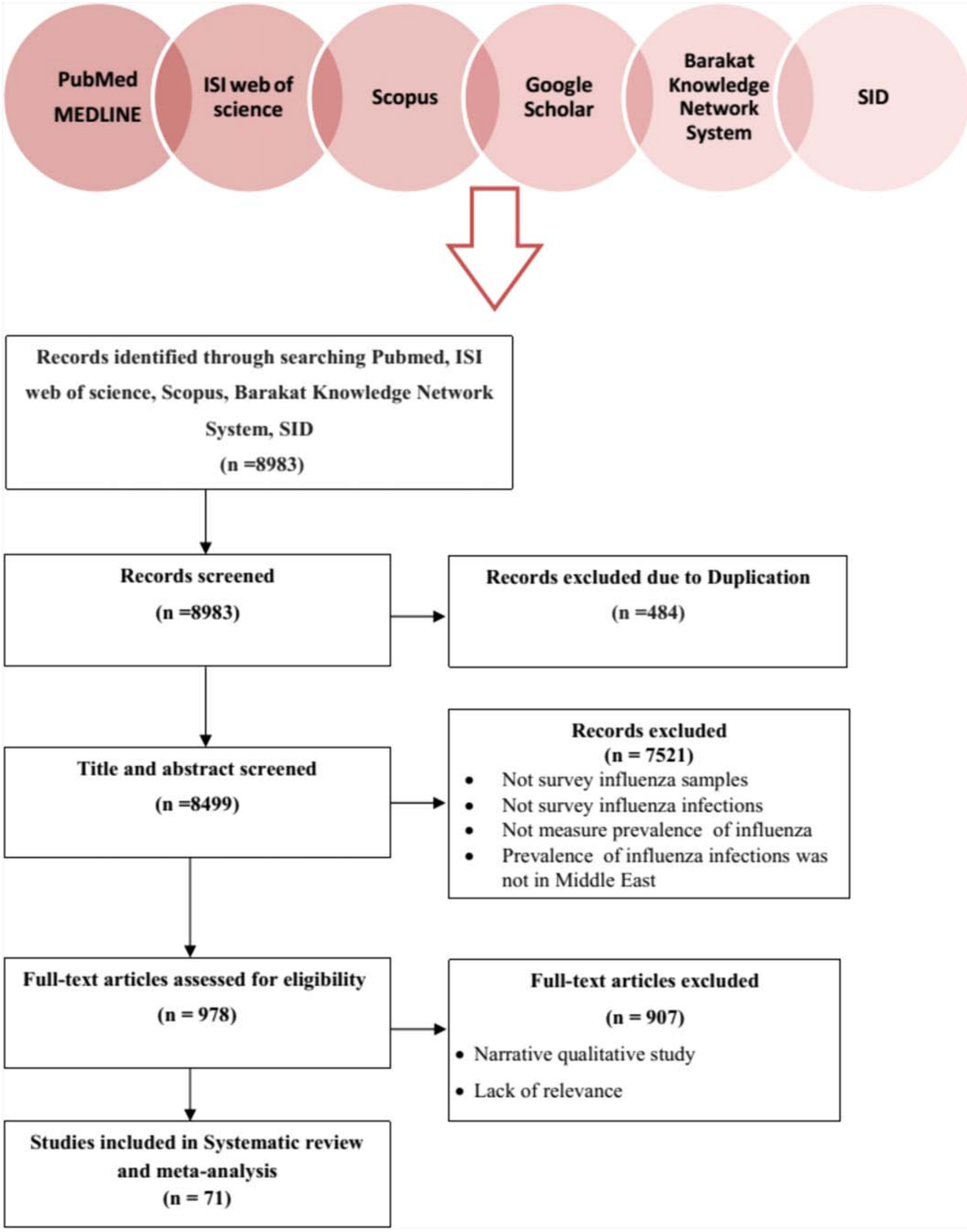

FIGURE 2 Flowchart of literature search and study selection

were found by the databases. In a primary screening process, 484 of the publications were excluded due to duplication. In the secondary screening process, 7521 of the publications were excluded based on title, abstract and keywords evaluation and 978 articles were retained for detailed full-text evaluation. After evaluation of full-texts, 71 articles (abstract with full-text articles) describing the prevalence of influenza infection in Middle East countries were selected for the present study and presented in Table 1. There were no confirmed reports of some countries, including Bahrain, Cyprus, Jordan and Palestine.

PCR based methods were the most dominant methods used for influenza detection; some studies had also used other more specific methods such as HI or culture. In total, 316 966 patients were analyzed for the pooled prevalence of influenza subtypes (Table 1). The characteristics of influenza in Middle East countries are represented in Table 2.

According to the results of the random-effects model, the pooled prevalence of influenza was found to be 10.2% [95% confidence interval (CI): 10.1%–10.3%]. However, the evident heterogeneity of influenza was observed among studies (Cochran Q test, P value <.001, $I^2 = 99.9\%$). No publication bias was observed in the Begg's adjusted rank correlation test and the Egger's regression test (P-value = .129; P-value = .460, respectively). Results of meta-regression were shown a statistically significant association between RF of

TABLE 1 Studies' characteristics

Subjects	Number of studies	Total of sample size	Total of cases	Types of influenza virus
Children	12	4964	1455	H1N1, H3N2
Pregnant women	2	98	29	H1N1
Poultry worker	2	196	34	H9N2
Haj pilgrims	10	7476	195	H1N1, H3N2
Healthcare workers	2	9801	538	H1N1
General population	43	293 831	29 391	H1N1, H3N2, H5N1
Total	71	316 966	31 642	4 types

influenza with a year of publication ($\beta = 0.017$; *P*-value = .046), type of subjects (*P*-value = .011) and location of the studies (*P*-value = .021). But the association between RF of influenza with studies' sample size and type of outbreak was not statistically significant ($\beta < -1.2 \times 10^{-6}$; *P*-value = .251), (*P*-value = .346), respectively. According to the sub-group analysis, the prevalence of influenza in Middle East countries was increased over year of publication (Figure 3), highest and lowest prevalence of influenza were related to Syria (70%; 95% CI: 60%–80%) and Qatar (0.5%; 95% CI: 0.1%–0.9%), respectively. According to the type of subjects, highest and lowest prevalence of influenza were related to pregnant women (29.6%; 95% CI: 20.7%–38.5%) and Haj Pilgrims (2.6%; 95% CI: 2.3%–3%). More details are shown in Table 3 and the Figures 4 and 5. Sensitivity analysis was performed by sequential omission of individual and group of studies. The combined RFs of the prevalence rate of influenza from sequential omission was not altered after omission (13.2%; 95% CI: 9.2%–17.2%), indicating that our results were statistically robust.

4 | DISCUSSION

Respiratory viral infection is very important in public health due to its ability to spread easily. So, influenza as one of these infections affects up to 5%-10% of the world's population annually.[89] The importance of influenza is increasing mainly because of the appearance of novel pandemic strains in swine and avian. Each year, influenza has spread around the world and causing about 250 000–500 000 deaths and more than 5 million cases of severe illness.[9] As mentioned in the previous part, this systematic review and meta-analysis are performed to estimate the prevalence of influenza infection in the Middle East. The authors of this study conducted a comprehensive search of 71 studies from 17 countries to presents the available epidemiological characteristics of influenza infection between 2000 and 2016. In this study, the pooled estimation of the influenza prevalence was 10.2%. The results of the current study revealed that the prevalence of influenza infection in the Middle East and the study population is variable. A multitude of factors such as population density, population movement, aging population, vaccination, herd immunity, geographical region, seasonality effects, etc., could be the effect on this variability.[90] In this systematic review, the most common influenza subtype was H1N1. The prevalence of H3N2 was reported in different parts of the world as follow: Thailand (18%), northern Iran (35.2%), National Influenza Centers (NICs) and other national influenza laboratories from 91 countries (92.5% during 06 February 2017 to 19 February 2017).[79,91] H5N1 is a highly infectious type of influenza virus that causes severe respiratory disease. Person to person transmission of this virus is difficult, although several outbreaks of the virus in humans were reported. The mortality rate of H5N1 is about 60%.[92] Prevalence of H5N1 has reported 856 cases during 2003–2017 and 452 of them was dead.[93]

Children, healthcare worker (HCW), pregnant women, Hajj pilgrim, poultry worker and the general population were included in this study. HCWs are the most vulnerable group because of close contact with patients. In the current study, pooled prevalence for HCWs was 5.5%. In an investigation, Kuster et al reported incidence rates of influenza in vaccinated and unvaccinated HCWs were 6.5% and 18.7%, respectively.[94] Children have the highest rate of influenza infection which led to hospitalization.[95] The prevalence of influenza in children was reported 9.7%–29.0% based on the region by US influenza Surveillance Report.[96] Also, in our study prevalence of influenzas in children was, 29.4% and 24.6%. Pregnant women are another high-risk group for influenza because the disease could be severe. In this meta-analysis prevalence of influenza in pregnant women was the highest rate, 29.6%. Previous studies have shown that these group of patients are associated with about 6% of influenza-related hospitalization.[97] One of the most common infections

TABLE 2 Characteristics of studies included in the systematic review and meta-analysis

First author	Year	Country/Province	Total of sample size	Number of cases	Technique	Subject	Types	Type of outbreak	No. references
Safaar	2003	Iran/Mazandaran	150	14	Indirect immunofluorescence	Children (1–7 month)	A	Seasonal	19
Balkhy	2004	Saudi Arabia	54	3	Viral culture	Hajj pilgrims	A	Seasonal	20
Moattari	2005	Iran/Fars	300	10	HI	Children (1–15 year)	H1N1, H3N2	Seasonal	21
Barati	2007	Iran/Tehran	160	7	Immunochromatographic assay	Children (3 month-15 year)	A	Seasonal	22
Moattari	2007	Iran/Fars	300	26	HA, Viral culture	General population	H1N1, H3N2	Seasonal	23
Imani	2007	Iran/Chaharmahal va Bakhtiari	338	12	ELISA	Haj pilgrims	A	Pandemic	24
Ciblak	2008	Turkey	524	111	ELISA	General population	A	–	25
Zaraket	2008	Lebanon	39	11	RT-PCR	General population	H1N1, H3N2	Seasonal	26
Ashshi	2009	Lebanon	1,600.00	120	RT-PCR	Haj pilgrims	A	Pandemic	27
Kandeel	2009	Egypt	6,355	63	RT-PCR	General population	H5N1	Avian	28
Shatizadeh	2009	Iran/Tehran	202	11	Multiplex PCR	Children (0–6 years)	–	Seasonal	29
Ayatollahi	2009	Iran/Yazd	1442	253	RT-PCR	General population	H1N1	Seasonal	30
Al-Lawati	2009	Oman	497	131	RT-PCR	General population	H1N1		31
Cheraghi	2009	Iran/Hamedan	633	245	PCR	General population	H1N1	Pandemic	32
Ziyaeyan	2009	Iran/Shiraz	305	13	rtRT-PCR	Haj pilgrims	H1N1	Pandemic	33
Kandeel	2009	Egypt	551	6	rtRT-PCR	Haj pilgrims	H3N2, H1N1	Seasonal	34
Örnek	2009	Turkey	56	33	rRT-PCR	General population	H1N1	Seasonal	35
Soydinc	2009	Turkey	16	2	RT-PCR	Pregnant Women	H1N1	Seasonal	36
Gäozalan	2009	Turkey	791	219	HI	General population	H1N1	Pandemic	37
Gäozalan	2009	Turkey	1164	281	HI	General population	H1N1	Pandemic	37
Torun	2009	Turkey	68	60	rRT-PCR	Children	H1N1,H3N2	Pandemic	38
Al-Busaidi	2009	Oman	5109	1388	PCR	General population	H1N1	Pandemic	39

(Continues)

TABLE 2 (Continued)

First author	Year	Country/Province	Total of sample size	Number of cases	Technique	Subject	Types	Type of outbreak	No. references
Ahmed	2009	Oman	393	231	RT-PCR	General population	H1N1	Pandemic	40
Ciblak	2009	Turkey	977	128	rtRT-PCR	General population	H1N1	Seasonal	41
Balkhy	2009	Saudi Arabia	9780	526	RT-PCR	Healthcare workers (HCWs)	H1N1	Seasonal	42
Al Subaie	2009	Saudi Arabia	1103	375	RT-PCR	Children (0–12 Years)	H1N1	Pandemic	43
Ertek	2009	Turkey	19 973	9459	RT-PCR	General population	H1N1	Pandemic	44
Al-Tawfiq	2009	Saudi Arabia	165	47	rRT-PCR	General population	H1N1	Pandemic	45
Herzallah	2009	Saudi Arabia	167 759.00	587	PCR	General population	H1N1	Pandemic	46
Mendelson	2009	Israel	2809.00	1082	PCR/sequencing	General population	H1N1	Pandemic	47
Nateghian	2009	Iran	10 005.00	4113	RT-PCR	General population	H1N1, H3N2	Pandemic	48
Memish	2009	Saudi Arabia	3218.00	11	multiplex RT-PCR	Haj pilgrims and departing pilgrims	H1N1	Pandemic	49
Roll	2009	Israel	2400.00	713	RT-PCR	General population	H1N1	Pandemic	50
Bijani	2009	Iran/Qazvin	518.00	76	RT-PCR	General population	H1N1	Pandemic	51
Moattari	2009	Iran/Fars	275.00	13	RT-PCR, Viral culture	Haj pilgrims	H1N1,H3N2	Pandemic	52
Özlu	2010	Turkey	285.00	151	RT-PCR	General population	H1N1	Pandemic	53
Soleimani	2009	Iran/Zahedan	132.00	20	RT-PCR	General population	H1N1	Pandemic	54
Bashir Aamir	2010	Pakistan	1287	262	RT-PCR	General population	H1N1	Pandemic	55
Alsadat	2010	Syria	80.00	56	PCR	General population	H1N1	Pandemic	56
Grassi	2010	Egypt	156.00	6	RT-PCR	Children (0–18 year)	H1N1	Seasonal	57
Husain	2010	Kuwait	194	62	RT-PCR	Children	H1N1	Pandemic	58
Nisar	2010	Pakistan	1243	262	RT-PCR	General population	H1N1	Pandemic	59
Khan	2010	United Arab Emirates	2806	934	RT-PCR	General population	H1N1	Pandemic	60
Afrasiabian	2010	Iran/Kurdistan	1059	157	RT-PCR	General population	H1N1	Pandemic	61
Hajikhezri	2010	Iran/Khuzestan	655	69	RT-PCR	General population	H3N2, H1N1	Seasonal	62
Kanmaz	2010	Turkey	82	27	rtRT-PCR	Pregnant Women	H1N1	Pandemic	63

(Continues)

TABLE 2 (Continued)

First author	Year	Country/Province	Total of sample size	Number of cases	Technique	Subject	Types	Type of outbreak	No. references
Elsalm Ahmed	2010	Egypt	198	20	RT-PCR	General population	H1N1	Pandemic	64
Affifi	2010	Saudi Arabia	21	12	RT-PCR	HCW	H1N1	Seasonal	65
Momn-Heravi	2010	Iran/Kashan	948	87	RT-PCR	General population	H1N1	Pandemic	66
Haghshenas	2011	Iran/Mazandaran	1363	205	rtRT-PCR	General population	H1N1	–	67
Asad Ali	2011	Pakistan	169	8	RT-PCR	Children	H1N1	Seasonal	68
Goodarzi	2011	Iran/Tabriz	96	17	HI	Poultry Worker	H9N2	Avian	69
Asadali	2011	Pakistan	812	27	rtRT-PCR	Children (<5 year)	H1N1	Pandemic	70
Guldemir	2011	Turkey	2601	404	RT-PCR	General population	H1N1, H3N2	Pandemic	71
Khattab	2011	Egypt	1200	570	Immunochromatographic assay	Children (2–60 month)	H1N1	Pandemic	72
Yavarian	2011	Iran	40169	5214	rtRT-PCR	General population	H1N1	Pandemic	73
Moattari	2012	Iran/Fars	450	205	rtRT-PCR	Children (1–60 month)	H1N1, H3N2	Seasonal	74
Benkouiten	2012	Saudi Arabia	27	6	rtRT-PCR	Pilgrims	A	Seasonal	75
El-Sayed	2013	Egypt	299	42	ELISA	General population	H5N1	Avian	76
El-Sayed	2013	Egypt	750	15	HI	General population	H5N1	Avian	77
Al-Awaidy	2013	Oman	423	273	rtRT-PCR	General population	H1N1, H3N2	Seasonal	78
Haghshenas	2013	Iran/Mazandaran	571	201	RT-PCR	General population	H3N2	Seasonal	79
Mohamed	2013	Iraq	869	255	RT-PCR	General population	H1N1	Pandemic	80
Barasheed	2013	Saudi Arabia, Qatar	1038	5	Multiplex RT-PCR.	Haj Pilgrims	A	Seasonal	81
Nasser	2013	Iraq	2222	672	RT-PCR	General population	H1N1	Season	82
Tavakoli	2013	Iran/Fars	200	77	rtRT-PCR	General population	H1N1	Pandemic	83
Benkouiten	2012	Saudi Arabia	70	6	rtRT-PCR	Haj Pilgrims	H1N1	Seasonal	84
WHO	2014	Egypt	24	13	RT-PCR	General population	H1N1	Pandemic	85
Alavi	2014	Iran/Khuzestan	318	167	RT-PCR	General population	H1N1	Pandemic	86
Cicek	2015	Turkey	6665	618	DFA, multiplex RT-PCR, Viral culture		A	Seasonal	87
Heidari	2015	Iran/Fars	100	17	Microneutralization	Poultry worker	H9N2	Avian	88

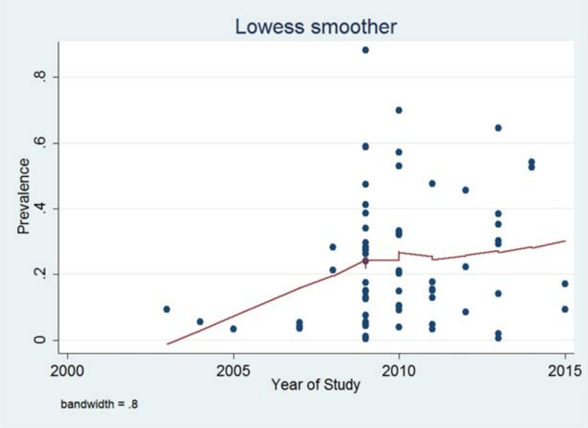

FIGURE 3 The prevalence of influenza diagram in Middle East countries over time

transmitted between pilgrims is viral respiratory infections, especially influenza.[98] In our study, the prevalence of influenza was 2.6%, whereas the prevalence of this virus in Hajj pilgrims were 93.4%, 90.7%, 97.0% in Malaysia (2013, 2012, 2009, respectively), 77.6% in Africa, 90.0% in Saudi Arabia based on previous investigations.[99] This difference can be due to several reasons such as vaccination, public health level, nutritional status, etc. Poultry workers are another group which studied in our investigations, with 17.3% prevalence of influenza. Pawar et al reported the prevalence of H9N2 in poultry workers 4.7% and 3.8% by HI and MN assay, respectively. H9N2 usually led to mild symptoms in humans and on the other hand easy to distinguish H9N2 symptoms with H3N2, H1N1; therefore, the accurate prevalence rate is not available.[100]

TABLE 3 Subgroup analysis for the type of outbreak, type of subjects, area and year of publication

Characteristics	Categories	No. of studies	Pooled prevalence (95% C.I)	Heterogeneity test (I^2%, *P*-value)	Publication bias (Begg's test, *P*-value; Egger's test, *P*-value)
All Studies	–	71	0.102 (0.101–0.103)	(100%; *P*-value <.001)	(Begg's test, .129; Egger's test, .46)
Type of outbreak	Pandemic	38	0.100 (0.099–0.101)	(100%; *P*-value <.001)	(Begg's test, .066; Egger's test, .001)
	Seasonal	24	0.110 (0.107–0.114)	(99.5%; *P*-value <.001)	(Begg's test, .637; Egger's test, .010)
Type of subjects	General population	42	0.103 (0.102–0.103)	(100%; *P*-value <.001)	(Begg's test, .013; Egger's test, .001)
	Children (<6 years old)	5	0.294 (0.279–0.309)	(99.8%; *P*-value <.001)	(Begg's test, .806; Egger's test, .276)
	Children (<18 years old)	7	0.246 (0.229–0.262)	(99.5%; *P*-value <.001)	(Begg's test, .072; Egger's test, .113)
	Haj Pilgrims	10	0.026 (0.023–0.030)	(98.6%; *P*-value <.001)	(Begg's test, .210; Egger's test, .011)
	Healthcare workers	2	0.055 (0.050–0.059)	(95.7%; *P*-value <.001)	(Begg's test, NA; Egger's test, NA)
	Poultry worker	2	0.173 (0.120–0.226)	(0.0%; *P*-value =.896)	(Begg's test, NA; Egger's test, NA)
	Pregnant women	2	0.296 (0.207–0.385)	(78.8%; *P*-value =.030)	(Begg's test, NA; Egger's test, NA)
Year of publication	≤2008	8	0.099 (0.086–0.112)	(95.4%; *P*-value <.001)	(Begg's test, .063; Egger's test, .158)
	>2008	63	0.102 (0.101–0.103)	(100%; *P*-value <.001)	(Begg's test, .102; Egger's test, .55)
Area	Iran	24	0.185 (0.182–0.188)	(99.5%; *P*-value <.001)	Begg's test, .021; Egger's test, <.001)
	Egypt	8	0.077 (0.073–0.081)	(99.8%; *P*-value <.001)	Begg's test, .63; Egger's test, .85)
	Saudi Arabia	9	0.009 (0.008–0.009)	(99.7%; *P*-value <.001)	Begg's test, .251; Egger's test, .162)
	Pakistan	4	0.159 (0.147–0.171)	(99.4%; *P*-value <.001)	Begg's test, .734; Egger's test, .81)
	Oman	4	0.315 (0.304–0.326)	(99.2%; *P*-value <.001)	Begg's test, .31; Egger's test, .16)
	Iraq	2	0.30 (0.284–0.316)	(0%; *P*-value <.623)	Begg's test, NA; Egger's test, NA)
	Turkey	12	0.346 (0.341–0.351)	(99.9%; *P*-value <.001)	Begg's test, .15; Egger's test, .01)
	Israel	2	0.345 (0.332–0.357)	(97.8%; *P*-value <.001)	Begg's test, NA; Egger's test, NA)
	Lebanon	2	0.08 (0.067–0.093)	(88.1%; *P*-value =.004)	Begg's test, NA; Egger's test, NA)
	Kuwait	1	0.32 (0.254–0.385)	NA	Begg's test, NA; Egger's test, NA)
	Qatar	1	0.005 (0.001–0.009)	NA	Begg's test, NA; Egger's test, NA)
	Syria	1	0.70(0.60–0.80)	NA	Begg's test, NA; Egger's test, NA)
	United Arab Emirates	1	0.333 (0.315–0.350)	NA	Begg's test, NA; Egger's test, NA)

NA: Not applicable.

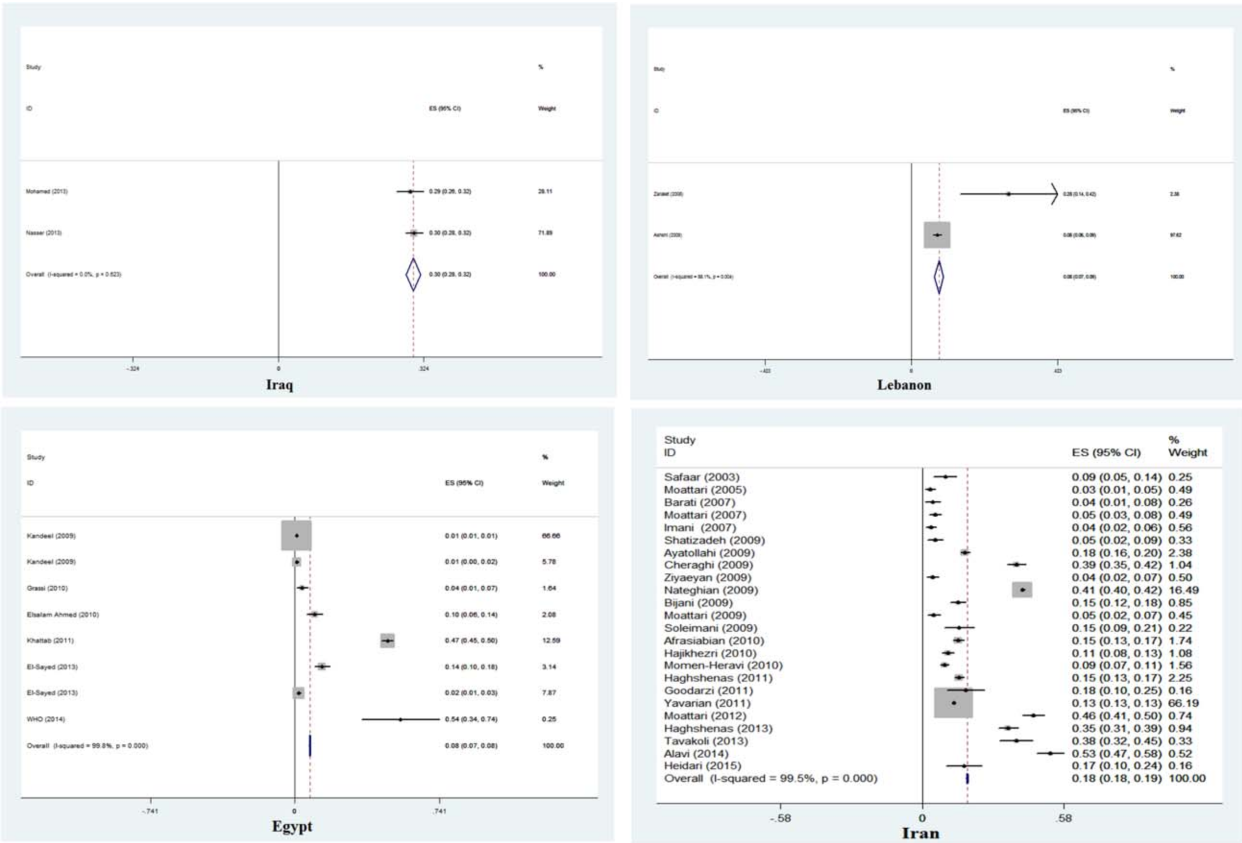

FIGURE 4 Forest plot is showing influenza infection prevalence estimates of patients in Iran, Iraq, Lebanon and Egypt

The time of occurrence outbreaks of influenza virus is different in several parts of the earth. For instance, in the Northern Hemisphere, it occurs between November and March; However, in the Southern Hemisphere, flu occurs between April and September; moreover, in the temperate and tropical zones, it occurs in winter and throughout the year, respectively.[101]

In this study, we demonstrated that most of the outbreaks of influenza were pandemic related to H1N1. Similar to our results, several investigations have shown that influenza A virus, especially H1N1, pdm09 and H3N2 were circulating subtypes in Iran, Afghanistan, Egypt and Yemen. Such subtypes were associated with increased hospitalization and death.[102] In another investigation, Nielsen et al reported influenza that the viruses subtype in clinical samples during 1994–2010 as follows: A/H3N2 seasonal during 1995–1999, 2005–2006 and A/H1N1 pandemic in 2009.[103] H1N1 was first reported in Mexico in 2009 and lead to 12 470 deaths and 274 000 hospitalizations in 2009–2010.[45] The highest mortality rate of H1N1 was reported in Damascus (51%), Mexico (41.4%) and Iran.[104,105]

The first human infections caused by H9N2 was reported in 1999, Hong Kong. Prevalence of H9N2 in Iran was reported 17%-18%.[69,88] These subtypes have repeatedly been isolated from patients in China and Hong Kong.[106] Khan et al reported that the seroprevalence of H9N2 ranged from 1% to 43%. Their results were based on HI methods and similar to WHO report.[107] One of the important limitation of Khan's investigation is that the immune responses of human against infections with avian viruses are poor. Badar et al in Pakistan tested 6258 specimens and showed that 72% of them were positive for influenza A viruses. Also, they demonstrated that the prevalence of subtype as following: 82% were H1N1 pdm09, 16% H3N2 and 2% seasonal A/H1N1.[14] It has been reported that 18% of clinical samples from patients were isolated human influenza viruses in Thailand (2004–2006).[79] Prevalence of influenza among Australian hospitals reported by Blyth et al. They detected influenza A in 90% of 402 patients. Among the positive samples, H1N1, pdm09 and H3N2 were confirmed as a most frequent subtype.[95] Epidemiological studies can be used for several purposes such as identify the dominant types of the virus to vaccination strategies for population and subgroups, identify high-risk groups and identification of the epidemiological pattern of the disease.

5 | CONCLUSION

The current study provides the overall influenza prevalence rate and information about circulating types of influenza virus in different geographical areas of Middle-East. The outbreak

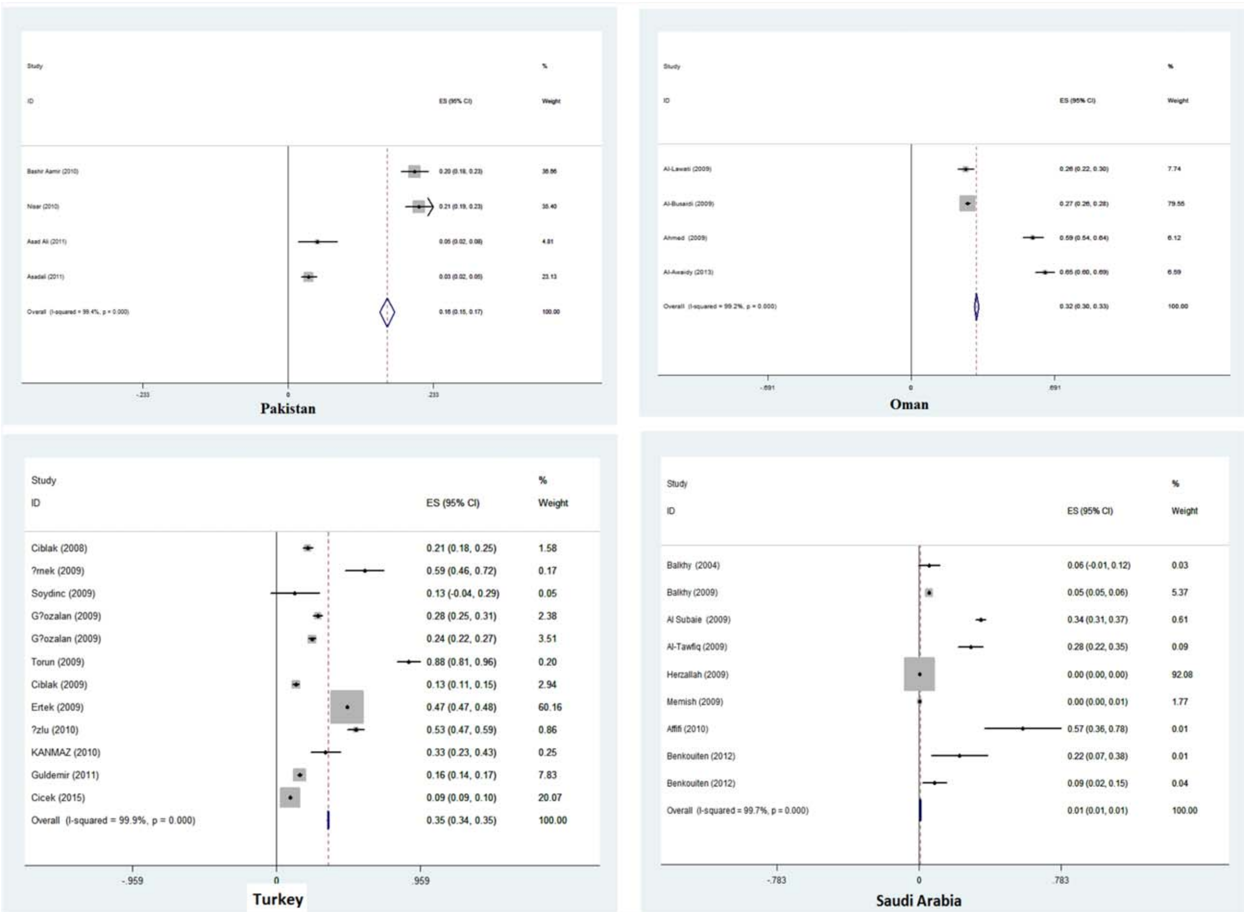

FIGURE 5 Forest plot is showing Influenza infection prevalence estimates of patients in Pakistan, Oman, Turkey and Saudi Arabia

is obtained will constantly increase over the next years. However, it should be noted that our results may be affected by several factors due to insufficient data on Middle East countries resulted from a small number of surveys, and low or inadequate geographical coverage of the studies. So, a comprehensive future population-based study is highly recommended to investigate the effects of all variable parameters.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Study design: Moghoofei, Esghaei
Acquisition of data: Hadifar, Ghasemi, Babaei, Kavosi, Tavakoli, Javanmard
Analysis and interpretation of data: Mostafaei
Drafting of the manuscript: Hadifar, Moghoofei, Khodabandehlou
Critical revision of the manuscript for important intellectual content: Monavari, Khodabandehlou, Esghaei

ETHICS

This study does not need ethical approval and patient consent. All analyses were according to previous published studies.

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