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Review article

COVID-19: An Epidemiological Puzzle

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ABSTRACT

Pneumonia of unknown etiology was reported from Wuhan, Hubei province of China on 31st December, 2019. WHO declared the outbreak a public health emergency of international concern on 30th January, 2020. Thereafter, it has spread throughout China and reached the level of a pandemic expanding to 210 countries with 9,653,048 confirmed cases and 491,128 deaths as per COVID-19 Situation Report issued by WHO based on data received upto 27th June, 2020. Manifold questions remain unanswered regarding pathogen associated variables for amplification dynamics, host environment and agent interaction. Multidimensional issues regarding the epidemiological spectrum have cropped up but still unresolved. This study makes an effort to analyse the information gathered from published articles of renowned journals and newsletters to explore the epidemiological characteristics of COVID-19 disease. Hereby, we have tried to assemble the questions epidemiological lacunae created by the divergent demographic characteristics, long incubation period, secondary attack rate and puzzling transmission dynamics of COVID-19 that remain unanswered.

Keywords: COVID-19, Novel coronavirus, transmission dynamics, pre-symptomatic.

1. Introduction

There is a Greek Myth in which Gods had given Pandora a locked jar and advised never to open. Driven by human weakness she nevertheless opened it, releasing the world's misfortune. Such is the scenario with COVID-19 [1]. Pneumonia of unknown etiology was reported from Wuhan, Hubei province of China on 31st December, 2019. WHO declared the outbreak a public health emergency of international concern on 30th January, 2020 [2]. Thereafter, it has spread throughout China, expanding to 210 countries and reached the level of a pandemic. On 11th February 2020 a name was announced for this novel coronavirus disease: COVID-19 [3]. Contact tracing, testing and treatment supported by social

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distancing are the gold-standards for harnessing this global pandemic. To this effect, on March 24th, the Government of India ordered a nationwide lockdown for 21 days at a point when the number of confirmed cases was approximately 500 in the country [4]. Currently, India has witnessed cases mostly related to travel and local transmission from imported cases. Community transmission has not been confirmed yet nationally. However, there is a state-wise difference in opinion regarding the same. Historically, if we look back, there were multiple viral pandemics and outbreaks globally. Corona virus also established previous pandemics, SARS (2003) and MERS (2012), but SARS-CoV-2 emergence takes a different trajectory. Despite the fact that each apparently has an origin in enzootic bat viruses [1], multiple questions remain unanswered regarding pathogen associated variables for amplification dynamics, host environment, agent interaction. With this present analysis of different documentations, we tried to understand the different variables pertaining to the COVID-19 disease transmission dynamics.

2. Objective

Descriptive analysis of COVID-19 epidemiological characteristics based on different published articles. We tried to analyse the information gathered from published articles of renowned journals and newsletters to explore the epidemiological characteristics of COVID-19 disease.

3. Discussion

A pooled analysis of confirmed COVID-19 cases reported in China estimated the median incubation period to be 5.1 days, similar to SARS. However, the symptoms appeared in 97.5% subjects within 11.5 days [5]. This infection has led in a multitude of knowledge gaps that has resulted in random spread and initiation of a pandemic of global proportion. A brief compilation of the major lacunae perplexing researchers worldwide:

3.1 Transmission dynamics:

Any infectious disease outbreak can be characterized by its reproductive number R_0 . If $R_0 > 1$, cases are statistically capable of secondary transmission. For COVID-19 outbreak in China, R_0 ranged from 2.5-2.9 [6,7] in contrast to 1918-19 Spanish influenza pandemic that killed 50 million people worldwide with estimated R_0 being 1.8. For SARS 2003 and MERS 2012 outbreak it was $R_0 < 2$ [8]. So, the current pattern of COVID-19 presents a concerning possible shorter doubling time of cases. Unlike SARS-2003 and MERS-2012 outbreaks where almost all onward transmission occurred after symptom onset, COVID-19 transmission can occur prior to that. Based on this fact 'contacts' have been defined as "those who have been in close contact since 2 days before onset of symptoms of suspected and confirmed cases, or 2 days prior to asymptomatic cases". This reflects that secondary transmission of COVID-19 virus is possible minimum 2 days prior to symptom onset [9]. Studies have also shown evidences of transmission by asymptomatic subjects who were later tested positive for SARS-CoV-2. This is an indication to the latent period extending from the point of infection to the onset of infectiousness which is shorter than the incubation period [10, 11]. The complete severe acute respiratory syndrome of COVID-19 is shown by only 5-10% of the total infected persons [12]. Whilst respiratory droplets and fomites have been advocated to be the major modes of transmission, studies have shown airborne transmission might be the cause of the extraordinary attack rate [13, 14]. Apart from oral swabs and bronchoalveolar lavage fluid (BALF) the virus has also been detected in anal swabs and blood [15, 16]. This can not be the possibility of viral shedding through feco-oral and body-fluid routes providing a lead for further interventions. Even though

the human coronavirus does not replicate outside the living cell, it remains viable on contaminated surfaces for varied durations, subject to humidity and temperature [17, 18]. A high stability was found at 4°C in-vitro but when temperature raised to 70°C, the inactivation time reduced to 5 min [19, 20]. Hence, delving into new factors and new temperature determinants can put light on the combination effect of temperature and humidity on the half-life of the virus. Droplet inoculation on different surfaces showed that the virus did not persist post 3 hour incubation on printing/tissue papers and 2 day incubation on wood. The viability was higher on smooth surfaces and recovery ceased on day-4 from glass and bank notes and day-7 on stainless steel and plastic. Persistence was observed on the outer layer of surgical mask even on day-7 [1]. Hence, the survival of the virus varies on different surfaces and gives an idea towards the safety and utility guidelines that can prove vital in breaking the transmission chain via inanimate objects in community setting.

3.2 Morbidity and mortality

Mean duration of onset of symptoms to death was found to be 17.8 days (95% CI 16.9-19.2) and to hospital discharge 24.7days (CI 22.9-28) [20]. Estimated fatality may vary between countries owing to difference in prevention, control and implemented policy utilization. Severity of a disease is usually measured by the fatality ratio that is the reported Case Fatality Ratio (CFR). Verity R. et al reported from a model based analysis, accounting for censoring and ascertainment bias, crude case fatality ratio of 3.67%. Best estimate from China reported, after adjustment of demography and ascertainment of CFR, to be 1.38% [20]. Even if the CFR of COVID-19 is lower as compared to 14–15% for SARS outbreak [21] and approximately 35% for MERS outbreak [22], rapid progression and evidences of multiple human-to-human transmission modes suggest SARS-CoV-2 to be more dangerous [23-26]. A preliminary study conducted in the Hubei province found that almost a four-fifth of the affected population were aged 30-69 years, indicating a major impact on the global workforce. The age group ≥ 80 have the highest case fatality ratio [27]. A new question is cropping up regarding role of ethnicity in incidence or outcome of COVID-19 [28]. A higher incidence and severity observed among ethnic minorities and first 10 doctors in the UK to succumb to COVID-19 identified to be from the ethnic section [29]. This could be due to socio-cultural, lifestyle, genetic predisposition and pathophysiological differences in susceptibility to infection. A higher mortality is observed in presence of co-morbidities [26] and hence, ethnic groups with higher rates of diabetes, hypertension and other co-existing conditions are at exemplified risk [28, 30-32] countries like India with a diverse geographic and demographic spectrum calls for further detailed studies. Even though data suggests no significant gender disproportion with 56% males being affected [30] but a higher COVID-19 related mortality among males may be the result of immunological or habitual differences such as smoking [33,34]. However it is too early to make any assumptions. Children of all age groups are sensitive to COVID-19 with neonates being the most vulnerable [35]. Disease severity and case fatality ratio is less as compared to adults [36, 37]. This is puzzling as children are often considered at higher risk of viral respiratory diseases owing to limited immune experience and incomplete airway development [38]. It indicates a knowledge gap that must be filled fast as children can be important transmission facilitators for COVID-19. As for pregnancy, no obstetric or neonatal complications related to COVID-19 have been reported so far [39]. But data being insufficient, the medical and social risk cannot be ruled out. Very recently a non-peer-reviewed article by Miller A. reported a correlation between universal BCG vaccination and reduced impact of COVID-19. Five countries without universal BCG

vaccination policy had 264.90 ± 134.88 cases per million and 55 countries having a current policy had 59.54 ± 23.29 cases per million inhabitants. A plausible explanation may be the broad spectrum protection against viral infection and sepsis conferred by BCG vaccine [40]. But this report was refuted as an ecological fallacy [41]. Reports of countries with high burden of leprosy being less vulnerable are also present [42]. Nevertheless this does not rule out the possibility of a higher proportion of asymptomatic cases in comparison to clinical cases.

3.3 Diagnostics

The detection of SARS-CoV-2 is conducted by real-time RT-PCR method and screened via serological tests. Although former is confirmatory, it can only detect the virus during acute stage of viral shedding which is uncertain in case of COVID-19, plus the sensitivity and specificity of the COVID-19 real-time RT-PCR test is not 100% [43]. The seroconversion kinetics shows a gap between end of convalescent phase and period of antibody response. Therefore, the conversion of a potential carrier of SARS-CoV-2 to seronegative state is one of significance in preventing/controlling community transmission. This might give serological testing an upper hand with respect to public health in the detection of asymptomatic/subclinical cases [44]. Thus, from different report analysis, a four months old disease appeared with total puzzling epidemiological characteristics, initiating a global pandemic. Multidimensional issues regarding the epidemiological spectrum came forward but could not be resolved. Animal-to-human viral transmission is yet to be confirmed by global medical fraternity as differences of opinion are cropping [45]. Regarding ethnicity, reports from developed countries are having perplexing implications. The reason isn't clear as to why minority origin countries are reporting lesser case incidences and symptomatic patients. Clinical manifestation is in line with airborne respiratory infections but gastrointestinal complications are now emerging [33]. The global diversity in mortality rates with highest being reported from developed countries is difficult to reason. Regarding diagnosis and treatment, the prevailing dilemma regarding the most suitable test is unresolved and preference of hydroxychloroquine by administrators without solid evidence with none other proper antiviral drug in pipeline except convalescent plasma showing some hope is perturbing.

4. Conclusion

Above analysis brings into fore the puzzling epidemiological characteristics of COVID-19 pandemic including identification of animal reservoir, determination of infective period, transmission dynamics, effective treatment and prevention methods including further test development, drug development and vaccine development which still remain unanswered. It is an attempt to briefly highlight the research gaps that still persist as limitations to the disease management strategies worldwide. In-depth and rigorous research is necessary to understand the puzzling epidemiological characteristics of COVID-19 disease. Though we tried to analyse different epidemiological studies, there are certain limitations of information collection and availability. Nevertheless this study will hopefully help to identify epidemiological lacunae and aid a direction for the development of solid evidences.

5. Declarations

5.1 Competing Interests

I declare that there is no conflict of interest.

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