

Socio-Demographic Factors Influencing Case Fatality Rate of Covid-19: A Review Article

Komal Mushtaq*, Ammal Mushtaq, Mushtaq Ahmad Shad and Muhammad Hammad Mushtaq

Ubeera Memorial Research Society, Allama Iqbal Medical College, Lahore, Pakistan

*Corresponding author: Komal Mushtaq, Ubeera Memorial Research Society, Allama Iqbal Medical College, Lahore, Pakistan



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ABSTRACT

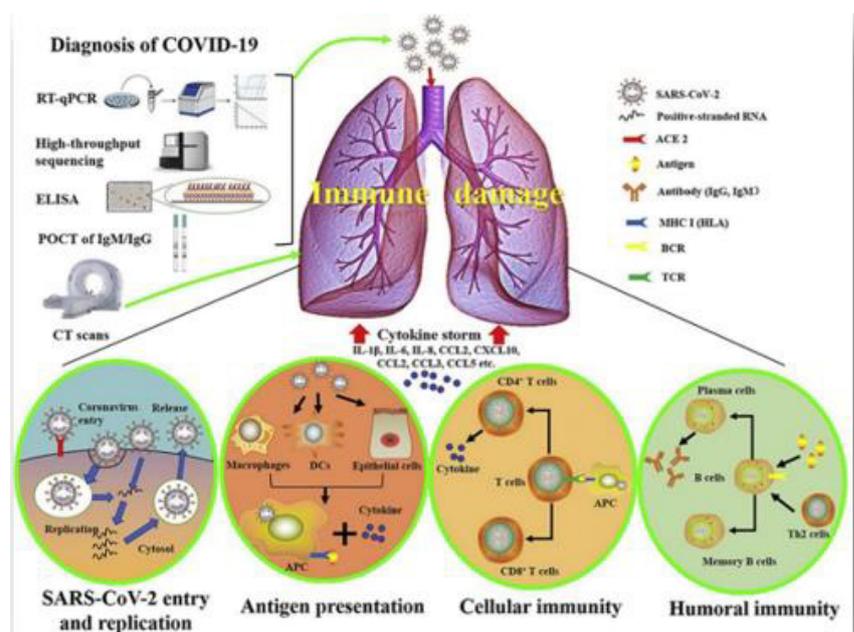
Aim: In this article, we analyze the socio-demographic factors that determine the case fatality rate of Covid-19 across developing and developed world.

Introduction: Covid-19's first case was reported in Wuhan, china and then it spreads throughout the world causing high fatalities. Contrary to prediction, it causes low fatalities in low-income countries. There are certain factors which need to be explored. Although currently there is limited data available about Covid-19 pandemic; however, there are number of factors which are strikingly different in both contrasting world and might be the reason for difference of covid-19 death ratio among different countries. Based on available data, our study will elaborate some factors such as population age structure, BCG vaccination, Malaria incidence and strain of human coronavirus and immune host response system as the main factors in determining this low case fatality rate of covid-19, in low-income countries.

Materials & Study: It is a review article analyzing various factors to emphasize the understanding of some key elements which are not focused yet.

Results & Conclusion: By reviewing original and review articles, moreover, the online material by webpage emphasize on the importance of health system and population age structure. It appeals further research on some factors which might help in some new discovery as medicine is a continuing education.

Molecular immune pathogenesis of Covid-19 (Graph 1) [1].



Introduction

The covid-19 pandemic has serious outcomes on world in terms of economic destabilization, mortalities, worsening of morbidities and a state of unreality. The SARS-COV-2 emerged as a viral illness in Wuhan province of china and in a short time becomes pandemic because of its high infectivity, virulence and having ability to spread in incubation period. This virus belongs to coronavirus family and it cause mainly respiratory tract illness. Covid-19 cause severity of symptoms in patients with comorbidities and elderly. Other than respiratory symptoms, it causes multi-inflammatory syndrome in children and presentation of this syndrome is unusual and has some features in similarities with Kawasaki disease [2].

There are various drug trials for treatment of covid-19; however, no drug regimen is approved by FDA till now.

This review article will explain the few factors that why there is difference in reported case numbers and case fatality rate in developing and developed countries. The symptoms, duration of symptoms and response to treatment vary in individuals; thus, it is different in countries and may be due to genetic variation along with difference of ethnicity. It is a debatable topic, and the results of research will help to understand the disease process and to combat

infectious diseases. The subsequent text will explain few factors which are currently not available in collaborative way.

Methods and Materials

This is a systematic review article. A literature search was done by using PubMed and google search engine for original and review articles, advisories from professional societies and expert publications since the onset of current covid-19 pandemic.

Discussion

Coronavirus are spherical or pleomorphic enveloped RNA viruses. They are transmitted via airborne droplets to nasal mucosa. Viruses replicate locally in cells of ciliated epithelium causing cell damage and inflammation. In animals, coronaviruses invade different tissues and cause a variety of disease; however, in human, it mainly causes mild upper respiratory infections [3]. However, we have witnessed severe lower respiratory tract infections (lung parenchymal infiltrates) due to coronavirus as SARS in 2002 and MERS in 2011. A novel human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) was identified in china in December 2019 and become pandemic affecting the world's population globally [4]. Coronavirus causes more cases and fatalities as compared to SARS and MERS [5] (Figure 1).

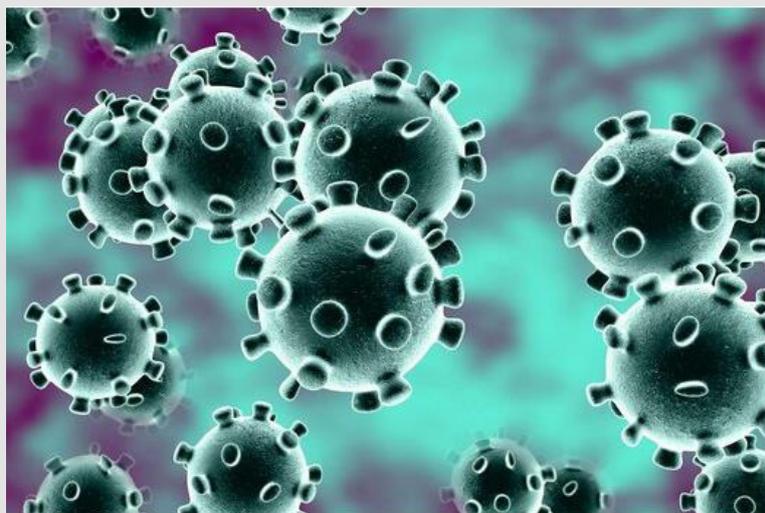


Figure 1: Virus causing covid-19 [5].

Mode of Transmission and Detection of Virus

SARS was first transmitted from civets to humans in china and then human-human by respiratory secretions (e.g. families, hospitals). It was mainly transmitted by respiratory droplets and invade via respiratory membrane. SARS-COV-2 was transmitted via

bat to humans and then human-human by respiratory secretions and close contact makes its spread more progressively [4,5]. Detection of virus is done by using antigen/antibody by ELISA, Nasopharyngeal/oropharyngeal swab by PCR to detect nucleic acid (Figure 2).

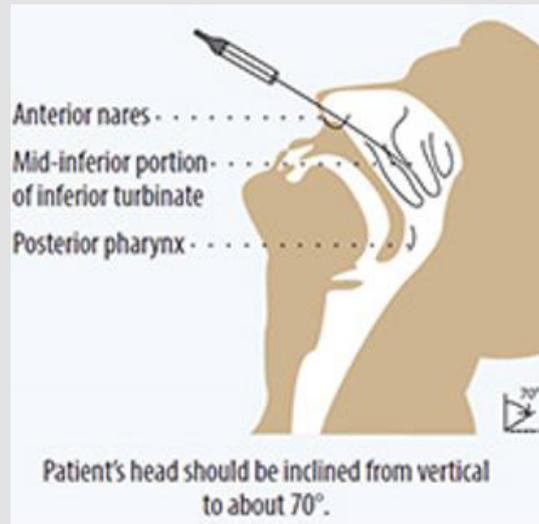


Figure 2: Taking Nasopharyngeal Swab²³.

Symptoms

The period between the introduction of virus into the body and the onset of symptoms is called incubation period and it usually lasts for 4-14 days in coronavirus infection. Symptoms varies from person-person in severity and duration; however, the percentage of symptoms [5,6] are as following;

1. Fever 80-90%
2. Cough 60-70%
3. Gastrointestinal complaints 40-50%

4. Loss of sense of smell and touch 30-40%
5. Shortness of breath 20%

The percentage of unusual symptoms are not available till date. It causes inflammatory syndrome in children and systemic vasculitis. It is also reported that it affects clotting pathway and cause death due to pulmonary embolism [1,7]. There are differences between symptoms of covid-19, common cold and other allergies (common cold is usually self-limiting and does not cause severe myalgias (Figure 3).

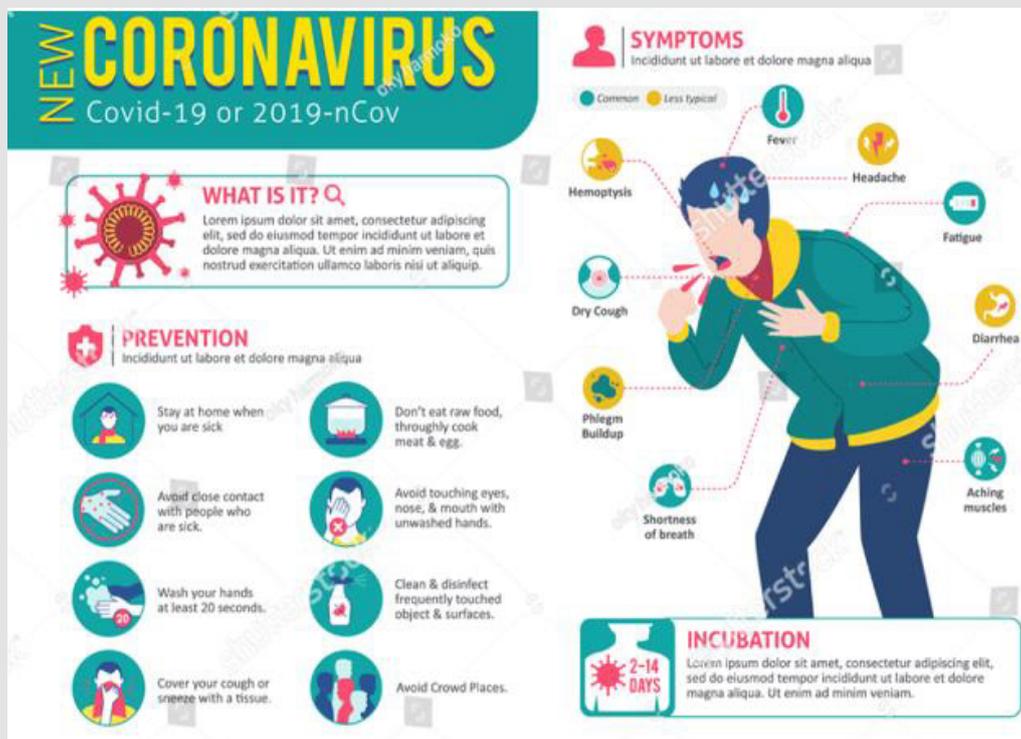


Figure 3: Symptoms ang Prevention of Covid-19.

Incidence and Mortality Rate

Reported case are increasing day by day. Total number of cases are 15,121,824 and deaths are 620,292 [8].

Case Fatality Rate

Definition: Case Fatality Rate is the proportion of deaths from a certain disease compared to the total number of people diagnosed with the disease for a particular period.

The case Fatality Rate of covid-19 varies in different countries and surprisingly higher in developed countries (e.g. Europe, USA) [8] (Table 1).

Table 1: Case number, death and case fatality rate of covid-19 in different countries [8].

Country Name	Case Numbers	Deaths	case Fatality Rate
France	154188	29209	18.94
Italy	235278	235278	14.44
U.S. A	2029660	113225	5.58
U.K.	287399	287399	14.13
Spain	288797	27136	9.4
Ireland	25207	1683	6.68
Pakistan	108317	2172	2.01
Ethiopia	2336	32	1.37
Nepal	4086	15	0.37
Bahrain	15731	29	0.18

Case Fatality Rate depends upon various factors; however, the major parameters of worth importance are:

- a. Population age structure
- b. BCG vaccination
- c. Malaria incidence and use of anti-malarials
- d. Viral strains and host-immune response

A. Population Age Structure

Population age structure of different countries varies and it is estimated that countries having high growth rate and young median age has low mortality rate by covid-19 pandemic; although, it opens a new debate and will surely lead to new aspect of population studies and control strategies [9] (Table 2).

Table 2: Median age of countries.

serial number	country name	Median Age (years)
1	Niger	15.4
2	Uganda	15.8
3	Angali	15.9
7	USA	37.1
8	Uk	39.8
4	Italy	45.5
6	Germany	47.1
5	Japan	47.3

Age has reciprocal relationship with the mortality rate of covid-19 [9] (Figure 4).

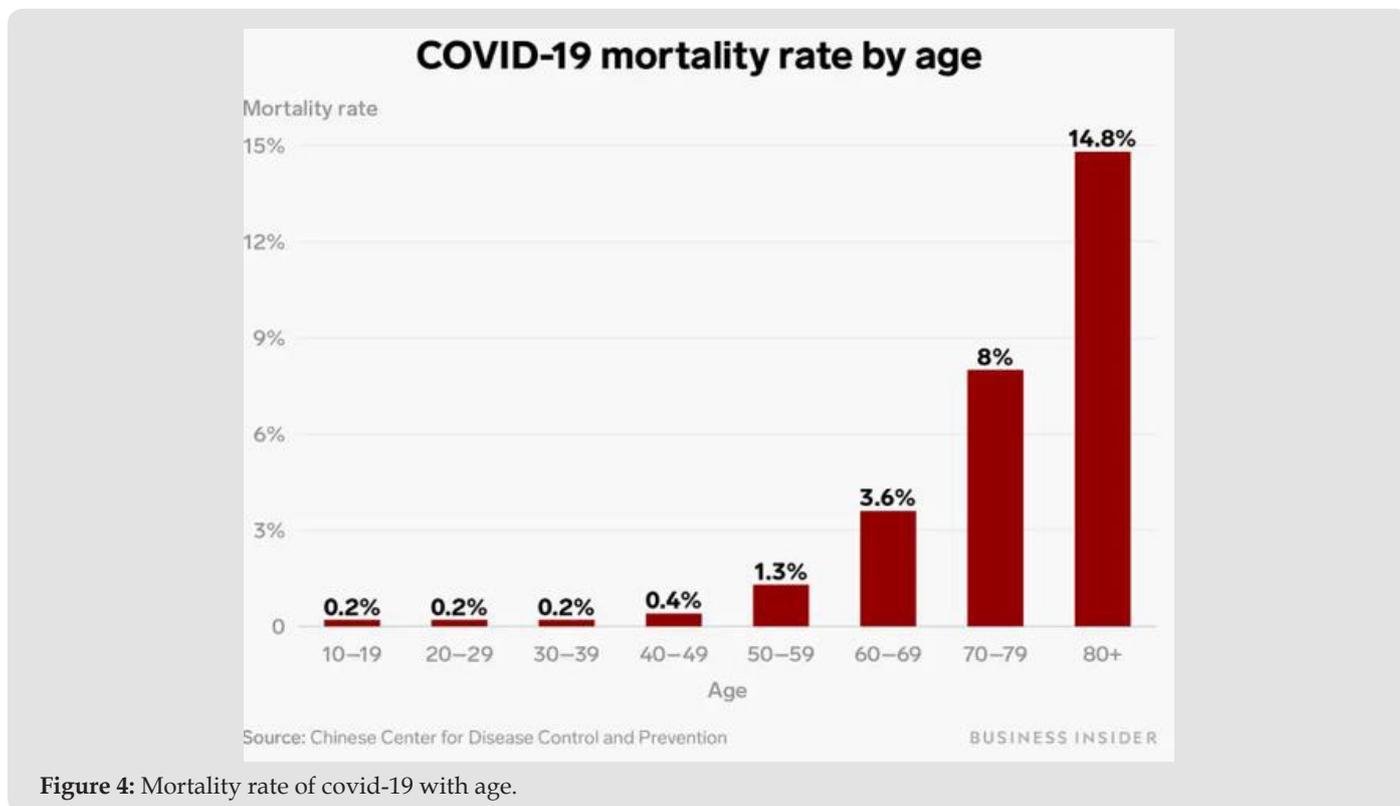


Figure 4: Mortality rate of covid-19 with age.

The mortality rate of covid-19 is surprisingly low in developing countries in contrast to predicted outcome as the countries having high growth rate and young median age shows low mortality rate as shown in below Figure 5 [10].

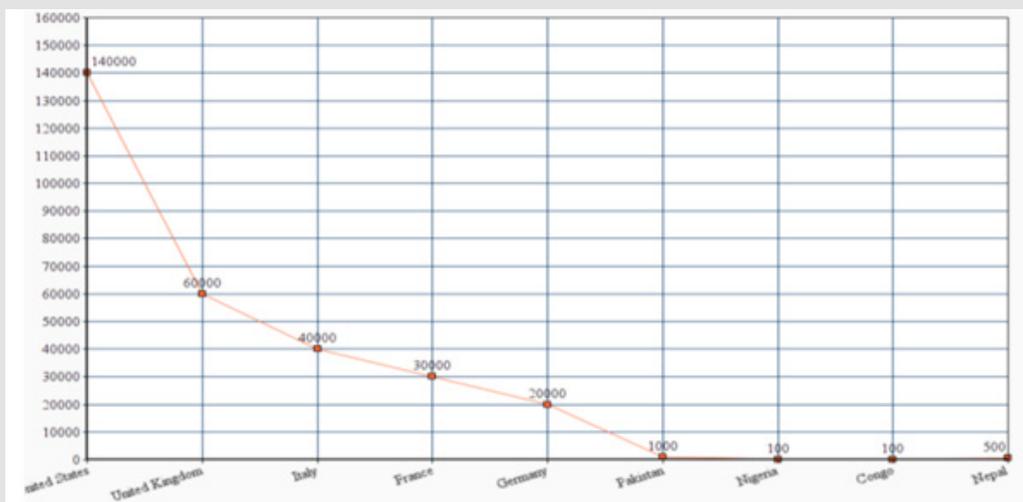


Figure 5: Graph showing case fatality rate of covid-19 in different countries.

B. BCG Vaccination and Covid-19

Bacillus-Calmette-Guerin is almost a 100-year-old vaccine against a dreadful bacterium known as Mycobacterium Tuberculosis which cause a disease Tuberculosis affecting different organs. Research indicates that it is 70-80% effective in protecting against few forms of tuberculosis (for example pulmonary tuberculosis, tuberculosis meningitis). It is recommended as a part of Expanded program of Immunization and administered to newborns immediately after birth. The countries which are prioritized for BCG vaccination due to high tuberculosis load has showed less fatality rate due to covid-19 [5]. Tuberculosis affects different organs with different severity; however, it initially affects lungs and spread via

respiratory droplets.

BCG protects us from Tuberculosis and other respiratory infection (influenza, pneumonia) [11]. There is currently no evidence that BCG helps in protection against covid-19; however, studies in Germany and Netherland support this evidence. In the midst of pandemic, it is early to jump on conclusion and surly it may help to build a vaccine against covid-19 and opens a new chapter in history [12]. Tuberculin Skin Test is an example of Type 4 hypersensitivity reaction; thus, it supports that BCG increase one's response to Type 4 hypersensitivity reaction (Potentiate the host response via T-Lymphocytes), immune system part which fight against covid-19.

C. Anti-Malarial and Covid-19

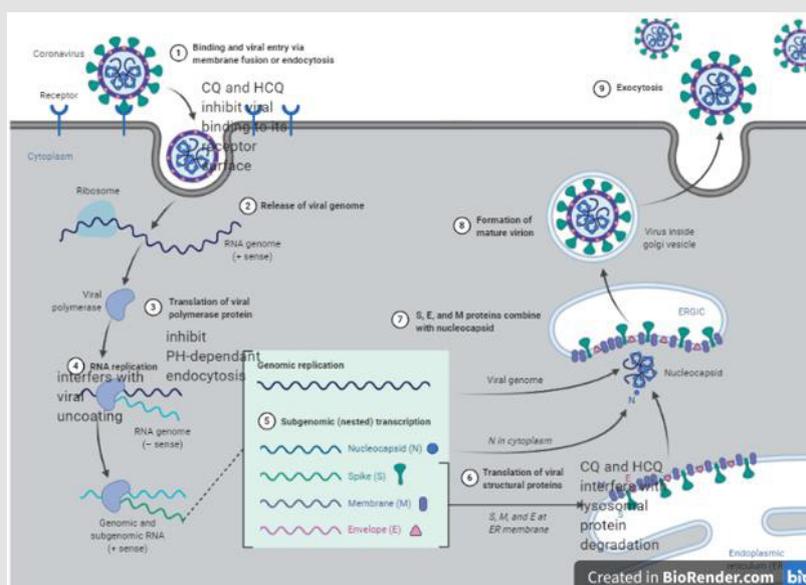


Figure 6: Chloroquine and Hydroxychloroquine interfering the viral replication cycle [14].

The Covid-19 Pandemic implies great stress and responsibility on clinicians. As morbidity and mortality rates are exceptionally high because of this pandemic, number of drug trials are used. Although Chloroquine and Hydroxychloroquine do not have enough literature in support to use as anti-viral agents. However, they are widely used as an antiviral agent in this pandemic [13] as they pose some properties to control viral replication which will be discussed below. The role of Chloroquine and Hydroxychloroquine in covid-19 will be illustrated by this Figure 6 [14].

Chloroquine and Hydroxychloroquine use in covid-19 must be rationalize due to their potential side effect as they cause renal, retinal toxicities and prolong QT interval [15]. If we look at the world map for infectivity of covid-19, there is low infectivity of

covid-19 in countries which have high index of malarial infection [16]. These countries use ways to decrease vector-human contact and prophylaxis drugs to decrease malarial incidence [14,17]. This topic has a worth importance in this pandemic.

D. Viral Strains and Host-Immune Response

When a virus (infectious particle) enters into one's body, the immune system protects it from virus. Virus considered as a foreign particle and presented to special host cells termed as T lymphocytes via Major Histocompatibility complex (MHC type 1 & 2). There are two types of T lymphocytes i-e Cytotoxic T cell and Helper T cell. Cytotoxic T cell kill the viral infected cells and remove from the body (Figure 7).

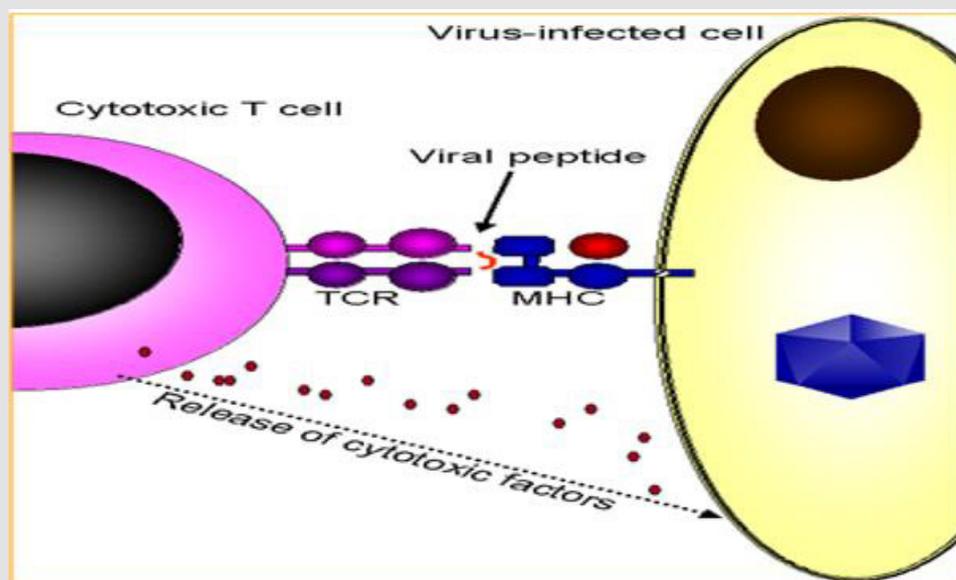


Figure 7: Viral Host Immune Response.

The immune system of body is potentiated by antibodies which are produced by *B lymphocytes* and help in not only augmentation of immune response but also to protect body next time by memory cells. This mechanism will not help us to save from a disease when there is a weak immune system or a different strain of infectious agent gain entry into one's body [18].

There are various strains of human coronavirus [17];

1. 229E
2. NL63
3. OC43
4. HKU1
5. MERS-COV
6. SARS-COV
7. SARS-COV-2 (the novel coronavirus which cause 2019 pandemic, COVID-19)

People around the world are commonly infected with 229E, NL63, OC43 HKU1 and it causes mild upper respiratory infections.

Although there is no data available to confer any immune response variation among people across the world [9]. As the people of Nigeria residing in USA are infected with covid-19 while the overall disease and mortality rate statistics of both countries varies. There is no convincing data available for genomic variation of SARS-COV-2 [19]. A study reveals changes in genomic sequence of human coronavirus and this variation makes changes in its virulence. That is may be another reason for high mortality rate in Europe, USA and China [18].

The major risk factor for covid-19 fatalities is also due to comorbidities which are more in elderly population as compare to young patients. Although younger people appear generally at lower risk, everyone must adhere to government restrictions to protect the millions of people at higher risk due to age or serious comorbidities [20-26].

Summary

This review article emphasizes the socio-demographic factors for difference of mortality rate due to covid-19 in developing countries. This difference of case fatality rate is surprising, and it urged many researchers worldwide to re-explore the facts. There is difference in population age structure, immunization practices and use of Malarial prophylaxis along with cultural, regional and societal differences. Medicine is a continuous education and it evolves with time. There is no specific theory, thus it demands research and analysis of various factors which in result help us to fight against infectious diseases. There is limited availability of data at time; however, it opens new chapters of research in public health too and thus help to save more lives.

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