MINI REVIEW

Comparison of Pattern and Outcome of COVID-19 in Pakistan and Its Neighboring Countries

Moniba Rafique¹ and Iqra Rafique²

ABSTRACT

The world is facing a severe and acute public health emergency due to the ongoing COVID-19 global pandemic. How individual countries respond in the coming weeks will be critical in influencing the trajectory of national epidemics. The mortality and morbidity rates reported so far and healthcare demands anticipated, are based on data from China and other high-income countries; marked variations in underlying health conditions of general public, capacity and strength of healthcare systems and vision of policy makers will likely result in different patterns in low income settings. This review is focusing on variations in pattern and outcome of SARS-COV-2 in Asian region in comparison with some neighboring countries. In conclusion, the aged population with co-morbidities has deadly outcome. As asymptomatic carriers are source of transmission of disease to vulnerable subjects, therefore, we need to continuously develop, monitor and implement prophylactic and therapeutic strategies to combat this deadly virus over the next months to years. A possible explanation of different outcome in different country can be ascribed by the presence of comorbidities, average age of population that are infected with virus and the use of some drugs that induce the cell expression of receptors for the virus.

KEYWORDS: Pattern, Outcome, Variations, COVID-19, Pakistan.

INTRODUCTION

COVID-19 Pandemic

After influenza attack in 1918, we are facing another pandemic of novelCoronavirus-2 which is causing severe acute respiratory syndrome (SARS), hence called now as SARS-COV-2. Coronavirus being protein enveloped RNA, attaches to the surface of cell. It hits differently to the different age groups, gender and has proven more lethal to the people with already present medical comorbidities. In this modern era of science and technology where Chinese and American were in the race of winning in the field of artificial intelligence, telecommunication and biotechnology the Coronavirus has hit upon all without discrimination of race, creed and religion. COVID-19 has touched every continent except Antarctica!!!! Back in December, 2019 some viral diseases in China were predicted. After that a series of cases were reported of pneumonia with unknown reasons in the province of Hubei, in Wuhan, China. On 31st December, 2019, a novel Coronavirus was informed to World Health Organization (WHO) of unknown etiology.[1] WHO announced this outbreak as Public Health Emergency of International Concern (PHEIC). Till far by May 10, 2020 Coronavirus has

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hit globally 3,884,434 people including 272,059 deaths.[2]

What is Coronavirus?

Coronavirus are RNA viruses having diameter of 60nm to 140nm. Its surface has spike like projections which appears like a crown under the electron microscope. Hence it is named as Coronavirus.[3,4] The spikes, oligomers of the spike(S) glycoprotein, bind to receptors on host cells and fuse the viral envelope with host cell membranes.[5]Coronaviruses in group 2 also have a hemagglutinin–acetylesterase (HE) glycoprotein that binds to sugar moieties on cell membranes. Curiously, the gene for HE was apparently introduced into an ancestral Coronavirus genome by recombination with the messenger RNA encoding HE of influenza C. The unique RNA-dependent RNA polymerase of Coronaviruses often switches template strands during replication, causing RNA recombination when a cell is infected with several Coronaviruses.[6]

Symptoms of Coronavirus

Based on statistical study by China medical treatment expert group for COVID-19, it was observed that out of 1099 patients, the most common symptoms were fever (43.8% on admission and during hospitalization 88.7%) and cough (67.8). Uncommon symptoms were diarrhea (38%). The incubation period's median remains 4 days. The patients who were admitted to the hospitals have ground glass opacity (56.4%) on chest computed tomography. A total of 83.2% patients were suffering from lymphocytopenia.[7]

Coronavirus Risk Factor

Attack of COVID-19 is usually mild, particularly in children and young adults. Risk of infection may be low, mild or high depending on the exposure.

People over 65 are most likely to get serious illness.[8] It has been observed that risk factors vary from person to person depending upon weakened immune system and having previous medical conditions including heart diseases, asthma, diabetes, liver disease, obesity, chemotherapy for cancer treatment, cigarette smoking, and kidney diseases where dialysis is frequently required.[9] The severity of COVID-19 depends on level of exposure and climatic conditions also. Depending on exposure, a person with strong immune system can also suffer worse symptoms. The transmission of this virus is very fast and it can be transmitted over various ways (Fig: 1).
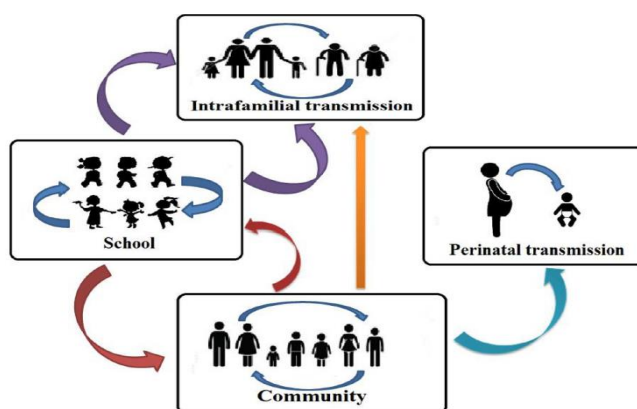

Fig. 1: Transmission of SARS COV-2.

Effect of Previous Diseases

SARS-COV-2 affects vigorously on patients with previous medical history.[10]In a research from Wuhan Pulmonary Hospital of 191 patients of COVID-19, 137 were recovered and discharged from hospital and 54 were declined. Out of 191 patients, 91 (48%) had co-morbidities as hypertension was observed in 58 (30%) patients followed by diabetes in 36 (19%) patients and coronary heart diseases in 15 (8%) patients (Table-1).[11]

Table-1: Demographics and clinical characteristics of 191 patients from Wuhan Pulmonary hospital.

	Total (n=191)	Non-Survivor (n=54)	Survivor (n=137)	p Value
Demographics and clinical characteristics				
Age, years	56.0 (46.0-67.0)	69.0 (63.0-76.0)	52.0 (45.0-58.0)	< 0.0001
Sex	..	..	..	0.15
Female	72 (38%)	16 (30%)	56 (41%)	..
Male	119 (62%)	38 (70%)	81 (59%)	..

Exposure history	73 (38%)	14 (26%)	59 (43%)	0.028
Current smoker	11 (6%)	5 (9%)	6 (4%)	0.21
Comorbidity	91 (48%)	36 (67%)	55 (40%)	0.0010
Hypertension	58 (30%)	26 (48%)	32 (23%)	0.0008
Diabetes	36 (19%)	17 (31%)	19(14%)	0.0051
Coronary heart disease	15 (8%)	13 (24%)	2(1%)	<0.0001
Chronic obstructive lung Disease	6 (3%)	4 (7%)	2(1%)	0.047
Carcinoma	2 (1%)	0	2(1%)	0.37
Chronic Kidney disease	2 (1%)	2 (4%)	0	0.024
Other	22 (12%)	11 (20%)	11(8%)	0.016

Effect of Delayed Hospitalization

In a study the risk factors associated with prolonged viral RNA shedding was observed in 113 COVID-19 patients especially of male sex. The study revealed delay in hospitalization after appearance of symptoms ended in prolonged SARS COV-2 RNA shedding. Patients with longer SARS-CoV-2 RNA shedding duration had slower recovery of body temperature and focal absorption on radiographic images than patients with early SARS-CoV-2 RNA clearance. Male gender, delayed hospital admission and invasive mechanical ventilation were independent risk factors for prolonged SARS-CoV-2 RNA shedding.[12]

Effect of Age & Gender

It is estimated that by 2050, there would be almost 2 billion population comprising older people.Aging itself produces negative changes in immune system and physical strength of a person.[13]Statistical data shows COVID-19 attacks more devastatingly on elderly male as compared to the young one and females according to a survey by The novel Coronavirus pneumonia emergency response epidemiology team, published in CDC Weekly, China. The results of the studies are shown in Table-2.[14]

Almost every kind of immune cells are negatively affected by aging which results in decreased response of antibodies to vaccinations, enhanced risk of infection on exposure to pathogens, more organ inflammation and ultimately weak safeguard system of immune system.[15]For initiation and regulation of inflammatory process, macrophages are basic cells. Metabolic and epigenetic profile of a cell reflects the polarization and activation of macrophages produced by intrinsic or extrinsic conditions.[16,17] In various studies it was observed male are affected 2.33 times more than a female.[18,19]The data in Table-2 also supports the same fact. There is low spread of Coronavirus in neonates, infants and children. The reason for the less infection in this age group is due to guard of fetal hemoglobin. The entry of Coronavirus in cell is inhibited by immature angiotensin converting enzymes (ACE).[20]

Table-2: Patients, deaths, and case fatality rates, as well as observed time and mortality for n=44,672 confirmed COVID-19 cases in Mainland China as of February 11, 2020.

Baseline Characteristics	Confirmed Cases, N (%)	Deaths, N (%)	Case fatality rate, %	Observed time , PD	Mortality , per 10 PD
Overall	44,672	1,023	2.3	661,609	0.015
Age , years					
0-9	416 (0.9)	-	-	4,383	-
10-19	549 (1.2)	1 (0.1)	0.2	6,625	0.002
20-29	3,619 (8.1)	7 (0.7)	0.2	53,953	0.001
30-39	7,600 (17.0)	18 (1.8)	0.2	114,550	0.002
40-49	8,571 (19.2)	38 (3.7)	0.4	128,448	0.003
50-59	10,008 (22.4)	130 (12.7)	1.3	151,059	0.009
60-69	8,583 (19.2)	309 (30.2)	3.6	128,088	0.024
70-79	3,918 (8.8)	312 (30.5)	8.0	55,832	0.056
≥80	1,408 (3.2)	208 (20.3)	14.8	18,671	0.111
Sex					
Male	22,981 (51.4)	653 (63.8)	2.8	342,063	0.019
Female	21,691 (48.6)	370 (36.2)	1.7	319,546	0.012

Diagnosis of SARS-CoV-2:

For early laboratory diagnosis conventional nested and/or real-time reverse transcription-polymerase chain reactions (RT-PCR) have been established to detect viral RNA in the patient that are clinically suspected SARS.Viral RNA detection is important for diagnosis.[21] Though, false-positive results have to be cautiously excluded, particularly samples that are collected from stool or urine. Nasopharyngeal aspirate collected by professional physician/ technician and detection from qualified real-time RT-PCR assays may enhance the method's sensitivity and specificity. Serology is the gold standard for detecting true-positive cases after 1 week of disease onset. We have deficient immunity against SARS-CoV as it is new to us. About 50 percent of pediatric population having disease isunable to develop detectable antibodies specific against SARS-CoV. Weakened humoral immune response in pediatric age may be responsible for these rare phenomena. Some adult patients expired after 4 – 6 weeks of illness before seroconversion occur and in some patient seroconversion can still occur during weeks 7 and 8 of illness. Delayed antibody response is one of the possible reasons of negative antibody detection. Other possible reason is that the antibody response of some patients is lower than the sensitivity of the ELISA test. Therefore, the SARS-Cov diagnosis also depends on clinical manifestations and characteristics on chest radiograph.[22]

Present Situation of SARS-COV-2 in Five Neighboring Countries of Asia

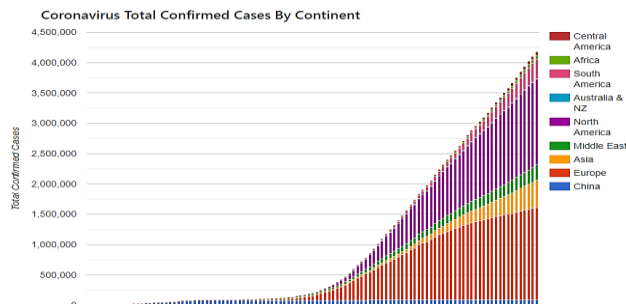Globally Coronavirushas hit upon all the continents. In Asia the confirmed cases are 510,498 (as on May15, 2020) (Fig:2).[23]

Fig. 2: Last updated 15 May 2020 03:00 GMT Data provided by Johns Hopkins CSSE.

Case Fatality Rate (CFR)

It is the proportion of deaths within a defined population of interest. Case fatality rate measures the severity of the disease that causes death. For instance, 60 patients with a particular disease died within 30 days out of 500 population; the CFR for this disease for 30 days is 60/500*100=12%.

The graphical presentation for the case fatality rate (CFR) for all these countries is as follows: (Fig: 3) [24]
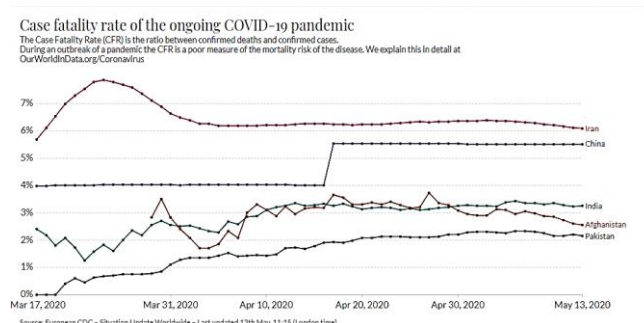
Fig. 3: Graph showing case fatality rate of Iran, China, India, Afghanistan and Pakistan. It shows highest fatality rate in Iran and lowest in Pakistan: Source:www.ouworldindata.org

Table-3: Case fatality and health index of five neighboring countries of Asia.

Country	Population	Confirmed Cases of COVID-19	Deaths due to COVID-19	Recovered cases from COVID-19	Health Index and Quality Index	CFR (Case Fatality Rate)
Iran	83,992,949	109,286	6685	87422	71.1	6.12%
India	1,380,004,385	707,688	2294	22549	44.8	3.24%
China	1,439,323,776	84,011	4637	79198	74.2	5.52%
Pakistan	220,892,340	32087	706	8555	43.1	2.20%
Afghanistan	38,928,346	4963	127	610	32.5	2.56%

Source: www.worldometre.com&www.ouworldindata.org

DISCUSSION

Different countries show different outcome of case fatality rate of COVID-19 outbreak depending upon their geographical and demographic data. By may15, 2020 except china all Countries were showing increase in confirmed cases of SARS-COVID-2. The reason of different outcome of COVID-19 in each country is that there's the "population pyramid" or distribution of age and gender in a given country.[25] And the medical or healthcare capacities of each country also vary. It also depends upon the testing capacity of each country, because knowing and recording exactly who has been infected will directly impact the accuracy of any published figures. In some countries, additional tests are also performed on the corpse and that would affect the statistics as well. Prolonged exposure to air pollution could lead to hyper-activation of an innate immune system and chronic inflammation even in young healthy subjects. Hence, living inindustrial/urban area with high levels of pollutants could lead a person to being more prone to develop chronic respiratory problems and as a result suitable to any infection , as peaks of concentration of fine dust and other pollutants, constitute an unfavorable element in cases of epidemics like COVID-19.The first line of defense of upper airways (namely cilia) is impaired by pollution. The persistent exposure to atmospheric pollutants above the threshold level alter the physiological conditions and lead to a greater predisposition to infection and symptomatic development of the air born disease.[26] The average age of a population is also important factor. Older residents are more prone to deleterious effects of COVID-19 as they often have other comorbidities. It is easier for a virus to overcome a diseased person's immune system as compared to healthy and young one. Immune systems become less effective and weak with progressive age. This would explain a higher prevalence and lethality of a novel, viral agent such as SARS-CoV-2, among a population living in air polluted areas. The cilia and upper airways defenses could have been weakened both by age and chronic exposure to air pollution in elder population living in such region, which could facilitate virus invasion in lower airways. Consequently, defective immune system activated by chronic air pollution exposure may lead to ARDS and ultimately death, particularly in patients having severe respiratory and cardiovascular comorbidities. As the continued exposure to atmospheric pollution could cause permanent modifications of the immune system, and short-term changes in the air quality may not be sufficient to reverse the situation. There are followings reasons that are applicable on all international data available on COVID -19 deaths which also highlight the root causes of statistical variation in different countries: It is scientifically demonstrated that there is existence of substantial correlations between high concentrations of atmospheric particulate matter and pronounced spread of some pathogenic microorganisms , such as the measles virus.[27] The actual number of total deaths from COVID-19 is likely to be greater than the number of confirmed deaths. This is due to limited testing capacity and problems in the designation of actual cause of death.[28]Therefore, there is persistent high fatality rate in spite of dramatically reduction of air pollution levelin lockdown of various region. We cannot ignore other critical factors accountable for the high contagiousness and fatality of this promptly spreading virus.

CONCLUSION

One current theory that appears fairly attractive favors that the chronic use of RAS blockers, antihypertensive drug such as Sartan, causes hyper-expression of the ACE-2 enzyme which is used by the virus as a receptor, that would lead to the worsening of pneumonia following intubation, because the holding of that drug orally would make the virus receptor available. The difference between reported confirmed deaths and total deaths varies from country to county. The reported death figures on a given date does not certainly include the new deaths on that day. This is due to delays in reporting new figures. Difference in counting of COVID-19 death also varies from place to place; at many places deaths in homes are not included in count as it is done in other place.

LIMITATIONS OF STUDY

The statistics of COVID-19 provided in this study are picked online from different statistical websites. A more comprehensive study and analysis is required to extract the useful information and trend from this data.

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CONFLICT OF INTEREST

None to declare

FINANCIAL DISCLOSURE

None to disclose

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Author's Contribution

MR: Conception and design of study, Acquisition of data and Final approval of the published version.

IR: Article drafting and critical revision for final approval of the manuscript.