CAPITAL UNIVERSITY OF SCIENCE AND TECHNOLOGY, ISLAMABAD

Comparison of COVID-19 Severity and Risk Factors between Developed, Underdeveloped and Developing Countries

by

Farhana Hamza

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To My Beloved Parents

Amir Hamza , Nazreen Akhtar

I'm here just because of their blissful love, always showered on me and their continuous encouragement at every step of my life, they taught me to pay respect to humanity and to love al

CERTIFICATE OF APPROVAL

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All Praises and thanks to **Almighty Allah**, The most beneficient and merciful, WHO is the source of all wisdom and knowledge, WHO knows whatever is there in the universe, hidden or evident and is entire source of all knowledge and wisdom to mankind. I offer my humblest thanks to the **Holy Prophet Hazrat Muhammad (peace be upon him)**, who is forever torch of guidance and knowledge for humanity.

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Farhana Hamza

Abstract

The world has encountered to a novel viral disease called the COVID-19 (Coronavirus disease) in December 2019.Since the first cases of the novel corona virus disease (COVID-19) were diagnosed in China, outcomes associated with this infection in terms of total numbers of cases and deaths have varied widely between countries. While some countries had minimal rates of infections and deaths, other countries were hit hard by the pandemic. Countries with highest numbers of cases continued to change over time. This study explores the relationship between risk factors and the incidence of COVID-19 in developed, underdeveloped, and developing countries. Coronavirus disease 2019 (COVID-19) has spread over the globe. However, it is unclear whether the disease has an equal impact on all countries. This research analyses the severity of COVID-19 in developed, underdeveloped, and developing countries by comparing the data of infections and registered deaths between March 2020 and August 2021. Data were segregated, summarized, visualized, and interpreted. The research found that the severity of the disease in terms of infection or death was significantly higher in developed, developing countries in comparison to under-developed countries.

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Abbreviations

ACE2	Angiotensin Converting Enzyme 2
COVID	Corona virus Disease
HCoV	Human Corona Viruses
M	Million
MERS	Middle East Respiratory Syndrome
SARS	Severe Acute Respiratory Syndrome Coronavirus 2
SARS	Severe Acute Respiratory Syndrome
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organization

Chapter 1

Introduction

1.1 Background

An enveloped, having diameter of 60 nm to 140 nm, positive sense RNA, with spike like outgrowth on the edge having appearance like crest under electron microscopy are named as Corona viruses [1, 2]. Severe respiratory infection with none of the reason is started reporting in people of Wuhan, in December 2019. The samples of these infected patients were sent to different laboratory for etiologic investigation. Due to its faster and exceptionally spread, its mortality rate is very high. China notified the outbreak to World Health Organization on 31st December 2019 [3]. As of 30th January, 7736 confirmed cases and 12,167 suspected cases were reported in China and 82 confirmed cases have been identified in 18 other countries [4]. According to the National Health Commission of China, the death rate for reported cases in China as of 4th February, 2020 was 2.1% [5].

Coronaviruses (CoV) are a group of specific, ancient and diverse viruses that infect many mammalian and avian organisms, causing respiratory, gastrointestinal and central nervous system diseases [6, 7]. Coronaviruses are a broad group of viruses that transmit to humans through animal host species (e.g. bats, civets, cats) causing life-threatening respiratory diseases such as respiratory syndrome of the Middle East (MERS) and severe acute respiratory syndrome (SARS [8]. Intermediate hosts were animals, whereas terminal hosts were humans, raw meat consuming activities and the physical closeness between humans and animals, as well as human-to-human contact, are risk factors for a new human CoV outbreak to arise [9].

Coronaviruses are zoonotic, which indicates that viruses are transferred between humans and animals [10]. As intermediate hosts, domestic animals may play a significant role in facilitating virus transmission from one species to human beings [11]. SARS, as defined by WHO, in individuals with a linked travel/contact history and severe acute respiratory symptoms in rare cases [12]. It was determined that MERS-CoV was spread to humans by dromedary camels and SARS-CoV was transferred to humans by civet cats (World Health Organization) Coronavirus [13].

SARS-CoV and MERS-CoV outbreaks both exhibit the rapid transmutation rates that all Virions possess [14]. The developing character and ability of transmission of CoVs from one species to another [15, 16]. A group of infected patients with an unidentified origin were revealed to the WHO on December 31, 2019, in Wuhan, Hubei Province, China [17]. On the same day, February 11, 2020, the WHO declared Pneumonia as Coronavirus disease-19 (COVID-19) [18]. SARS-CoV-2 is the term given to a novel human CoV member that appeared recently in Wuhan, China [19]. The severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) emerged in China at the end of 2019 and rapidly expanded to other countries and continents, forcing the WHO to declare an international national emergency at the end of January 2020 [20]. In March 2020, COVID-19 announced a pandemic [21].

COVID-19 has been reported to be established across over 230 countries worldwide [22]. Some countries have shown limited growth and spread of COVID-19 cases, whereas others have seen extensive community transmission and a virtually exponential increase in infection numbers [23]. Pakistan has also been affected by COVID-19,and the incidence of COVID-19 victims is expanding with each day. To prevent the rise of COVID-19 incidence across Pakistan, the Pakistani government has taken absolutely remarkable steps. Public transportation has been restricted, educational institutes and colleges have been closed, and a general alert has been declared in the nation, as well as national standards to quarantine COVID-19 patients and serious incidents [24]. This is the first time that any such epidemiological condition has been caused by any coronavirus, although several other coronaviruses are already known to exhibit human pathogenicity [25].

SARS-CoV-2 is believed to have evolved in the large seafood and livestock markets of Wuhan, China's Hubei province capital [26]. This is systematic disease that can pass after the lungs with circulation of blood to affect muscles, kidney, liver, spleen and nervous system. Due to immense lung infection in many cases, emergency signs appear including difficulty in breathing due to pneumonia [27].

1.2 COVID–19 Symptoms

This is a new RNA virus strain that has never before been seen in humans [27]. Humans, rodents, dogs, cats, camels, pigs, chickens, and bats are all susceptible to the virus, which can cause fatal infections [28]. Fever, dry cough, dyspnea, weakness, diarrhea, and headache are all signs and symptoms of SARS-CoV-2 infection in humans [29]. Human infections can cause issues such as pneumonia, organ failure, severe acute respiratory syndrome (SARS), and even death [30, 31]. Infection spreads through droplets in the air released by infected patients coughing and sneezing, but infection can also spread through unaffected people before symptoms appear[32]. Infected persons show a variety of clinical symptoms. It is asymptomatic or causes moderate upper respiratory tract symptoms in 80% of cases. However, pneumonia, which is accompanied by fever, cough, breathlessness, and tiredness in 20% of patients, resulting in respiratory failure as well as a variety of other complications, develops in some cases. The severity and outcome of the disease varies with age and other health factors in symptomatic individuals [33].

1.3 COVID–19 Transmissions

The SARS-CoV-2 sequence is alike to a bat-isolated coronavirus, so the postulate is that SARS-CoV-2 comes from bats that then mutate and infect humans

[34].Transmission of the virus is observed to be quick in both direct and indirect paths, including as respiratory droplets, direct contact with an infected individual, and on surfaces and objects [35]. Infected droplets can disperse 1.2 meters and deposit on surfaces; the virus can remain on surfaces for days in favourable air conditions, but conventional disinfectants such as sodium hypochlorite, hydrogen peroxide, kill it in less than a minute [36]. There is currently no indication that COVID-19 is transferred through food. The virus can't replicate in food since it needs an animal or human host to do it [37].

The transmission of coronavirus from animal to human was made possible by human involvement in nature, wildlife commerce, and especially consuming wild animals. In this scenario, the coronavirus in the bat was transferred to humans after being transmitted to the intermediated host and a slight alteration in the virus's transmission capacity [38].

In China, the virus spread quickly among humans, and it has since spread to over 200 countries. The number of affected people, the speed and ease with which the infection is transmitted, and the clinical severity of the infection and the spread of zoonotic viruses[39].Infected persons transfer the particles through their mouths to others when they come into close contact[40].

1.4 Vulnerable People

Solid organ transplant recipients, persons with cancer, respiratory illnesses, atypical diseases, or congenital metabolic defects, people on immunosuppressive treatments, and pregnant women with severe cardiac disease are among these populations [41]. Before getting any infection immune system play vital role in human health system to keep them healthy, while it becomes open invitation for various diseases like cancer, COVID-19, diabetes if immune system response will be weak, low or damage [42].

The rapidly spreading Corona virus disease 2019 (COVID-19) has generated a lot of concern in the epidemic's treatment and prevention [43].There is no approved treatment for COVID-19, but a number of clinical trials have been started, including Hydroxychloroquine, Remdesivir, tocilizumab, anesthetics, immunoglobulin, and convalescent plasma. Patients who are infected are stressed and attempt to avoid social contacts. They may not even reveal their true symptoms for fear of disease-related stigma. The likelihood of community transmission increases as a result of this. Frequently empathic dialogue with such patients can aid in the reduction of stigma, the facilitation of social support, and the provision of basic necessities [44]. Because stigma may derail communal cohesiveness, a clear description of the pandemic can aid in reducing confusion, avoiding misconception of data, and intervention programs.

At present, the primary source of transmission is the spread of SARS-CoV-2 from humans to humans, so the spread is more powerful. The virus has been found in stool and water sources, with subsequent transmission by aerosol feco- oral route [45]. Human behaviour habits influence the rates of contact between infected and vulnerable individuals. Moreover, personal hygiene is essential to preventing infectious disease spread. SARS-CoV-2 can only survive three hours in aerosols, although it can live for days on other surfaces. On copper surfaces, this virus is believed to last for four hours, twenty-four hours on cardboard, forty-eight hours on stainless steel surfaces, and seventy-two hours on polypropylene plastic surfaces[46]. More recently, the virus's ability to spread through the air has been reported [47].

1.5 Incubation Period of SARS-CoV

SARS-CoV was predicted to take 2 to 10 days to incubate, with a maximum of 14 days [42]. Furthermore, the time from the onset of COVID-19 symptoms to mortality ranged from 6 to 41 days, with an average of 14 days [43]. This period varies depending on the patient's immune system and age, with 70-year-old patients experiencing a shorter period than younger people [43, 44].SARS-CoV-2 may infect the lower respiratory tract in immunocompromised patients and in older patients with underlying health conditions, leads to severe pneumonia [45].

1.6 Precautions and Prevention for Covid-19

Hands can become infected during a variety of tasks, and the virus can then spread to the eyes, nose, or mouth, gaining access to bodily fluids [46]. One of the ideal ways to inhibit illness is to keep less prone to the virus. Hands should be washed often with detergent and water for at least 20 seconds, and the nostrils and face should be covered with any form of mask, by putting elbow while coughing and sneezing, keep distancing about 1 to 3 meter with infected persons, stay at home avoid gathering and touching your eyes and nose with un-washed hands and self-isolate immediately in case of feeling unwell [47].

It is the initial stage in the preventive process. Whereas hand hygiene program are successful in decreasing disease transmission, the level of protection provided varies depending on the environment and community compliance. Hands must be washed often with soap (as prescribed by the WHO), or with an alcohol-based hand-rub and then air-dried [47, 48]. If the immune system response is weak, poor, or damaged, it becomes an open invitation for diseases such as cancer, diabetes and COVID-19 [49].

The WHO and the Centers for Disease Control and Prevention have suggested hand washing with soap and water before and after coughing/sneezing, attending a public venue, physical contact surfaces outside the residence, and caring for an infected individual as well as before and after meal, in the context of Coronavirus disease 2019 (COVID-19). Alcohol- based sanitizers can be utilized when soap and water aren't accessible [49]. As per the WHO, consistent physical activities offers many medical benefits, including lowering blood pressure, weight maintenance, and lowering the risk of type 2 diabetes, stroke, heart disease, and different malignancies, all of which are factors that can enhance vulnerability to the Acute respiratory infection outbreak [50]. The infection of COVID-19 spreads among individuals through respiratory droplets and interaction courses. The droplets transmission occurs where an affected COVID-19 person is coughing or sneezing openly in public or other surrounding environment. This enhances the risk of getting the virus by normal persons through mucosae (mouth and nose) or conjunctiva (eyes). Similarly the transmission may take place through fomites nearby the infected person. The COVID-19 virus can transfer the surfaces and objects used by the infected person to others through direct contact with the infected person or indirectly. It involves the presence of microbes inside the nucleus of the droplet, which are usually known to be particles smaller than 5 μm in diameter [57].

Excessive stress, disturbance of normal routines, limited gym access, workplace closures, and restricted physical exercise can all have negative impacts on people's general health and well-being, even if they are physically active on a regular basis. As a result, physical exercise and relaxation are recommended at this period since they promote awareness and maintain one's health. The WHO advises 150 minutes of moderate-intensity 75 minutes of vigorous intensity physical exercise each week, or a mix of both [58]. As per the WHO, consistent physical activities offers many medical benefits, including lowering blood pressure, weight maintenance, and lowering the risk of type 2 diabetes, stroke, heart disease, and different malignancies, all of which are factors that can enhance vulnerability to the Acute respiratory infection outbreak [59].

Due to frequent human interaction, the disease spread from China to other parts of the world, resulting in a deadly outbreak and a fast spike in the proportion of affected individuals [60]. Infected persons in self-isolation must stay away from the public to limit the occurrence of illness to others. They are advised to seek medical help as needed and to keep in touch with doctors because the virus's intensity can have devastating effects [61].

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COVID-19 can live in the air for a long time and be transmitted for distances of about 1 m to humans. World Health Organization recommends precautionary measures to control the transmission of COVID-19 disease among people i.e. Use of Face masks, Sanitizers, Gloves etc [51].

1.7 COVID-19 Properties and Phenotype

SARS corona virus 2 (SARS-CoV-2), a virus which is a causative agent of COVID-19, is a current beta corona virus (with a large RNA), that shares 80 percent of the sequence similarity with the previous SARS outbreak in 2003. The COVID-19 virus surface have many spike glycoproteins (s) which consist of homotrimers protruding far from the surface of virus, that give it a halo like shape. The spikes protein allows the virus to engage its target cell reporter, angiotensin converting enzyme 2 (ACE2).There are two subunits of s protein, S1 and S2 which facilitate the internalization of the target cell. Due to many characteristics of SARS-CoV-2 which make a more potent infection virus than SARS-CoV.

Perhaps the most important receptor binding domain SARS-CoV-2 preserved the entire structure of the SARS-CoV binding domain, which included 8 of the 14 residues being absolutely similar. However, the three- dimensional form of the SARS-CoV-2 binding site shows that it is much more compact. Increased binding stability and hence increased ACE2 binding interactions [65]. The second difference is that SARS-CoV-2 has a polybasic (furin) (site into which the increasing incidence of S1 / S2 protein is inserted at the border. This furin binding site is very rare and it improve the ability of the cells to internalize into the cells and it shares features with recent extremely pathogenic viruses, including avian influenza. In general, RNA viruses are prone to higher mutation rates. Viruses are expected to mutate during the epidemic. In order to facilitate their transmission viruses tend to adopt to local environment [66].

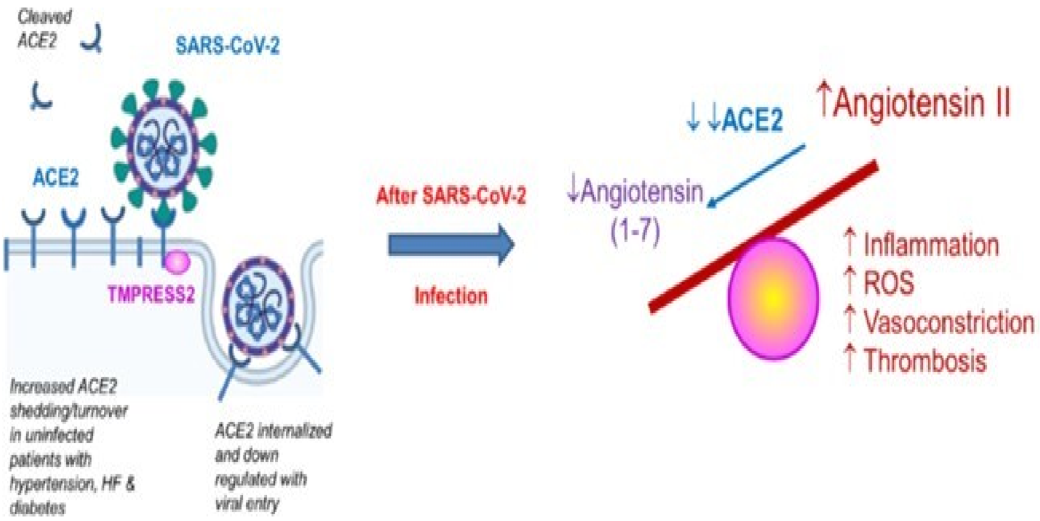

FIGURE 1.1: SARS-Cov-2 Uses the ACE2 as a Internalization Receptor, that is Promoted by TMPRSS2 Protease [65].

1.8 Classification of COVID-19

CoVs belong to the Nidovirales order, which is a subfamily of the Coronaviridae family, according to the International Committee on Virus Taxonomy [55]. In the 1960s, coronaviruses (CoVs) were discovered and classified as Coronaviridae ,is the vast family in the Nidovirales order. Thousands of people have been infected with the virus thus far, according to reports [56]. The Orthocoronavirinae and Torovirinae subfamilies belong to the Coronaviridae family [9, 57]. There are four genera in the Orthocoronavirinae subfamily: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus [11, 58]. In mammals, including bats, alpha and beta coronaviruses disperse [59]. Gamma coronaviruses mostly infect birds, whereas delta coronaviruses affect both birds and mammals [59, 60]. Human-infecting coronaviruses belong to two of these genera (alpha and beta coronaviruses) (HCoVs) [61]. HCoV-229E and HCoVNL63 are the alpha coronaviruses infecting humans and HCoV-HKU1, HCoV-OC43(MERS-CoV, SARS-CoV)and SARS-CoV-2 are the beta coronaviruses infecting humans [62].

Prior to 2019, only six CoVs were known to infect humans and cause respiratory diseases. Four of the six human CoV infectious diseases (HCoV-229E, HCoV-OC43, HCoV-NL63, and HKU1) cause only mild upper respiratory disease, while others frequently cause serious infections in babies, small children, and the elderly [63]. The current pandemic in 2020, named coronavirus disease-2019 by the WHO, is caused by another novel coronavirus, now known as SARS-CoV-2 (COVID-19). The ultimate origin of SARS-CoV-2 is believed to be bats with an unknown intermediary host (perhaps pangolins) that spreads the virus to humans [64, 65]. Animal CoVs are suspected to promote severe animal diseases and may be to responsible for the economic loss of pets and birds [66-68]. Despite the fact that these CoVs can infect humans and spread from person to person [69].

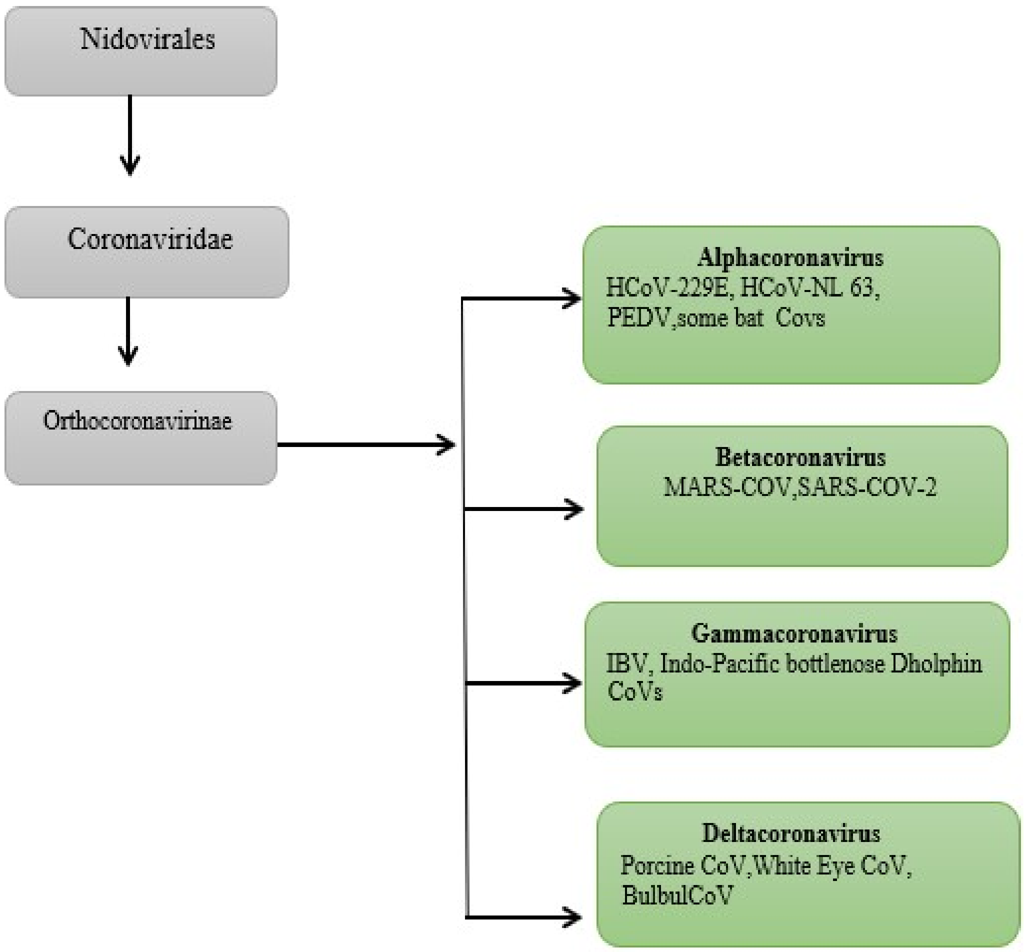

Figure 1.2: Classification of Different Types of Coronaviruses

1.9 Coronavirus Structure

CoVs are globular positive single-stranded RNA viruses, like the recently discovered SARS-CoV-2, distinguished by spike proteins extended from the surface of the virion[82]. The cylindrical structure of the viral particle along with the spike projections, due to the presence of the virus as a royal crown under the electron microscope, led to the name coronavirus from the Latin word corona meaning "crown" [83].

In some betacoronaviruses, CoVs are enveloped viruses (the envelope is a lipid bilayer originating from the host cell membrane) with a viral structure primarily made up of structural proteins such as spike (S), membrane (M), envelope (E) and nucleocapsid (N) proteins, and hemagglutinin esterase (HE) protein [84].

The S, M, and E proteins are all located in the viral envelope, however the N protein interacts with the viral RNA and forms the nucleocapsid in the nucleus of the viral envelope. [85]. The S protein is a highly glycosylated protein that forms homotrimeric clusters on the surface of the viral envelope, mediating viral entry into the host cells[86].

Each homotimeric S protein monomer appears in some CoVs as two subunits (S1 and S2) on the viral particle due to S protein cleavage by host furin-like proteases during viral replication [87]. The M protein is one of the most essential proteins in the structure of the virus, it remains in greater amounts than any other protein in the viral particle, as compared to the E protein found in small quantities within the virus [88].

Due to the fact that M protein gives the virus its shape and is essential together with E protein in the interpretation of the virus assembly and the production of mature viral envelopes, the E protein also helps in the release of viral particles from host cells, in response to other functions [89]. The N protein binds the viral RNA and is essential during viral assembly to package the viral RNA into the viral particle[90, 91].

1.10 Coronavirus Cell Entry Mechanisms Mediated by the Viral Spike Protein

Coronavirus can enter human body cells through an amazing mechanism explains as; the spike (S) protein of coronavirus attaches the special receptors found on several human cells, containing in the lungs called angiotensin converting enzyme 2 (ACE2) receptors, that allow virus to enter the cells. The host proteases trypsin and furin performing the proteolytic cleavage of Coronavirus S protein among the S1 and S2 subunits, whose sites are located on the boundary. The separation of the S2 domain at the S20 site takes place at a later point for the release of fusion peptides.

This phenomenon triggers the binding process of the membrane. Antibody research can find molecular levelling sustenance that can manipulate the organizational content of the binding region that is present in the receptor of the angiotensin-converting enzyme 2. The provided procedure could thus ruse a therapy to obstruct the entry of the virus. Human cells can absorb the virus by endocytosis, where, unlike other viruses, COVID-19 exhibits a special 3-step process involving membrane fusion; mediated configuration in glycoprotein Spike(S) and receptor binding; cathepsin L proteolysis by intracellular proteases; and the third step is to activate further membrane fusion pathways within endosomes [92].

After that, the endosome releases the virus to the cytoplasm, where the proteasomes continue to uncoated viral nucleocapside (N), that hydrolyzes endogenous proteins and is also able to degrade exogenous proteins such as the nucleocapsid protein SARS [93]. The target cells receptor via its S1 subunit on the surface and the host proteases are attached to the Spike and then the fusion of the host target membrane virus via the S2 subunit at low pH is expected [94].

Lastly, a single stranded RNA, the genetic material of the virus, is completely released into the cytoplasm, where replication and transcription processes take place to form a replication-transcription complex (RTC), which is composed of non-structural proteins (nsp) encoded in the viral genome. The complex of replication-transcription is alleged to be an induced double membrane structure in cytoplasm infested cells [95]. In the open, reading frame 1a / b (ORF 1a / b), the positive RNA genome can be converted into replica proteins. In the cyto-plasm, M, S and E (structural viral proteins) are produced, introduced into the endoplasmic reticulum and then moved to the intermediate ERGIC (endoplasmic reticulum-Golgi) compartment. The N protein also creates nucleocapsids through the encapsidation of repeated genomes in cytoplasm, resulting in the shifting of self-assembly inside the ERGIC membrane into new virions. In order to infect the other cells, the new virions packaged in smooth walled vesicles are now secreted by the exocytosis process. The tension of viral development in the endoplasmic reticulum, meanwhile, eventually contributes to necrosis of the cells [96].

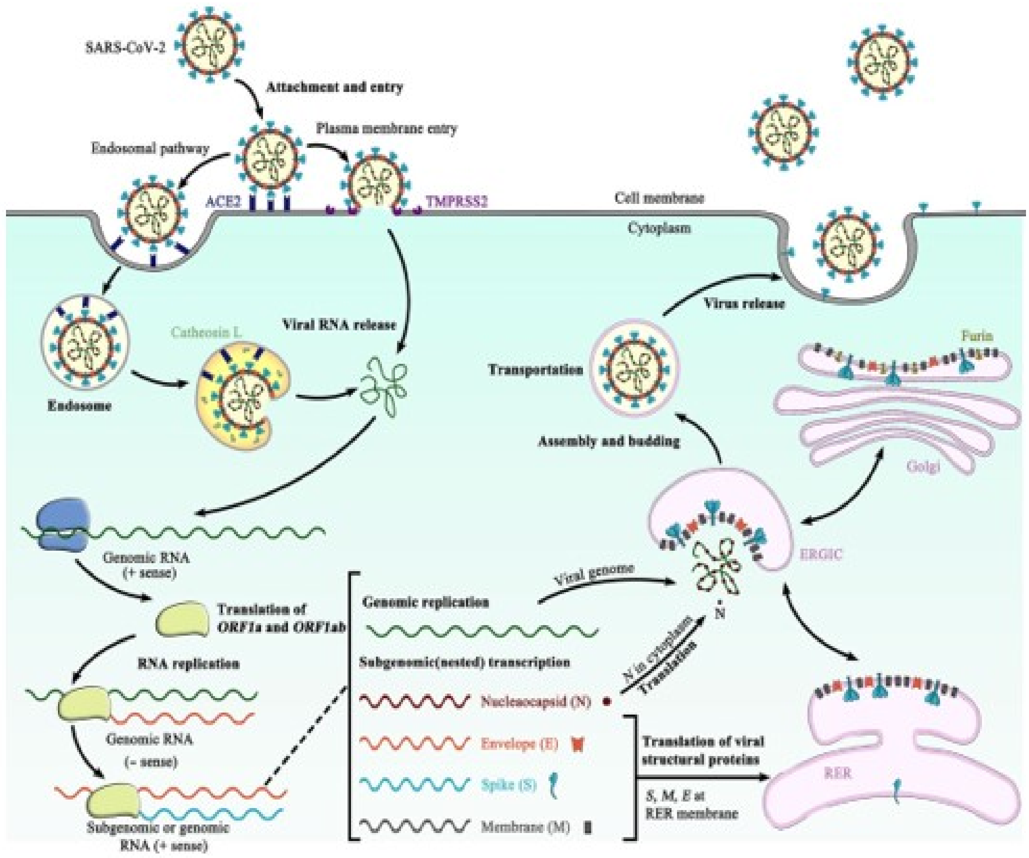

Figure 1.3: Mechanism of Corona Virus Entry [97]

1.11 Etiology of COVID-19

COVID-19 is a member of the family of Beta coronavirus. The results of the phylogenetic study revealed that this infection entered a subgenus similar to that of COVID that triggered the 2002-2004 episode of (SARS), namely Sarbecovirus [69]. On this basis, the name SARS-CoV-2 was suggested by the International Committee on the Taxonomy of Viruses [70].

1.12 Coronavirus Main Reservoirs and Hosts

It is necessary to decide the cause of initiation and transmission in order to establish prevention systems to control the disease. Scientists have previously concentrated on raccoon, canines and palm. Civets were the primary source of infection in SARS-CoV reservoirs, but only the sample taken from civets Positive findings have been seen on the food market for The role of viral RNA, suggesting that civet palms might well be secondary hosts [71].

In 2001, the sample was taken for antibodies test from healthy people from Hong Kong, so the result revealed that antibodies formed against SARS-COVID were 2.5 percent frequency levels. These indicators indicated that SARS-COVID might be running in people before triggering the epidemic in 2003 [72]. Rhinolophus bats have also been later found to have antibodies to SARS-CoV, revealing bats as a viral replication vector [73]. COVID'S Middle East Respiratory syndrome (MERS) first rose in Saudi Arabia in 2012 [74].

MERS-COVID also links to beta-COVID and camel as a zoonotic. or primary host origin [75]. MERS-COVID has also been recognized in Pipistrellus and Perimyotis bats [76]. In the ongoing study that bats are the primary host and mode of communication for infection. At first, a group of researchers said that snakes were imaginary hosts, but after discovering the genomic similarities of the current coyote with bat-like infections such as storks, it was claimed that bats could be important water reservoirs, not snakes [77].

1.13 Problem Statement

The COVID-19 is a global problem which is spreading almost all over the world, so, in the light of universal problem, this study is designated to investigate and compare the COVID-19 severity rate, risk factors, and casualties rate in various developed, under developed and developing countries.

1.14 Aims and Objectives

This study requires following objectives:

- To calculate the severity rate of COVID-19 in the intended countries and compare the severity rate in various developed, under developed and developing countries.
- Assessment of spread of COVID-19 risk factors in developed, underdeveloped or developing countries.
- To determine prevalence of COVID-19 and their recovery ratio in various developed under develop or developing countries.
- To compare number of tests with cases (1M population) and mortality rate in various developed, developing and under develop countries.

Chapter 2

Literature Review

2.1 Comparative Study of Beginning and Spreading of Coronaviruses

A provincial health committee in Wuhan, Hubei province identified a cluster of pneumonia cases with an unknown origin in December 2019. For the first diagnosed patient, the symptom onset date was December 1,2019 [107]. With strong evidence linking the epidemic to the Huainan Seafood Wholesale Market in Wuhan, the market was shuttered on January 1, 2020. Individuals may find it hard to adapt with their distress, which can lead to a variety of psychiatric problems like depression, anxiousness, frustration, and discouragements [108].

The virus was identified as a novel coronavirus on January 7, 2020 [109]. Thailand identified the first incident outside of China on January 13, 2020 [110]. In addition to China, cases of COVID-19 have been reported in Thailand, South Korea, Japan, Taiwan, Australia, Iran, and the United States. As of March 10th, 2020, over 114,430 COVID-19 cases had been identified in 115 countries around the world, according to the Worldometer. COVID-19 infections are most severe in South Korea and Iran (outside of China), while the European countries with the most severe outbreaks are Italy, France, and Spain [105].

The total number of cases has surpassed 12M by early July 2020, with over 500,000 casualties. While the United States had more than 3M instances, Brazil had over

1.7M, India had over 0.7M, Russia had over 0.7M. With only 83,000 cases reported, China, a heavily populated nation where the COVID-19 was initially discovered, has been slightly less afflicted than some of the other world countries [105]. The death rate among the elderly in care centers is significantly greater than the rate among the elderly in the general population. This could be attributed to the fact that disease spreads more quickly among this vulnerable population because they are all isolated in the same location[112]. According to reports, elderly people in certain Countries in Europe were abandoned in nursing homes, with some being discovered dead in their beds [113].

The current pandemic of coronavirus occurred in China's Wuhan city, which is known as the 2019-nCoV infection, originally named SARS-CoV-2 or COVID-19 outbreak [85, 86]. The Chinese population in 2003 Guangdong Province became infected with a sever acute respiratory syndrome (SARS) virus, As a member of the Subgroup on Beta Coronavirus the virus has confirmed and called SARS-CoV [87]. Affected patients showed signs of pneumonia with scattered ovular injury that escalated to acute respiratory distress syndrome (ARDS). In Guangdong, China, SARS first rose and then spread exponentially across the world with more than 8,000 infected individuals, 776 expiring. In 2012, after 10 years, a few Saudi Arabian nationals were hospitalized with another COVID infection. The WHO described in detail that MERS-COVID affected more than 2428 people and 838 passersby [88].

On the basis of sequences analysis, the virus is considered as a novel coronavirus. Similarly other evidence such as genetic sequence also proved it is the viral infection. In the beginning it was considered this infection is due to the use of stuff available in seafood market in Wuhan city of china, but later other cases has reported, the investigation showed that there were no history of contact to the seafood market from this observation it is concluded, there is great chances of human to human transmission, as it mentioned in more than 100 countries in the world [89].

Two major coronavirus infections, SARS-CoV (2002) and MERS (2012), have arisen during the last two decades [79]. The third coronavirus to appear in the human population has been SARS-CoV-2 or COVID-19, threatening the globe overall [80]. Travel poses the greatest risk of transferring COVID-19 over the world, as it is responsible for the disease's regional and global spread [81].

2.2 COVID -19 Case and Death Rates are Influenced by a Variety of Factors

The risk factors related with the outbreak's transmission routes, severity, and death risks were unknown at the beginning. Several research have been carried out to better understand the disease's prognosis, while there is still a lot of confusion about viral shedding, risk of transmission, and disease severity remains high [82]. Individual-level factors such as sociodemographic factors, behavioural characteristics, and pre-existing medical complications have been noticed to influence vulnerability to infections, the risk of becoming severely infected, and the possibility of dying[83, 84]. For many people, the COVID-19 outbreak is a once-in-a-lifetime experience. Such a traumatic scenario might affect people's mental health, creating dread, uncertainty, isolation, or discrimination [85].

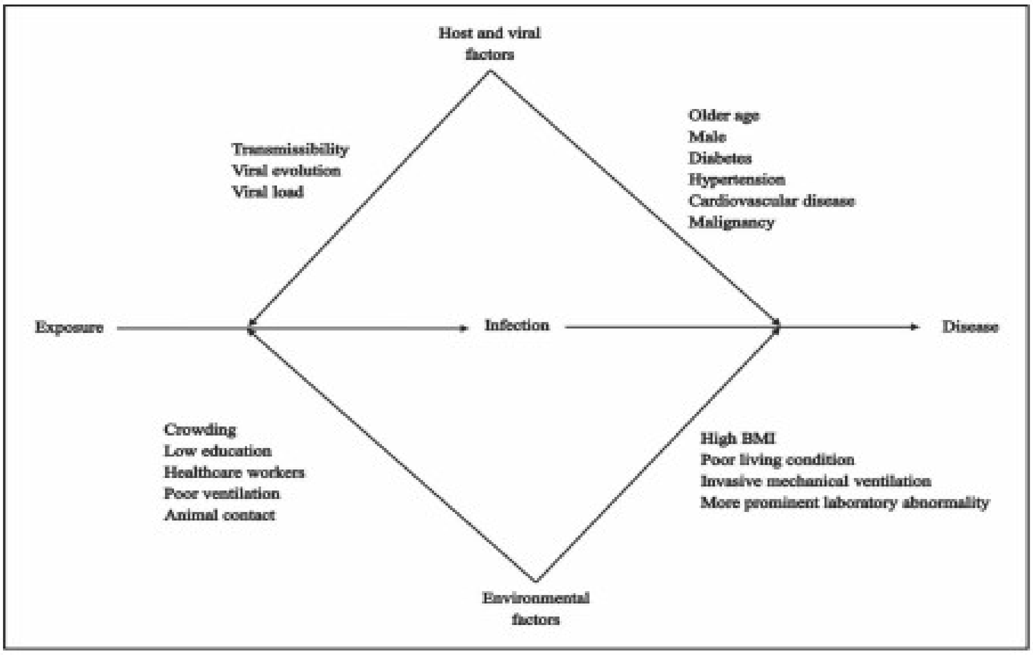

FIGURE 2.1: Risk Factor for COVID-19 [118].

2.2.1 Age and Sex

COVID-19 levels rise with age, suggesting ageing a risk factor for the disease [86]. Elderly people have a higher mortality rate [87]. As a result of aging's negative effects on lung function and the delayed activation of the acquired immune system, the virus can become more replicated, resulting in more pro-inflammatory responses and an increased risk of death [88].

Initial findings from China indicated that COVID-19 mostly infects the old, with those aged 60 and up being the most susceptible [74]. COVID-19 has been linked to significant death rates in older male patients with numerous metabolic comorbidities, according to reports from China and Italy [89].

By global standards, Africa continues to have the lowest number of persons infected with the virus, which may be due in part to the population's youthful age structure and in part to poor infrastructure for large-scale testing [90]. The impact of sex is clear, as the virus affects more men than women. The male sex is one of the risk factors for COVID-19 because men are more susceptible to SARS-CoV-2 [72].

According to study, males and female's immunological responses to COVID-19 virus and inflammatory illnesses differ dramatically. Women have become less vulnerable infections than men due to differences in innate immunity, steroid hormones, and chromosomal traits. In comparison to the immune-enhancing hormone, estrogen, testosterone has an immunosuppressive effect [91].

Women with two X chromosomes have a stronger immune system, even if one is dormant. When compared to male sex, the immune modulatory genes expressed by the X chromosome result in lessen viroin amount and inflammation, as well as a larger amount of CD4 + T cells with better immunological response.

Women also generate more antibodies, which last longer inside the bloodstream [92]. In Iceland, women and children under the age of ten were shown to be less vulnerable to COVID-19 infection [103].

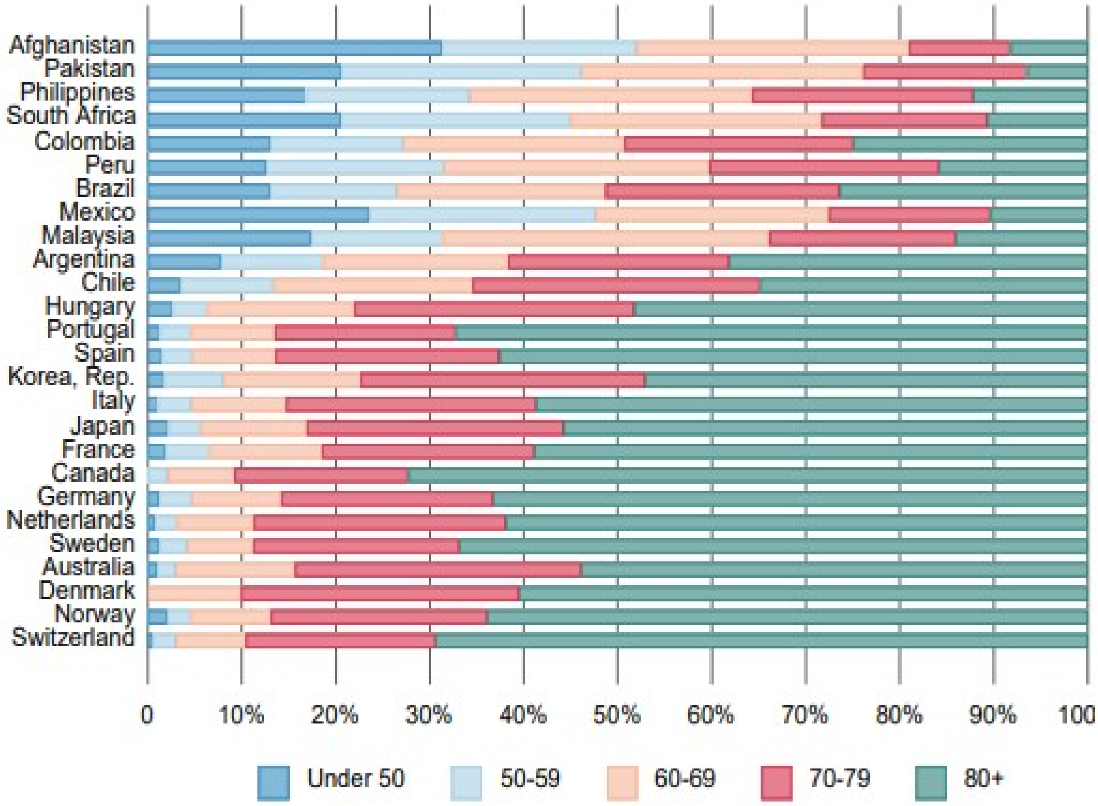

FIGURE 2.2: Distribution of COVID-19 Deaths by Age Group for Each Country[104]

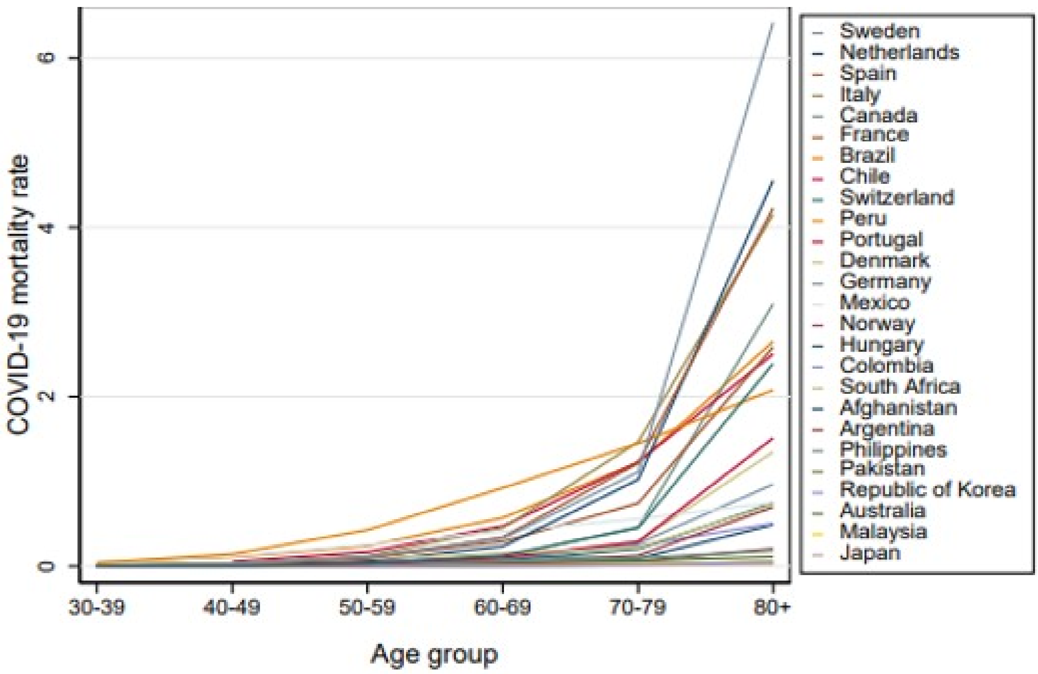

FIGURE 2.3: Unnormalized COVID-19 Mortality Rates (Deaths per 1000 Population) by Age Group and Country[127].

2.2.2 Children with COVID-19

It has reported only 1-2% of children and young people affected by COVID-19 . Children of all ages were affected by COVID-19, although there was no significant difference in sex. Though the clinical presentation of childhood cases of COVID-19 was usually less serious than that of adult patients, young children, particularly babies, remained vulnerable to infection [128].

2.3 Underlying Health Condition Poses Higher Risk of Death

The most significant risk factor for severe COVID-19 outcomes is age. In the United States, there are approximately 54.1 million people aged 65 and up; more than 80% of COVID-19-related deaths occur in this age group [94]. COVID-19 does not affect all populations in the same way, according to studies. As the number of underlying illnesses in an individual increases, so increases the possibility of severe COVID-19 [95]. Vulnerable populations, such as children and pregnant women with severe cardiac disease, who are at high risk of severe sickness from COVID-19 because of a pre-existing health condition [96].

2.3.1 Diabetes

It has been found that older patients with diabetes are at higher risk of extreme COVID-19 and mortality. Diabetes and different comorbidities are important measures of morbidity and mortality in COVID-19 victim [97]. Diabetes is a major metabolic disorder in the entire globe. It is a condition that causes the immune system to deteriorate. Diabetes is becoming more prevalent over the world, particularly in developing countries. Diabetes has been linked to an increased risk of COVID-19, according to studies [98].

Diabetic patients have a lower response to treatment and a greater mortality rate (14 % vs 31 %) (p=0.0051). Because innate immunity is compromised in diabetic individuals due to high blood glucose levels, glycosylation of cytokines affects the function of cytokines produced by type I helper T cells (Thl). Patients are predisposed to COVID-19 by pulmonary microangiopathy, tissue damage induced by oxidative stress in hyperglycemia, and lung inflammation, which also occurs in tuberculosis patients [99].

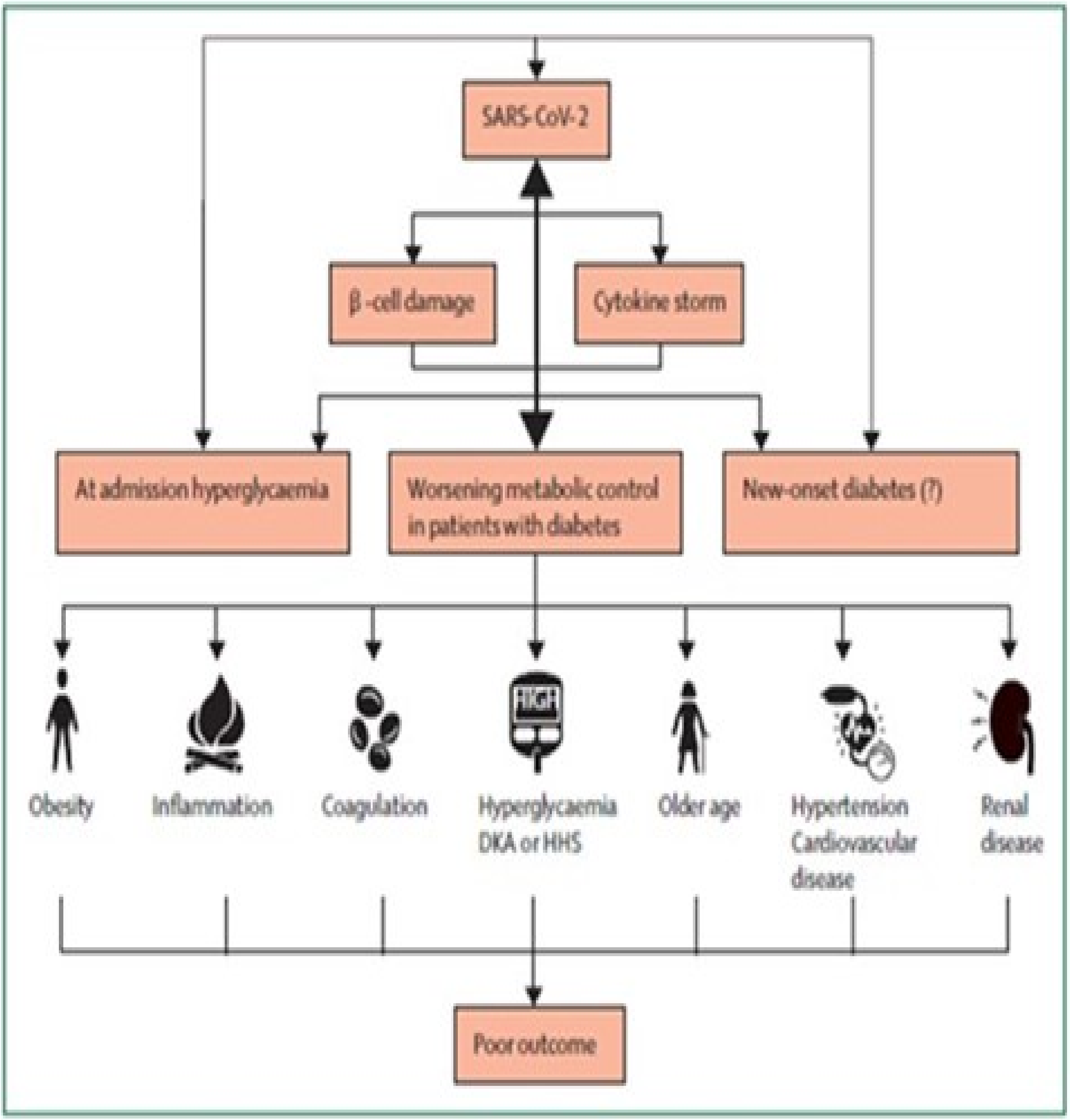

FIGURE 2.4: Interactions between Diabetes and COVID-19 [98]

2.3.2 COVID-19 and Hypertension

Hypertension is frequently a genetic illness that is amplified by external factors like lifestyle, nutrition, and stress.

Table 2.1: The Absolute Number of Deaths of Patients with Underlying Conditions was Actually Higher. Coronavirus Age, Sex, Demographics (COVID-19) –Worldometer [135]

Country/City **USA(New York)**	Age	**Number of Deaths Due to COVID (14,april, 2020)**	**with Underlying Condition(Diabetes, Lung Disease, Cancer, Hypertension)**	**without Underlying Conditions**
	0 to 17 years of age	3	3	0
	18 to 44 years of age			
	45 to 64 years of age	1,581	1,343	59
	65 to74 years of age	16,83	1,272	26
	66 to74 years of age	3,263	2,289	27

Blood pressure rises with age, mainly due to a blood vessel disorder such as atherosclerosis. COVID-19 and its death rate are both high in these people, according to researchers. The virus was believed to be linked to the renin-angiotensin-aldosterone system (RAAS) via ACE2 receptors because SARSCoV-2 penetrates cells via ACE2 receptors. As a result, angiotensin-receptor blockers (ARBs) like losartan may be linked to increased ACE2 expression in COVID-19 vulnerability. High blood pressure appears to enhance COVID-19 mortality by reducing oxygen delivery and impairing lung function [100].

2.3.3 Cardiovascular Disease

Patients with cardiovascular disease are more sensitive to COVID-19. The expression of ACE2 in myocytes and vascular fibroblasts might be the reason. The existence of the virus in cardiovascular cells can cause damage and trigger the infiltration of mononuclear inflammatory cells into the heart tissue, aggravating the infection [102].

2.3.4 Cancer

About 15,590 cases of confirmed corona virus disease (COVID-19) were reported in 2019 in 18 patients with a history of cancer. It is stated that COVID-19 cancer patients are much more likely than people with no cancer history [103]. Cancer is one of the most major co-morbidities that increase the risk of COVID-19, according to a recent study comprising 1,590 COVID-19 positive patients in China. Cancer is also believed to promote COVID-19 pathogenesis, according to the WHO [104].

Cancer is characterized by inappropriate cell proliferation caused by mutations in DNA, particularly in damaged DNA repair genes and proto-oncogenes. Cancer patients are more susceptible to infection than non-cancerous individuals because malignancy and treatment processes such as chemotherapy decrease immune cell growth and proliferation, resulting in an immunosuppressive state in the body [127]. As a result, cancer patients are more likely than non-cancer individuals to develop COVID-19.COVID-19-positive cancer patients are more likely than non-cancer patients to develop a crisis state (8 percent vs 39 percent) ($p=0.0003$) [140].

2.3.5 Risk of COVID-19 by Blood Group

Several risk factors, including age, sex, and multiple chronic and complex diseases and laboratory results, are reported for COVID-19 inflammation, ill health, and death. They discovered a relationship between ABO blood group type and infection in a study performed on COVID-19 patients in Wuhan and Shenzhen.7, 770 COVID-19 patients examined at the New York Presbyterian (NYP) hospital, we concluded that blood B group is more susceptible, and O blood group is less susceptible [141]. It has been revealed that blood group and COVID-19 have a linkage. Blood O group is considered is a protective against the SARS-Cov-1 [142]. Other report mentioned that blood group O have no such link with COVID-19 while blood group A was more prone to COVID-19 [143]. Another investigation has been done on the ABO blood group system; they found different association of blood group with COVID-19. Blood group A more prone to COVID-19 than blood group O. It is concluded that ABO system is a somewhat associated with COVID-19 and it can be used as biomarker for COVID-19. The susceptibility of COVID-19 to blood group system were studied in Hong Kong [31]. A study has conducted on blood group system, they compare non O blood group to O blood group system they found that having blood O group is less chances of getting infection than others blood group types. But it needs further studies to find the very basic cause of ABO system and COVID-19 association [144].

2.3.6 Older Age

SARS-CoV-2 can infect individuals of all ages, however it is significantly less common in children under the age of 14 and generally goes unnoticed in young adults [133]. COVID-19 levels rise with age, making ageing a risk factor for the disease [134]. Elderly people have a greater mortality rate than younger persons. Coughing and sneezing from other infected family members and acquaintances or hospitalizations are the most common ways for older persons to become infected in the population [135]. As a result of aging's negative effects on lung function and the delayed activation of the acquired immune system, the virus can become more replicable, resulting in more proinflammatory reactions and an increased risk of death[136].

2.3.7 Gender

Men are more susceptible to SARS-CoV-2, making male gender one of the COVID-19 risk factors[137].Because this is a community-acquired disease and men are more likely to be out of the house owing to working conditions and more present in the community in some countries, such as Iran, it appears that they are more likely to become infected. Men and women have different behavioural patterns, especially when it comes to health advice, and they pay less attention to the issue of social separation. This is an issue that should not be disregarded. A disintegrin and metalloprotease 17 (ADAM17) is a protein that is more abundant in the lungs and liver and is involved in the shedding of surface proteins like ACE2[138].Increasing ADAM17 increases dropping and thus the amount of soluble ACE2, which helps to prevent SARS-CoV-2 from infecting cells. Estradiol, which is abundant in women, boosts the expression and activity of certain genes.ADAM17 increases soluble ACE2 in women, which may be one of the reasons for the lower prevalence of COVID-19 in women compared to men[139].

2.4 Environmental Risk Factors

2.4.1 Travel and Tourism

Travel is the first and most visible factor influencing the disease's spread. Most countries imposed quarantines to prevent the virus's spread, with the primary parameters being travel restrictions and social isolation. The origination and spread of a pandemic is influenced not just by the infective agent's virulence and transmission pattern, but also by population migration. Before the pandemic, the busiest and most heavily travelled travel routes on the world were in Europe, the United States, and China. This applies to both internal and international travel inside and between selected countries [152].

Tourism is very necessary for a country's economy as it not only brings investment it makes a country's image in international market. Countries like Switzerland are earning a lot from tourism. Tourism is connected to the spread of COVID-19. Tourists are the people who spread the whole world. That is, if an individual from China visited some other country, that individual could spread the corona virus throughout the whole country. This situation happened in the first 2 months of the year, as governments were not aware of the issue and unknowingly, tourists caused the spread of the corona virus, and countries welcomed corona with a smile [153].

Humans are a vector of transportation for this virus so more tourists visiting a country means more transportation to the country of virus, that's why among the first steps travelling was banned with infected countries [154]. In the terms of the actual 2019 coronavirus disease (COVID-19) pandemic, which has spread to 206 countries or territories, the world is experiencing such a crisis. Tourism obviously plays a part in counteracting the associated crisis in public health. Given that tourist arrivals increases COVID-19 spread and contributes to the pressure on the local healthcare system, the most affected are destination residents. More the tourists more the COVID-19 spread [155].

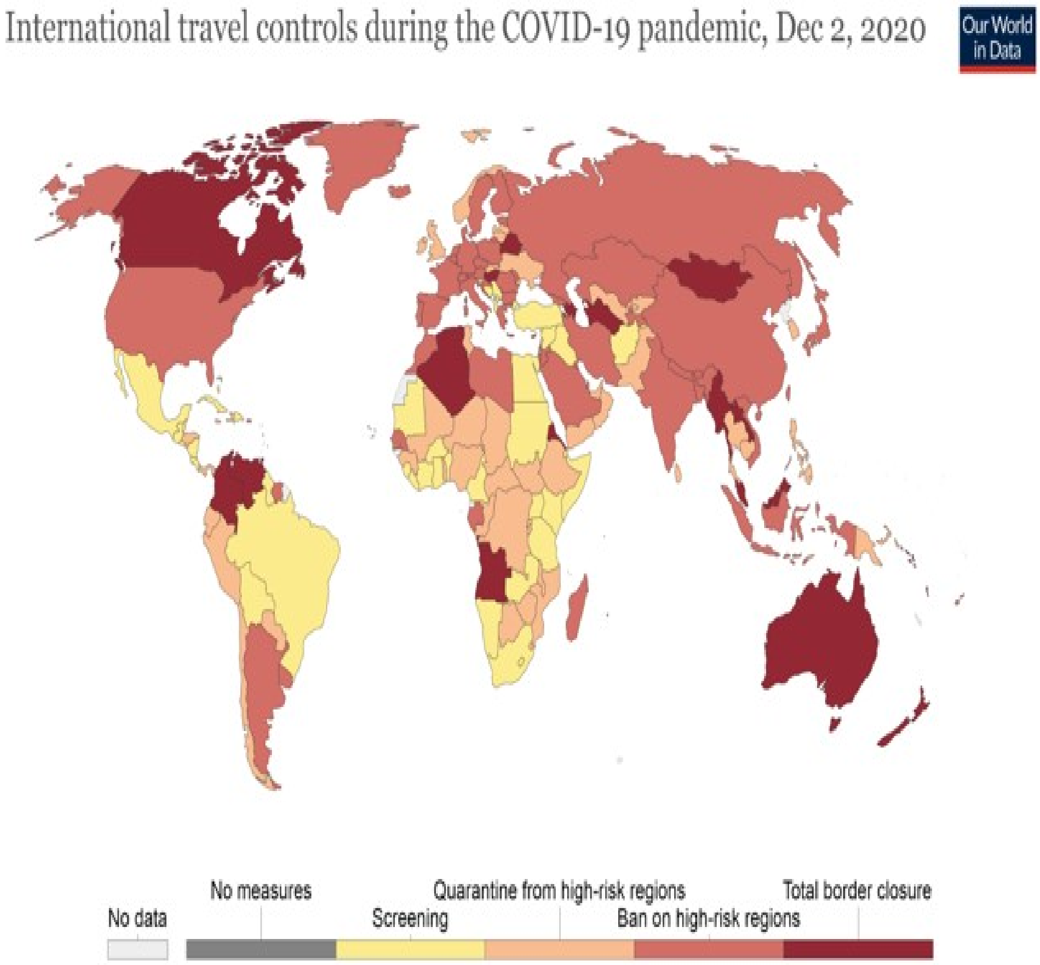

Figure 2.5: International Travel Controls During the COVID-19 Pandemic December [108].

2.4.2 Climate

Another environmental component that was examined was the climate. The virus was formerly thought to be a heat-sensitive RNA virus that causes different symptoms in temperate and cold countries. In November–December 2019, the first cases of COVID-19 were detected, indicating that colder temperatures play a role in the virus's spread. At the start of the epidemic, Latin America had fatality rates of around 0.6 percent. COVID-19 case fatality data in European countries (mostly Mediterranean) with 4 seasons annually represent a massive mortality rate in Italy, France, and Greece. The Northern countries, on the other hand, where the cold weather is prolonged (up to eight months of snowfall and rain),have a low mortality rate (below 1%) [109]. COVID-19 transmission is thought to be reduced to some extent as the temperature rises. Relative humidity measurements in New York during the winter indicated a vapour pressure of less than 10 mb and an indoor RH of less than twenty four percent, enabling cold season viruses to survive. It's thought that SARS-survivability COVID-19 would be enhanced by the minimal moisture and high heat [110].

2.4.3 Crowding

The presence of unprotected people at gatherings where there is a chance of an infected person is the most important way to transmit SARS-CoV-2. As a result, if the social distancing is not observed, a person's presence in public vehicles such as buses, subways, trains, and airlines will be a risk factor for contamination. Being in crowded stores, temples, sporting events, and other crowded areas could also raise increased risk of exposure [111].

2.5 Low Education

Although sufficient and adequate training is an important factor in breaking the transmission chain, those who lack proper training in this field may unconsciously transmit the virus. For example, uneducated people attempting to distribute disinfectants to individuals can cause social gatherings; or, health care workers (HCWs) wearing personal protective equipment (PPE) such as gowns, masks, and gloves that were present with the patients; they go to the hospital's administrative centers and contaminate the environment, and because the virus stays on the devices for a long time , they provide the possibility of infecting people [112].

2.6 Population Density

Population density can be determine as the abundance of individuals living per unit square feet of space, population density directly affect the spread of disease, as the disease is pandemic that it spread from one person to the other through atmosphere so if there is a large population density that is large number of people living in a certain locality the risk of spread of disease will increase. When an infected individual breath in atmosphere the viruses along with micro droplets of sneeze comes to the atmosphere, people passing from that atmosphere and breathing in that are more likely to inhale that virus along with air and it is more fatal because virus will directly reach lungs where its binding sites are present [113].

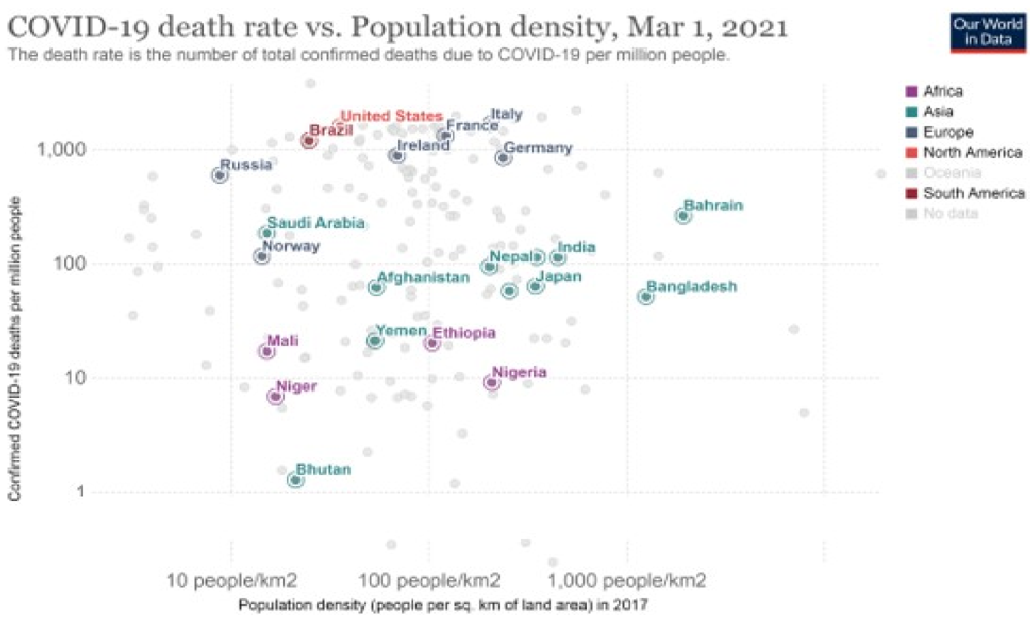

FIGURE 2.6: Population Density and Total Confirmed Deaths Per Million People Due to COVID -19 [116].

The spread of the pandemic is influenced by population density. Overcrowding promotes air pollution [114]. The degree of transmission will be linked to the density of the population. This was not the case with SARS-CoV-2, as evidenced by lower than expected incidence in some of the largest and most populous lands (e.g., Egypt, Bangladesh, and Indonesia). It may be claimed that these nations had more time to get ready because they were not the first to be hit by the outbreak. Diseases spread more quickly as population density rises. The sensitivity of a specific location to the virus is likely determined by various factors, including population density [115].

TABLE 2.2: COVID-19 Cases, Deaths and Recoveries Worldwide by WHO [171]

Country	**Total cases**	**Total Deaths**	**Total recovered**
USA	15,370,339	290,474	8,983,641
India	9,703,908	140,994	9,178,946
Brazil	6,628,065	177,388	5,801,067
Russia	2,515,009	44,159	1,981,526
France	2,295,908	55,521	170,285
Italy	1,742,557	60,606	933,132
UK	1,737,960	61,434	
Argentina	1,466,309	39,888	1,300,696
Germany	1,200,006	19,539	863,300
Iran	1,051,374	50,594	742,955
Turkey	860,432	15,103	436,270

Continued Table: 2.2 COVID-19 Cases, Deaths and Recoveries Worldwide by WHO [171]

Country	**Total Cases**	**Total Deaths**	**Total Recovered**
South Africa	817,878	22,249	745,750
Indonesia	581,550	17,867	479,202
Iraq	566,015	12,460	495,725
Romania	517,236	12,447	409,121
Bangladesh	479,743	6,874	398,623
Pakistan	423,179	8,487	370,474
Canada	423,054	12,777	338,735
Saudi Arabia	358,922	5,977	349,168
Switzerland	354,306	5,495	279,900
Hungary	256,367	6,120	75,281
Nepal	241,995	1,614	227,433
UAE	177,577	594	159,711
Bulgaria	164,185	5,010	65,616
Japan	162,067	2,335	136,903
Azerbaijan	149,765	1,675	90,278
Kuwait	144,599	897	140,341
Oman	125,115	1,452	116,506
Egypt	118,847	6,790	103,703
Denmark	92,649	894	71,882
Algeria	88,825	2,527	57,648
Kenya	88,579	1,531	69,414
China	86,646	4,634	81,732
Ireland	77,678	2,143	23,364

Continued Table: 2.2 COVID-19 Cases, Deaths and Recoveries Worldwide by WHO [171]

Country	**Total cases**	**Total Deaths**	**Total recovered**
Nigeria	76,207	1,201	67,110
Uzbekistan	75,675	612	72,961
Singapore	58,377	29	58,252
Afghanistan	50,202	2,032	38,686
Norway	42,776	404	34,782
Sri Lanka	35,387	160	26,353
Finland	32,228	484	22,500
Uganda	29,361	228	10,172
Sudan	22,265	1,408	12,873
Hong Kong	7,900	124	6,534
Thailand	4,297	60	4,005
New Zealand	2,110	25	2,034
Yemen	2,087	606	1,384
Mauritius	524	10	489
Tanzania	509	21	183
Bermuda	485	9	255
Bhutan	442		419
Zimbabwe	11,866	314	9,836
Tajikistan	12,852	89	12,295
Maldives	13,418	48	12,828
Ethiopia	118,481	1,831	99,751
Palestine	117,755	1,078	92,979

Brazil has the third greatest reported cases and the 2nd highest number of fatalities in the world [118].

2.7 Other Environmental Factors

Poor hygiene, prisons, nursing homes, dormitories, poor living conditions, unemployment, a high body mass index (BMI), stress, taking the subway, eating in a restaurant, and more prominent laboratory malformations are some of the other environmental factors that can cause COVID-19 and its severe form.

2.8 Social Interaction

Social interaction played a key role in spread of virus, people who live in narrow streets and usually multi-story houses must communicate with one another and interact socially with each other in order to spend the day, whereas there are people who are unaware of their neighbors. This type of culture is only found in the western and upper class colonies of Asia, while people in villages and the lower middle class must interact with their neighbors, these types of societies were more vulnerable to spread of virus as this time humans were a vector for transportation [137].

2.9 Susceptibility

Susceptibility refers to how vulnerable you are to disease [138]. Everyone knows that the immune system fights all invaders. If the immune system succeeds, antibodies are developed against that invader; if invaders dominate, disease occurs. According to indications, those over the age of 65, as well as those with compromised immune systems or medical issues, are at a higher risk of becoming far sicker from the virus [139].

2.10 Isolation Number

As the term suggests, the isolation number indicates how many people have isolated them from infected individuals. It is clear and well known that humans are the vectors of disease spread, so the more people interact and socialize, the more they help the virus and spread the disease. Isolating ourselves is like blocking the way or channel of transmission. Corona virus spread is inversely proportional to the number of isolates [140].

2.11 COVID-19 Pandemic in Asia

The COVID-19 outbreak started in Asia, in the city of Wuhan in the Chinese province of Hubei, and has since spread across the continent. As of June 8, 2020, every country in Asia had at least one case of COVID-19, with the exception of North Korea and Turkmenistan. India, Iran, Bangladesh, Iraq, and Saudi Arabia. Thailand, Japan, South Korea, Taiwan, and Vietnam were among the first nations to report COVID-19 cases after the epidemic in China, but the pandemic had been successfully controlled in these countries [119].

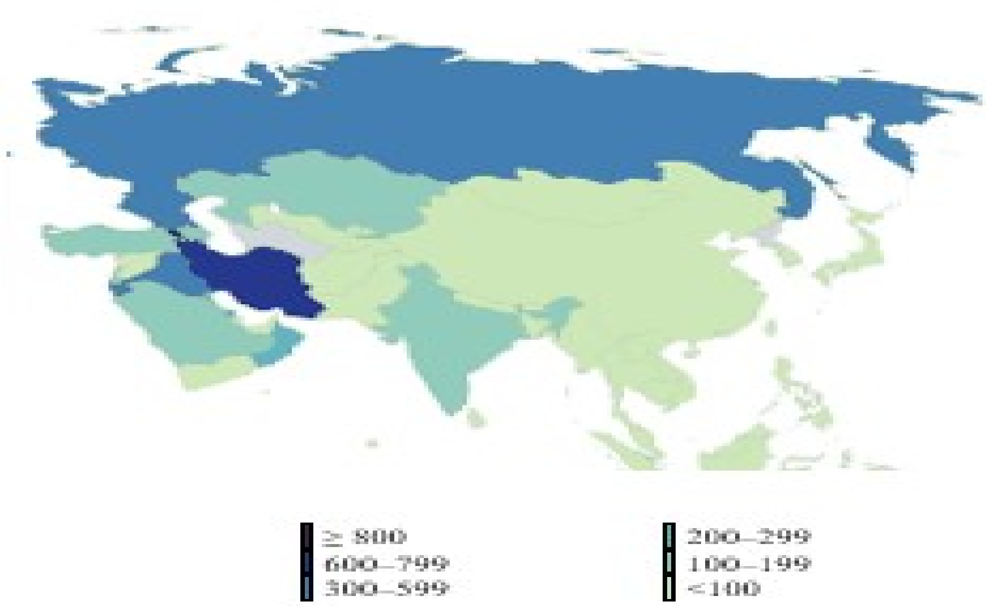

FIGURE 2.7: Confirmed COVID-19 Deaths Per Million Residents as of December 10, 2020 [100].

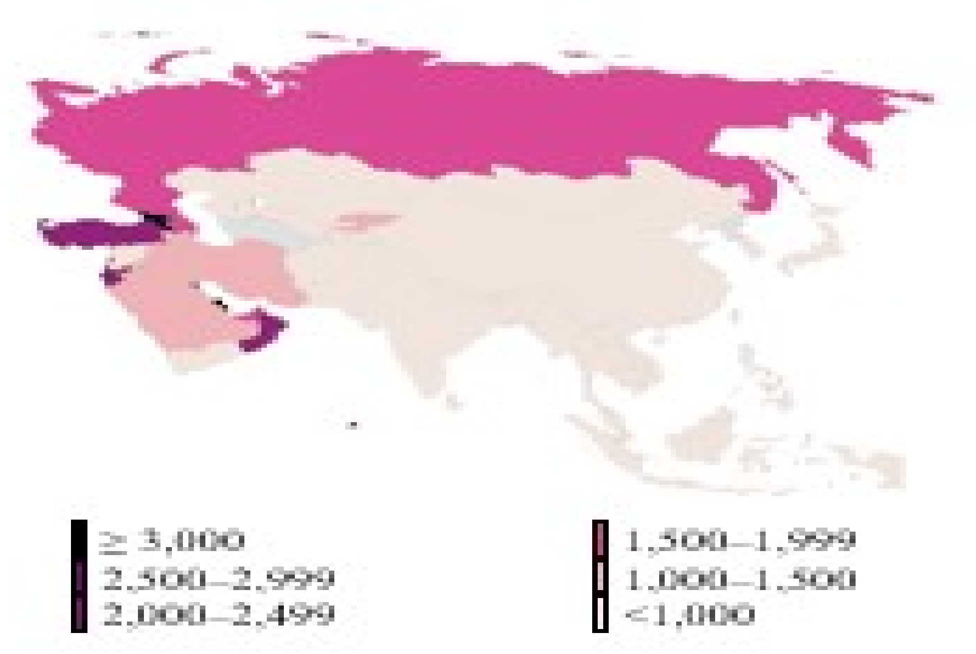

FIGURE 2.8: Cumulative Confirmed Cases of COVID-19 per 100,000 Ppeople as of December 10, 2020 [100].

Chapter 3

Research Methodology

3.1 Study Design

Countries were categorized as developed, developing, and least developed. The United Nations provided the list for developing, least developed, and developing countries ,based on gross domestic product (GDP), gross national product (GNP), per capita income, Human Development Index (HDI), level of industrialization, infrastructure development, and general living standard [180].

The cases and mortality rate of COVID-19 differ so greatly across countries. Such high variability indicates that there are variables that influence COVID-19 mortality, severity other than patient characteristics. COVID-19 data from various developed, underdeveloped, and developing countries was collected and compared.

3.2 Data Collection

The data was collected from reliable databases, including Worldometer [181], WHO [182]. The selected countries share the maximum reported COVID-19 incidence, tests /1M population and deaths. These countries were selected deliberately based upon their COVID-19 caseload, mortality rates and outcome (deaths and recovered).Due to the rapid increase in data, the analysis in this study was performed from March, 2020 to August 8, 2021.

3.3 Data Analysis

Data were entered in Microsoft excel and later imported into Statistical Package for Social Sciences (SPSS) version 22.0 for statistical analysis .After data collection and data entry, SPSS version 22.0 was used to analyze the data. Several types of analyses were done based on study objectives. The ANOVA test was used to check the severity rate and mortality rate of developed, developing and under-developed countries. Pearson's correlation and linear regression were implemented to determine the number of cases reported /1M population and deaths per million population, respectively. Spearman's correlation was used to determine the relationship between population density per Km2 and cases reported per million population, as well as median age and cases reported per million population.

This chapter includes frequency tables representing profile of different countries. After running inferential statistics, it was found out that there is an association between cases per million population and deaths per million populations. Moreover, it was found out that the severity of COVID-19 in developed and developing countries were significantly higher in comparison to under-developed countries.

Chapter 4

Result and Discussion

4.1 Descriptive Statistics

Table 4.1: Frequency Table of COVID-19 Data of Developed Countries from March 2020 to August 2021

Country Name	Total Population	Total Tests /1Million Population	Total Number of Reported Cases /1 Million Population	Total Mortality /1 Million Population
USA	333140783	1829614	109693	1900
Germany	84079193	836797	45170	1098
Norway	5467920	1388007	25757	147
China	1439323776	111163	65	3
Singapore	5901007	3081464	11157	7
Switzerland	8724324	1172272	82983	1250
Ireland	4998483	1382667	62512	1009
United Kingdom	68278881	4193781	4642198	1909
Japan	126049332	185923	8182	121
France	65432718	2019692	96361	1715
Canada	38108288	1090573	37877	700

Note. n = 11 Developed Countries.

According to the data of developed countries, most of the cases were reported in United Kingdom (4.6 million), United States of America (1.09 lacs) and France (96 thousand). The United States and the United Kingdom had the highest number of reported cases because they did not take it seriously at first. The federal government did not quarantine people in their homes. That is why COVID-19 spread in the USA and the UK at an extraordinary speed. In China where it all started, they fought COVID–19 fearlessly. China has taken it seriously and did preventive measures, set effected cities in strict lockdown and restricted travelling and all these factors counted in so much control of spread of COVID-19. In China, there were only 65 reported cases per million people.

TABLE 4.2: Frequency Table of COVID-19 Data of Developing Countries from March 2020 to August 2021

Country Name	**Total Population**	**Total Tests Per 1Million Population**	**Total Reported Cases / 1 Million Population**	**Total Casualties/1 Million Population**
India	1394938788	389928	22919	229
Pakistan	225603806	82153	4750	106
Thailand	69993027	131433	11088	91
Indonesia	276706842	-	13324	392
Iraq	41213273	359064	41557	466
Russia	146003457	1262246	44313	1135
Philippines	111185350	178523	14999	262
Saudi Arabia	35409944	793738	15067	235
Bahrain	1766315	3480986	152895	784
Bangladesh	166495380	55826	8131	136
Nepal	29712650	135896	24060	340

Note. n = 12 Developing Countries.

According to the data of developing countries, most of the cases were reported in Bahrain (1.5 Lacs), Russia (44 thousand), India (23 thousand) and Nepal (24 thousand). However, lowest number of cases and deaths were reported in Pakistan and Thailand respectively.

TABLE 4.3: Frequency Table of COVID-19 Data of Under Developed Countries from March 2020 to August 2021

Country Name	**Total Population**	**Total Tests /1Million Population**	**Total Reported Cases /1 Million Population**	**Total Casualties /1 Million Population**
South Sudan	11338126	-	979	11
Liberia	5188138	-	1052	29
Nigeria	25165436	5919	226	8
Mozambique	32215423	27184	4111	50
Mali	20890165	19110	701	26
Yemen	30547109	8665	235	45
Bhutan	780958	1435874	3258	3
Ethiopia	118087799	28133	2406	37

Note. n = 08 Under Developed Countries.

According to the data of under developed countries, least number of the cases were reported in Nigeria (226 cases) and Yemen (235 cases). Out of over three thousand cases reported in Bhutan, only three people died representing the lowest casualty rate.

4.2 Inferential Statistics

TABLE 4.4: ANOVA Table for Country wise COVID-19 Fatality Rate

Casualty Rate	**Sum of Squares**	***df***	**Mean Squares**	**F**	***Sig.***
Between Groups	0.79	2	0.39	0.32	0.73
Within Groups	32.24	26	1.24		
Total	33.03	28			

Note. Dependent Variable: Fatality Rate, Independent Variable: Country Type. n = 28 Countries.

Table 4.4 and **Figure 4.1** shows the results of Analysis of Variance (ANOVA) that was conducted to compare the difference in the fatality rates of COVID-19 among different countries. According to the findings, there is statistically a non-significant difference in the fatality rate among all three, developed, developing and under-developed countries ($F(2, 26) = .32$, $p = .73$). The calculated fatality rate for COVID-19 varies according on the area and situation, as well as the degree of testing performed.

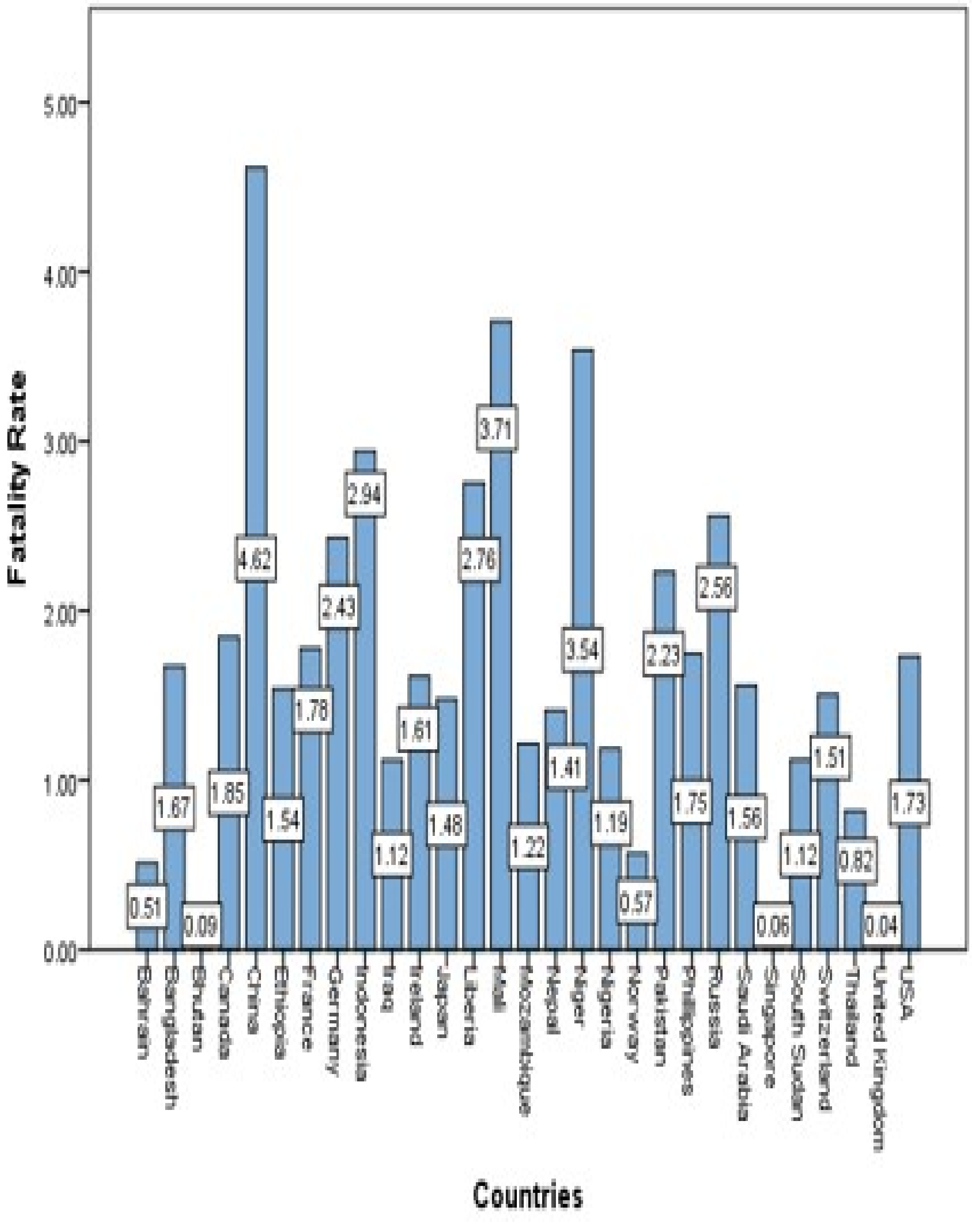

FIGURE 4.1: Bar graph showing COVID-19 Fatality rate of different countries (x-axis representing different countries and y-axis represents fatality rate)

4.3 Severity of the Disease

The severity of the disease refers to how critical of an effect it has [175]. The severity of COVID-19 is determined by the total number of cases per million persons. The reason for utilizing this severity criterion is that it gives a more accurate representation of how widespread the disease has become among the populations of different countries. This is more precise than simply counting the number of confirmed instances. For example, ten affected people in a country with a population of 1,000,000 are not as severe as ten affected people in a country with a population of 100.

$$S = (N \div P) \times 1,000,000$$

S, severity; N, total number of cases; P, population.

The severity calculations for all countries were examined, and it was revealed that there is a statistically significant difference in severity between underdeveloped and developed developing countries.

4.4 Severity Rate Country Wise

Table 4.5: ANOVA Table for Country wise COVID-19 Severity

Fatality Rate	**Sum of Squares**	***df***	**Mean Squares**	**F**	***Sig.***
Between Groups	10114985296	2	5057492648	8.54	.001***
Within Groups	15402061018	26	592386962.2		
Total	25517046313	28			

Note. Dependent Variable: Severity (Cases per Million Population), Independent Variable: Country Type. n = 28 Countries. ***. $p < .001$.

Table 4.6: Multiple Comparisons ANOVA Table for Country wise COVID-19 Severity

Country Type	**Country Type**	**Mean Difference**	**Std. Error**	***Sig.***	**95% Confidence Interval**	
					Lower Bound	Upper Bound
Developed	Developing	29698.52	12923.01	0.098	-5140.92	64537.96
	Under developed	46354.7	12224.34	.011*	12246.66	80462.77
Developing	Developed	-29698.52	12923.01	0.098	-64537.96	5140.92
	Under developed	16656.18	4254.81	.007**	5047.72	28264.65
Under Developed	Developed	-46354.7	12224.34	0.011	-80462.74	-12246.66
	Developing	-16656.18	4254.81	0.007	-28264.65	-5047.72

Note. Dependent Variable: Severity (Cases per Million Population), Independent Variable: Country Type. n = 28 Countries. *. $p < .05$. **. $p < .01$.

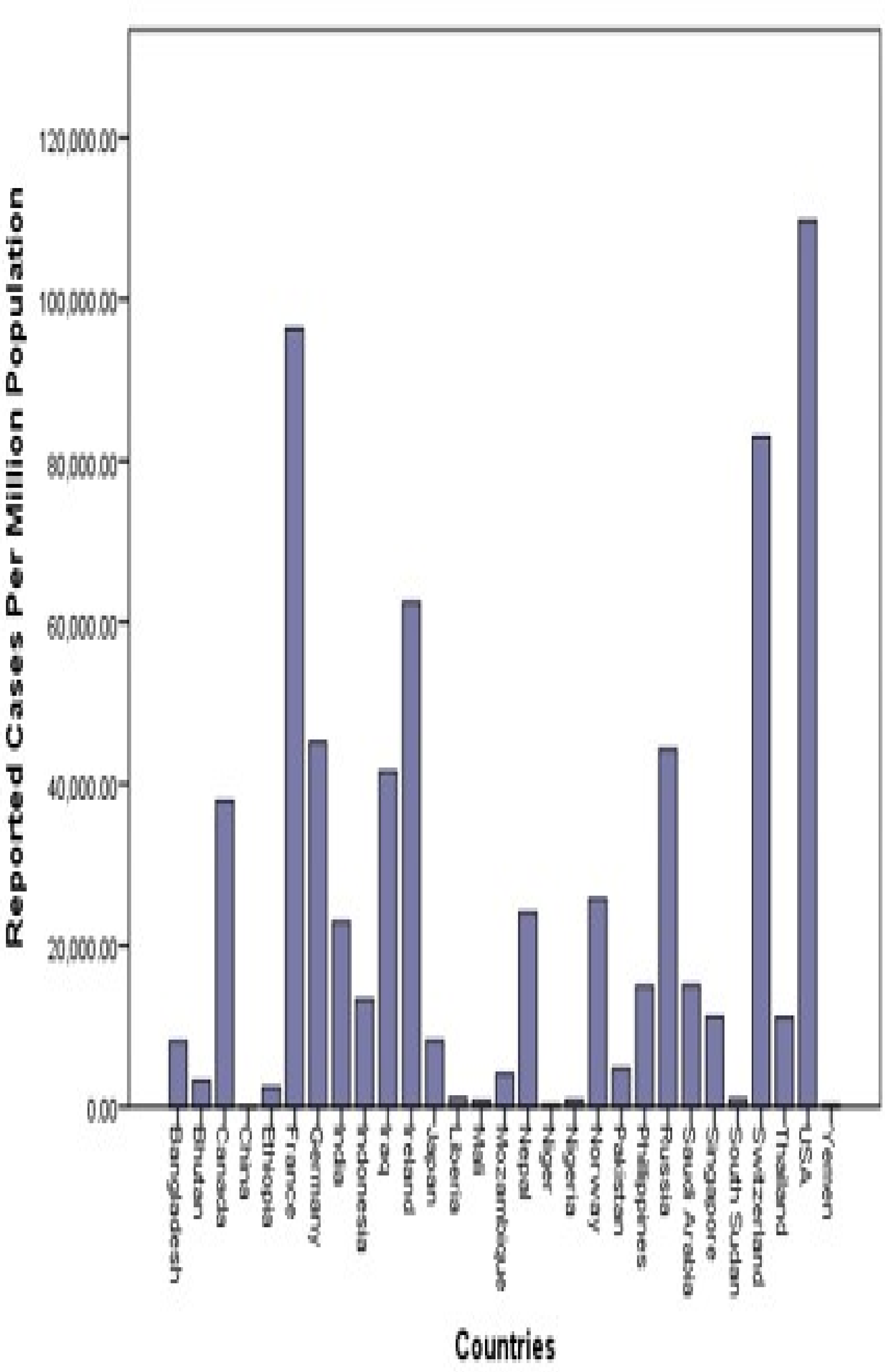

Figure 4.2: Bar Graph Showing Severity of COVID-19 in Different Countries (X-axis Representing Different Countries and y-axis Represents Reported Cases per Million Population)

Table 4:5, 4: 6 and **figure 4:2** shows the results of Analysis of Variance (ANOVA) that was conducted to compare the difference in the severity of COVID-19 among different country types. According to the analysis, there is a statistically significant difference in the severity of under-developed countries with both developed and developing countries ($F(2, 26) = 8.54$, $p = .001$). A Post Hoc test revealed that the severity of developed (47975.70×38622.24, $p = .011$) and developing countries (18277.18×14007.22, $p = .007$) were significantly higher in comparison to under-developed countries (1621.00×1461.19).

To test the association between cases reported /1Mpopulation and deaths per million populations, a Pearson's correlation was conducted (see the table below):

Table 4.7: Pearson's Correlation Table Showing the Association between Reported Cases and Deaths Per 1Million Population

		Reported Cases	**Reported Deaths**
Reported Cases	Pearson Correlation	1	0.83
	Sig (2-tailed)		.000***
	N	29	29
Reported Deaths	Pearson Correlation	0.83	1
	Sig (2-tailed)	.000***	
	N	29	29

Note. Variables: Reported Cases and Deaths. n = 29 Countries **. = $p < .000$.

A Pearson's correlation was conducted to analyze the association between reported cases (M = 28405.17, SD = 38529.77) /1M populations and the reported deaths (M = 417.79, SD = 546.44). It was found out that there is a strong, positive relationship between reported cases and death due to COVID-19 (r = .83, p < .001).

TABLE 4.8: Regression Analysis with Reported Deaths due to COVID-19 /1 million Population as a Dependent Variable and /1 million Population Reported Cases due to COVID-19 as a Predictor

Model	**Sum of Squares**	***df***	**Mean Square**	**F**	**Sig.**
Regression	5792575.68	1	5792575.68	60.9	.000***
Residual	2568049.08	27	95112.93		
Total	8360624.76	28			

Note. Dependent Variable: Reported Deaths in /1M Population due to COVID-19. Predictor: /1M Population Reported Cases due to COVID. n = 28 Caregivers. ***. = p < .001 level.

Tables 4.8 and 4.9: shows the results of simple linear regression for cases per million populations due to COVID-19 predicting deaths per million populations due to COVID-19. Reported cases per million population (M = 28405.17, SD = 38529.77) was found to be the significant predictors of deaths reported in per million population due to COVID-19 (F (1, 27) = 60.90, p < .001). A large amount of variance is explained in deaths /1M populations due to predictor (R^2 = 0.69). The correlation between cases /1M population and reported death /1M population was found to be statistically significant (r = .83, p < .001). A significant linear regression equation exists ($\hat{y}$ = 82.47 + 0.012×). Results suggest that as the number of reported cases increases /1M population, the deaths in /1M population also increases and vice versa. Reported deaths increases 0.012, points with each increase in reported cases /1M population. These findings support the hypothesis.

TABLE 4.9: Regression Coefficients of Reported Deaths in per million Population due to COVID-19 with Reported Cases in per million Population due to COVID-19

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	***t***	***Sig.***	**95.0\% Confidence Interval for B**	
	B	Std. Error				Lower Bound	Upper Bound
(Constant)	82.47	71.6		1.152	0.259	-64.428	229.377
RCPMPa	0.012	0.002	0.832	7.804	.000***	0.009	0.015

Note. Dependent Variable: Reported Deaths in /1M population due to COVID-19. Predictor: Reported Cases in Per Million Populationa due to COVID-19. n = 28 Caregivers. ***. = p < .001 level.

4.5 Risk Factors for COVID-19 (Population Density)

To test the association between population density per Km2 and cases reported / 1 million population, a Spearman's correlation was conducted (see the table below):

TABLE 4.10: Spearman's Correlation Table Showing the Association between Population Density per Km2 and Reported Cases

		Population Density Per Km2	**Reported Cases Per 1 Million Population**
Population Density per Km2	Correlation Coefficient	0.024	1
	Sig (2-tailed)	0.91	-
	N	26	28
Reported Cases per million population	Correlation Coefficient	1	0.024
	Sig (2-tailed)	-	0.91
	N	26	26

Note. n = 28 Countries.

A Spearman's correlation was conducted to analyze the association between Population Density per Km2 (M = 116.65, SD = 109.40) and Reported Cases (M = 25060.27, SD = 31667.05). It was found out that there is a non-significant relationship between Population Density per Km2 and Reported Cases ($r_s = .024$, $p >$

.05). There is no connection between population density and COVID-19 reported cases in countrywide statistics.

To test the association between population density per Km2 and deaths reported per million population, a Spearman's correlation was conducted (see the table below):

TABLE 4.11: Spearman's Correlation Table Showing the Association between Population Density per Km2 and Reported Deaths

		Population Density Per Km2	**Reported Deaths /1million Population**
Population Density per Km2	Correlation Coefficient	1	0.07
	Sig (2-tailed)	-	0.72
	N	26	26
Reported Deaths per million population	Correlation Coefficient	0.07	1
	Sig (2-tailed)	0.72	-
	N	26	26

Note. n = 28 Countries.

A Spearman's correlation was conducted to analyze the association between Population Density per Km2 (M = 116.65, SD = 109.40) and Reported Deaths /1 million population (M = 430.35, SD = 564.77). It was found out that there is a non-significant relationship between Population Density per Km2 and Reported Deaths ($r_s = .07$, $p > .05$). It means that population density is not linked to the number of casualties, so a country with a large population density is not at high risk of casualties due to COVID-19.

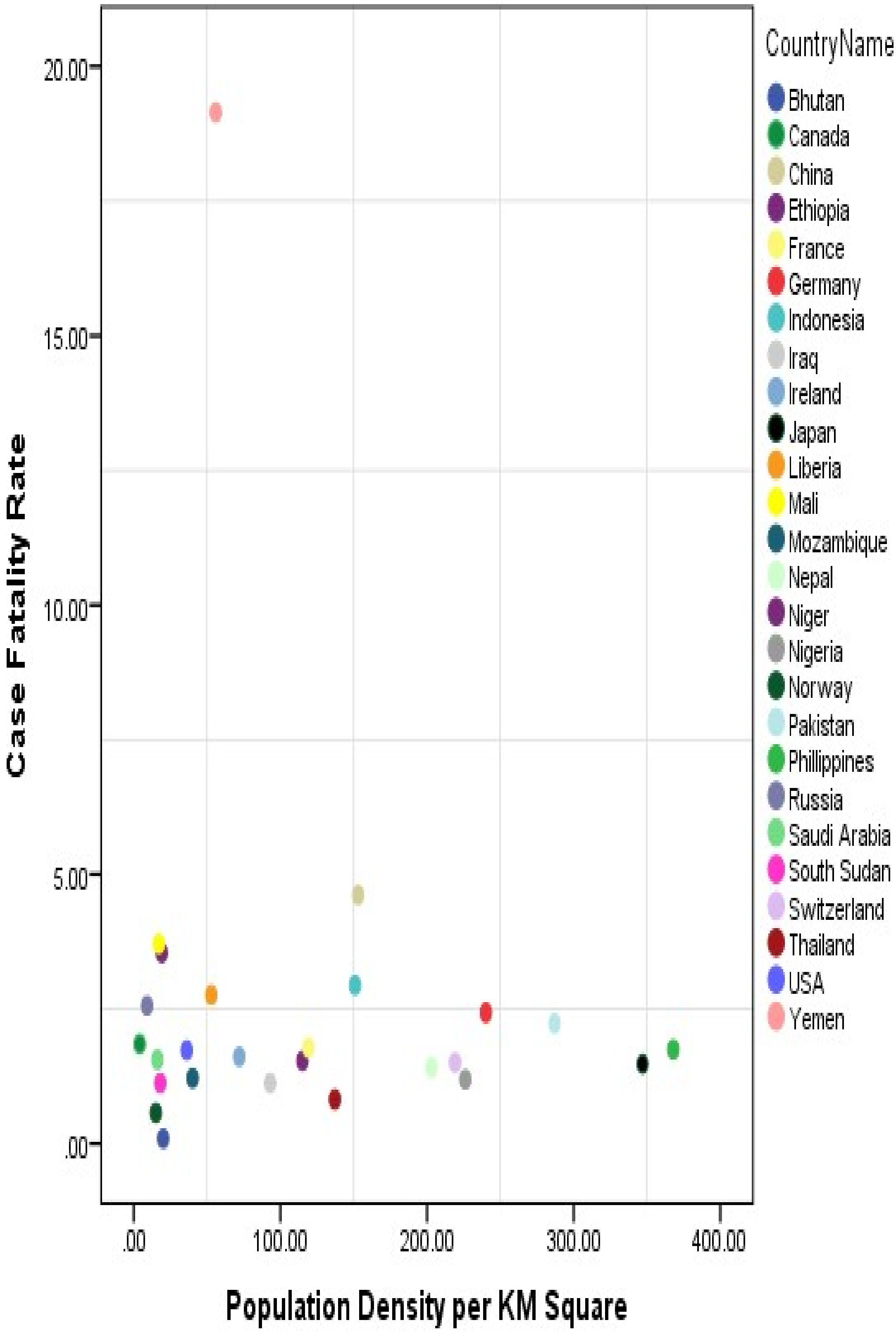

FIGURE 4.3: Scatter Plot Showing Case Fatality Rate of Different Countries Based on Population Density per km2 (x-axis Representing Population Density and y-axis Represents Case Fatality Rate)

The above scatter plot (figure4.3) shows the case fatality rate of different countries based on population density per km2. The scatter plot represents that Yemen despite having low population density had high case fatality rate. However, developing country like Bhutan had lowest case fatality rate.

4.6 Risk Factor for COVID-19 (Median Age)

To test the association between median age and cases reported / 1 million population, a Spearman's correlation was conducted (see the table below):

TABLE 4.12: Spearman's Correlation Table Showing the Association between Median Age and Reported Cases

		Median Age	**Reported Cases /1 million Population**
Median Age	Correlation Coefficient	1	0.7
	Sig (2-tailed)	-	.000***
	N	24	24
Reported Cases per million population	Correlation Coefficient	0.7	1
	Sig (2-tailed)	.000***	-
	N	24	26

Note. n = 28 Countries. ***. p < .001 level.

A Spearman's correlation was conducted to analyze the association between Median Age (M = 32.01, SD = 10.21) and Reported Cases (M = 25060.27, SD = 31667.05). It was found out that there is a strong positive relationship between median age and cases reported per million population (rs = .70, p < .001).

To test the association between median age and deaths reported /1 million population, a Spearman's correlation was conducted (see the table below):

TABLE 4.13: Spearman's Correlation Table Showing the Association between Median Age (2020/2021) and Reported Deaths/1million population (March 2020 to August, 2021)

		Median Age	**Reported Deaths /1million Population**
Median Age	Correlation Coefficient	1	0.63
	Sig (2-tailed)	-	.001**
	N	24	24
Reported Deaths per million population	Correlation Coefficient	0.63	1
	Sig (2-tailed)	.001**	-
	N	24	26

Note. n = 28 Countries. **. $p < .01$ level.

A Spearman's correlation was conducted to analyze the association between median age (M = 32.01, SD = 10.21) and Reported Deaths /1 million population (M = 430.35, SD = 564.77). It was found out that there is a strong positive association between median age and deaths reported / million population ($r_s = .63$, $p < .01$).

The below scatter plot (figure 4.4) shows the case and fatality rate of different countries based on median age. The scatter plot represents that median death age in France was forty-eight years with the case fatality rate of around 2%. However, median death age in Yemen was twenty-years with the case fatality rate of nineteen percent.

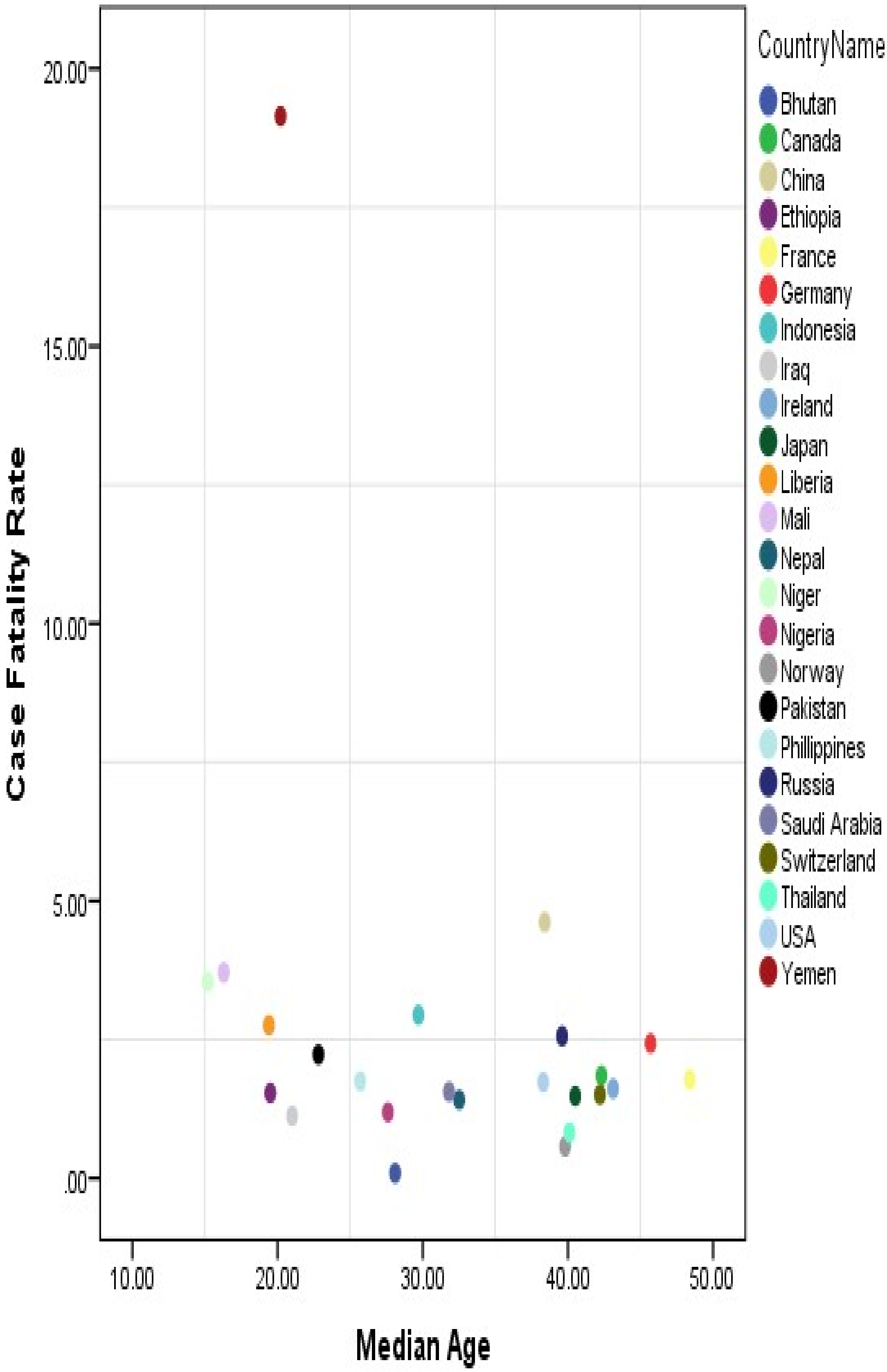

Figure 4.4: Scatter Plot Showing Case Fatality Rate of Different Countries Based on Median Age (x-axis Representing Median Age and y-axis Represents Case Fatality Rate)

There are a few exceptions with these two countries, where other variables play an important role. In comparison to developed countries, the median age in underdeveloped countries is lower. Developing countries, on the other hand, have a younger population.

TABLE 4.14: Regression Analysis with Reported Cases due to COVID-19 in per million population as a Dependent Variable and Tests conducted in per million Population due to COVID-19 as a Predictor

Model	**Sum of Squares**	***df***	**Mean Square**	**F**	**Sig.**
Regression	20952520767	1	20952520767	27.92	.000***
Residual	18763469886	25	750538795.4		
Total	39715990653	26			

Note. Dependent Variable: Reported Cases in per million population due to COVID-19. Predictor: Tests conducted in per million population due to COVID-19. n = 27 Countries. ***. = $p < .001$ level.

Table 4.14 and 4.15 shows the results of simple linear regression of tests conducted in per million Population due to COVID-19 (M = 796544.96, SD = 954805.36) predicting cases reported in per million population due to COVID-19 (M = 30789.41, SD = 39083.73). Tests conducted per million was found to be a significant predictor of reported cases per million population (F (1, 25) = 27.92, $p < .001$). A large amount of variance is explained in reported cases due to predictor ($R^2 = .53$).

TABLE 4.15: Regression Coefficients of Reported Cases in per million Population due to COVID-19 with Tests conducted in per million Population due to COVID-19

Model	**Unstandardized Coefficients**		**Std. Coeff.**	***t***	***Sig.***	**95.0% Confidence Interval for B**	
	B	**Std. Error**				**Lower Bound**	**Upper Bound**
(Constant)	7106.94	6920.13		1.03	0.314	-7145.34	21359.22
TPMPa	0.03	0.01	0.73	5.28	.000***	0.02	0.04

Note. Dependent Variable: Reported Cases in per million Population due to COVID-19. Predictor: Tests conducted in per million Populationa due to COVID-19. n = 27 Countries. ***. = p < .001 level.

The correlation between tests conducted in per million population and reported cases was found to be statistically significant (r = .73, p < .001). The regression equation for predicting the reported cases from tests conducted was ($\hat{y} = 7106.94 + .03\ times$). Results suggest that with each unit increase in conducted tests, cases due to COVID-19 increase by .03 times. These findings support the hypothesis.

The below bar graph shows COVID-19 recovery ratio of different countries of the world.

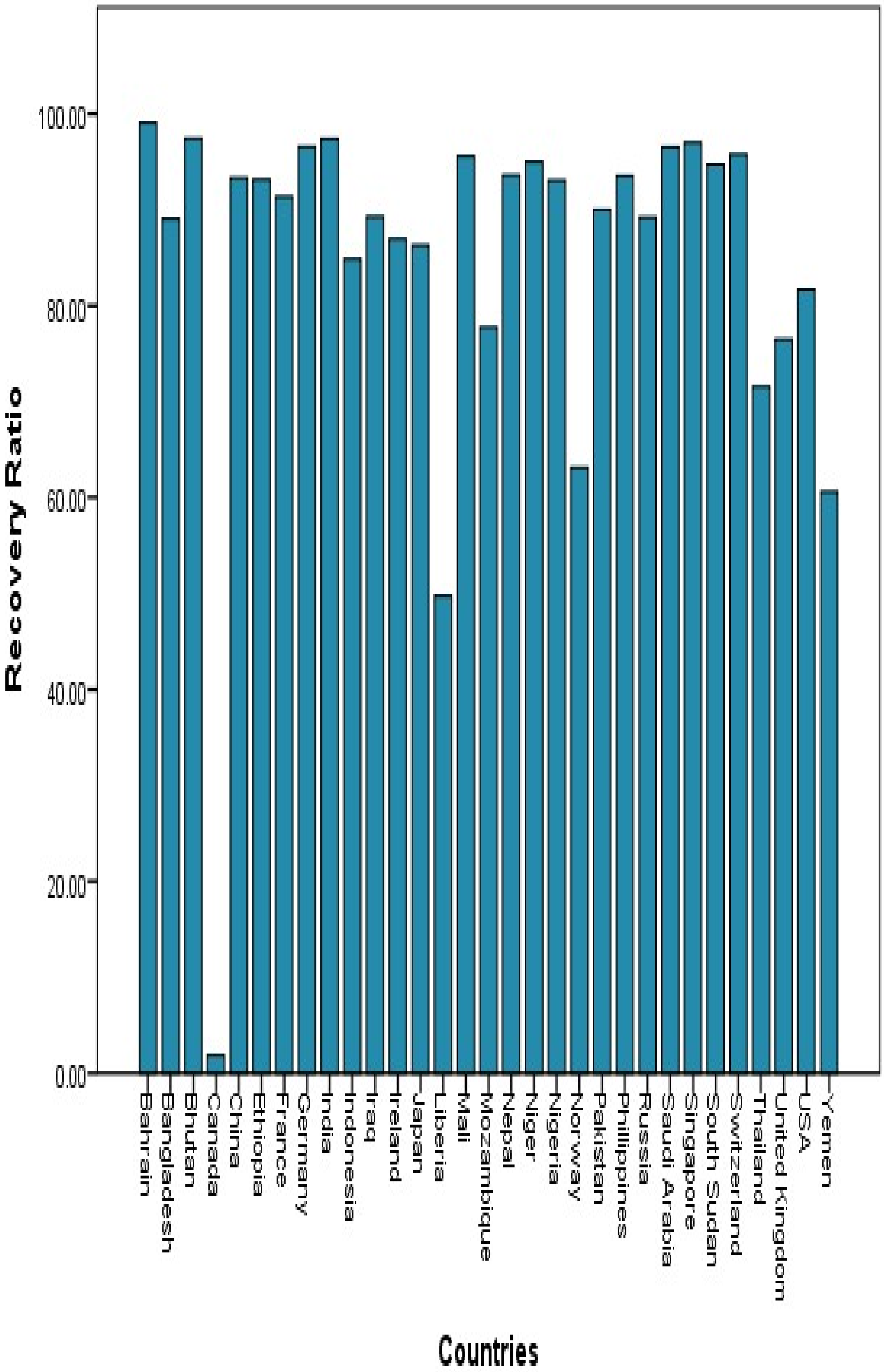

FIGURE 4.5: Bar Graph Showing Recovery Ratio of COVID-19 in Different Countries (x-axis Representing Different Countries and y-axis Represents Recovery Ratio)

In **Figure 4.5** the graph represents that highest recovery ratio was observed in developing countries like Bahrain, Bhutan, and Saudi Arabia. In terms of developed countries, highest recovery ratio was observed in Singapore and Switzerland. Lowest recovery ratio was observed in Canada.

COVID-19 at first when it started spread at a frightening rate, everyone was getting infected, people dying but there was one element which brought a visibility of relief, its recovery rate. People who got infected recovered soon, although due to their negligence they infected many more but they themselves got recovered, people with other health issues in bonus had severe problems and they reached to ventilators and thus many left us.

Chapter 5

Conclusion and Recommendations

It is concluded that developed and developing countries failed to combat the COVID-19 pandemic. This study analyzed the COVID-19 severity between developed, underdeveloped and developing countries. In developed and developing countries, the severity of the disease (in terms of infection and fatality) was significantly higher than in underdeveloped countries.

It is also concluded that there is no connection between population density and COVID-19 reported cases in countrywide statistics. Population density is not linked to the number of casualties, so a country with a large population density is not at high risk of casualties due to COVID-19.

Considering the rapid spread of COVID-19 and the increase in the number of cases and deaths in various countries, it is necessary to investigate which countries are more affected by COVID-19.According to the analysis, the majority of reported cases per million people were found in developed countries. In comparison with developing countries, underdeveloped countries had the lowest number of cases and deaths/1million population. The COVID-19 pandemic was uncontrollable in both developed and developing countries. It happens because of the population's negligence .In most countries, even in Pakistan, people consider it a rumor. Due to the negligence of people, COVID-19 spreads quickly. According to the findings, if the number of incidence increases by /1M population, the number of deaths /1M people increases as well. Results suggest that with each unit increase in conducted tests, cases due to COVID-19 increase by 0.3 times.

Accordings to the findings, the majority of incidents and mortality from COVID-19 rises when the median age rises above 40. It was revealed that the median age and the number of fatalities per million population have a strong positive association. Highest recovery ratio was observed in developing countries Bahrain, Bhutan, and Saudi Arabia. In terms of developed countries lowest recovery ratio was observed in Canada.

In comparison to developed countries, the median age in underdeveloped countries is lower. Developing countries, on the other hand, have a younger population. Health care in underdeveloped countries is of lower quality, and proper water and sanitation are rare. The virus has little effect in underdeveloped countries, as it does in developed and developing countries (in terms of cases and mortality).

There were numerous reasons why underdeveloped countries had lesser impact related to COVID-19. Due to a lack of COVID-19 testing infrastructure and improper fatality counting and recording; and a higher number of young individuals who are more resistant to infection. Further research is needed to identify the COVID-19 virus's specific components that favor underdeveloped countries. The results suggest that the fatality difference in all three countries, developed, developing, and underdeveloped, is statistically non-significant.

5.1 Recommendations

This conclusion was based on the first wave of COVID-19, because of the research we did, we know that old aged people are more sensitive to the coronavirus as compared to others. We can suggest that further research should take place on "why" elderly people are more prone to the coronavirus. More research is needed to figure out why COVID-19 has a lower infection rate in underdeveloped countries and also investigate the COVID-19 virus's specific components that favor underdeveloped countries.

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Appendix-A

Tests/M Population	Deaths/1M Population	Total Population (agust 2021)
1,829,614	1,900	333,140,783
836,797	1,098	84,079,193
1,388,007	147	5,467,920
111,163	3	1,439,323,776
3,081,464	7	5,901,007
1,172,272	1,250	8,724,324
1,382,667	1,009	4,998,483
4,193,781	1,909	68,278,881
185,923	121	126,049,332
2,019,692	1,715	65,432,718
1,090,573	700	38,108,288

389,928	22,919	1,394,938,788
82,153	106	225,603,806
131,433	209	69,993,027
	392	276,706,842
359,064	466	41,213,273
1,262,246	1,135	146,003,457
178,523	262	111,185,350
793,738	235	35,409,944

3,480,986	784	1,766,315
55,826	136	166,495,380
135,896	340	29,712,650
13,864	10	211,744,938

	11	11,338,126
	29	5,188,138
5,919	8	25,165,436
27,184	50	32,215,423
19,110	26	20,890,165
8,665	45	30,547,109
1,435,874	3	780,958
28,133	37	118,087,799

Total Deaths After the onset of COVID-19 from (March 2020, Agust 2021)	**Median Age (2020 to 2021)**	**Population Density/km2**	**Total Land Area**
633,116	38.3 years	36 per Km2(94 people per mi2)	9,147,420 Km2 (3,531,837 sq. miles)
92,281	45.7 years	240 per Km2 (623 people per mi2)	348,560 Km2 (134,580 sq. miles)
804	39.8 years.	15 per Km2 (38 people per mi2)	365,268 Km2 (141,031 sq. miles)
4,636	38.4 years.	153 per Km2 (397 people per mi2)	9,388,211 Km2 (3,624,807 sq. miles)
42	42.2 years	8358 per Km2 (21,646 people per mi2)	700 Km2 (270 sq. miles)
10,909	43.1 years	219 per Km2 (567 people per mi2)	39,516 Km2 (15,257 sq. miles)

5,044	38.2 years	72 per Km2 (186 people per mi2)	68,890 Km2 (26,599 sq. miles)
130,320	40.5 years	281 per Km2 (727 people per mi2)	241,930 Km2 (93,410 sq. miles)
15,280	48.4 years	347 per Km2 (899 people per mi2)	364,555 Km2 (140,755 sq. miles)
112,220	42.3 years	119 per Km2 (309 people per mi2)	547,557 Km2 (211,413 sq. miles)
26,683	41.1 years.	4 per Km2 (11 people per mi2)	9,093,510 Km2 (3,511,022 sq. miles)
428,339	28.4 years.	464 per Km2 (1,202 people per mi2)	2,973,190 Km2 (1,147,955 sq. miles
23,918	22.8 years.	287/km2(742people/mi2)	770,880 Km2 (297,638 sq. miles
6,353	40.1 years	137 per Km2 (354 people per mi2)	510,890 Km2 (197,256 sq. miles)
108,571	29.7 years.	151 per Km2 (391 people per mi2)	1,811,570 Km2 (699,451 sq. miles)

19,203	21.0 years.	93 per Km2 (240 people per mi2)	434,320 Km2 (167,692 sq. miles)
165,650	39.6 years	9 per Km2 (23 people per mi2)	16,376,870 Km2 (6,323,142 sq. miles)
29,128	25.7 years	368 per Km2 (952 people per mi2)	298,170 Km2 (115,124 sq. miles)
8,334	31.8 years	16 per Km2 (42 people per mi2)	2,149,690 Km2 (830,000 sq. miles)
1,384	32.5 years	2239 per Km2 (5,799 people per mi2)	760 Km2 (293 sq. miles)
22,652	27.6 years	1265 per Km2 (3,277 people per mi2)	130,170 Km2 (50,259 sq. miles)
10,093	27.6 years.	203 per Km2 (526 people per mi2)	143,350 Km2 (55,348 sq. miles)
2,187	18.1 years	226 per Km2 (586 people per mi2)	910,770 Km2 (351,650 sq. miles)
120		18 per Km2 (47 people per mi2)	610,952 Km2 (235,890 sq. miles)

148	19.4 years	53 per Km2 (136 people per mi2)	96,320 Km2 (37,189 sq. miles)
196	15.2 years.	19 per Km2 (49 people per mi2)	1,266,700 Km2 (489,075 sq. miles)
1,613		40 per Km2 (103 people per mi2)	786,380 Km2 (303,623 sq. miles)
534	16.3 years	17 per Km2 (43 people per mi2)	1,220,190 Km2 (471,118 sq. miles)
1,386	20.2 years	56 per Km2 (146 people per mi2)	527,970 Km2 (203,850 sq. miles)
2	28.1 years	20 per Km2 (52 people per mi2)	38,117 Km2 (14,717 sq. miles)
4,426	19.5 years	115 per Km2 (298 people per mi2	1,000,000 Km2 (386,102 sq. miles)