Wave-wise Comparison of COVID 19 Based On SARS-CoV-2 Variants of Concern (VOCs) in Bangladesh, India, Sri Lanka, Pakistan, Nepal and the Probable Reasons Behind The Less Devastating Effects of Delta variant in Bangladesh: A Review.

By

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A thesis submitted to the Department of Mathematics and Natural Sciences in partial fulfillment of the requirements for the degree of
Bachelor of Science in Microbiology

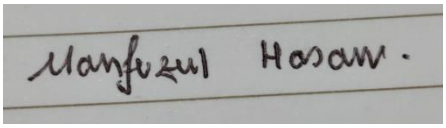
Department of Mathematics and Natural Sciences
Brac University
January, 2022.

Declaration

It is hereby declared that

1. The thesis submitted is my/our own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I/We have acknowledged all main sources of help.

Student's Full Name & Signature:



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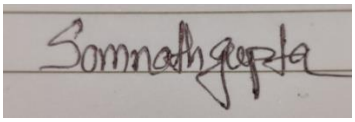

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Approval

The thesis/project titled “Wave-wise comparison of COVID 19 based on SARS-CoV-2 Variants of Concern (VOCs) in Bangladesh, India, Sri Lanka, Pakistan, Nepal and the probable reasons behind the less devastating effects of Delta variant in Bangladesh: A Review.” submitted by

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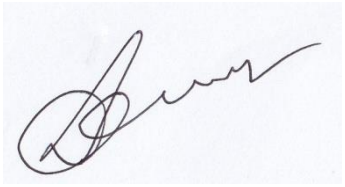

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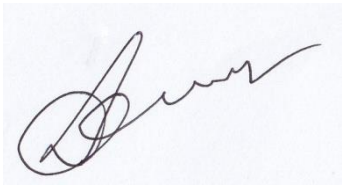

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Ethics Statement

For completion of our study, we collected data from many sources. Firstly, we used sources such as PubMed, Scopus and Google scholar for collecting relevant research articles. Moreover, we have also collected data from sources such as different national and international databases and websites for acquiring relevant information.

Abstract:

Background: The world is currently facing the devastating effects of COVID-19. Increasing spread of SARS-CoV-2 Variants of Concern (VOCs) has an impactful effect on different waves of this pandemic. Every country tried to tackle the pandemic by administering COVID specific vaccines. In this scoping review, we aimed to find out the association between SARS-CoV-2 Variants of Concern (VOCs), vaccination and waves in Bangladesh, India, Sri Lanka, Pakistan and Nepal along with the possible reasons behind the less severe effects of Delta variant in some of the countries.

Knowledge Gap: Although there are many studies emphasizing on effects of different Variants of Concern (VOCs), vaccinations and country specific pandemic patterns, there is shortage of information regarding the direct association of VOCs contributing to waves of the pandemic in our selected countries. Therefore, we tried to highlight on the infectivity patterns of the VOCs which resulted in different waves of the pandemic in the mentioned countries.

Methods: We used two electronic search engines (PubMed and Scopus) and one database (Google Scholar) for collecting articles published between December 2020 to November 2021 which highlighted on SARS-CoV-2 VOCs and waves in our desired countries. Besides, we also included some grey data from some websites and databases (World Health Organizations and Ministry of Health, Sri Lanka). After collecting data based on selected parameters, we created wave-wise graphs based on confirmed cases, death rate and vaccinations for our selected countries along with summary table highlighting effects of different VOCs in our selected countries during those time periods.

Result: After analysis of the data based on different waves (Confirmed cases, death rate, variant wise infectivity at a particular time period), we came to a conclusion that, the less severe effects of Delta variant in Bangladesh and Pakistan is due to high prevalence of beta variant before the spread of Delta variant. Although immunization by vaccination aids to reduce the effects of the virus, in our selected countries the vaccination campaign did not contribute much to the dynamics of the pandemic till October 2021.

Conclusion: Variant specific analysis of the pandemic is important for proper identification of causes behind the waves. The casualties of the pandemic can be mitigated if proper identification of different VOCs is performed before mass spread. Therefore, for containment of the pandemic in the future, the relevant authorities can emphasize on steps such as genetic screening when a new variant emerges. Besides, the vaccination facility must be accessible to a large proportion of the population in order to ensure community level protection.

Keywords:SARS-CoV-2 , VOCs, COVID 19, Vaccine.

Acknowledgement

First and foremost, we are grateful to the Almighty for allowing us to complete our work within time without experiencing any major obstacles. Then we want to express our gratitude to our supervisor, Mahbubul Hasan Siddiqee, PhD, for bearing with our mistakes and providing frequent input to assist us improves our research. We would like to thank all of the helpful faculty members for their assistance. We would also like to thank our parents and teammates for their constant support over the entire semester. This journey was not successful without them. Thank you.

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List of Acronyms

VOCs: Variants of Concern.

VOI: Variant of Interest.

VOHC: Variant of High Consequences.

WHO: World Health Organization.

UN: United Nations.

CHRF: Child Health Research Foundation.

ACE2: Angiotensin-Converting Enzyme 2

mAbs: Monoclonal Antibodies.

CDC: Centers for Disease Control and Prevention.

ICU: Intensive Care Unit.

RT-PCR: Reverse Transcription Polymerase Chain Reaction.

Glossary

Pandemic:	The term pandemic generally refers to the outbreak of a particular disease which spread across a large region, for example multiple continents or worldwide.
Variants of Concern:	A Variant of Concern (VOC) is considered to be more infectious along with increased likelihood of causing breakthroughs or re-infections in individuals who were previously infected or vaccinated. These variants cause comparatively more severe diseases and have the tendency to resist antiviral treatments or may evade diagnostic tests.
Variant of Interest	A SARS-CoV-2 variant with mutations that are predicted to affect characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape and have been known to cause significant community transmission or multiple COVID-19 clusters, in multiple countries.
Waves	The wave of a disease is generally defined to have certain characteristics such as rising number of confirmed cases along with a certain peak of the outbreak followed by a decline.

Chapter 1

[Introduction]

The world has been dealing with the COVID-19 pandemic for over two years now. The main causative agent responsible behind this outbreak is severe acute respiratory syndrome virus type 2 (SARS-CoV-2) which is a member of the coronavirus family. Although the actual origin of SARS-CoV-2 is unknown till now, the bat coronavirus strain RaTG13 is considered to be the closest relative (Afrin et al., 2021). Back in December of 2019, the first cases of the COVID-19 were reported in Wuhan, Hubei Province, China (Zeng, J. H. et al, 2020). From then, globally there had been approximately 293 million confirmed cases of SARS-CoV-2 infection along with nearly 5.45 million deaths till the December of 2021 (World Health Organization., n.d.). The infection is initially associated with the respiratory tract of the infected individuals while the common symptoms mainly include fever, cough, chest pain, lack of appetite, body aches, mild gastrointestinal diseases, myalgia, and/or fatigue. In severe cases, complications such as acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infection are also commonly evident (Zeng, J. H. et al, 2020). The causative agent SARS-CoV-2 is a positive sense single stranded RNA virus in which the genetic material is easily prone to mutations (Afrin et al., 2021).

1.1 [VOCs of COVID]

As COVID 19 is a single Stranded RNA virus it has intention to get accustomed with genetic changes thus the Corona virus also starts to form genetic lineages (Basics of covid-19,2021). For these genetic changes the world has witnessed different variants of COVID 19. Among all of the variants some of the variants has been declared as Variants of Concern (VOCs), some of them classified as Variant of Interest(VOI) and variant of high consequences (VOHC) by World Health Organization (WHO) (SARS-COV-2 variant classifications and definitions,2021).

As per definition of the UN health body, we can declare a variant as a variant of concern when it has increased rate of transmissibility in epidemiological sectors of a virus (Team, 2021). The declared VOCs are Alpha, Beta, Delta and Gamma.

The HO label, Pango lineage, earliest documented samples and date of designation of VOC'S has been written here. The HO label and Pango lineage of Alpha variant is Alpha and B.1.1.7.

This variant was first documented in United Kingdom during the September of 2020 and it has been designated as VOC on 18th December, 2020. The HO label and Pango lineage of Beta variant is Beta and B.1.351, respectively. Beta variant was documented first in South Africa during May of 2020 and was designated as a VOC on 18th December, 2020. The HO label and Pango lineage for the Gamma variant is Gamma and P.1. It was documented first in Brazil during the November of 2020 and had been designated as a VOC on 11th January, 2021. The HO label and Pango lineage of Delta variant is Delta and B.1.617.2. It was documented first in India on the month of October, 2020 and it was designated as a VOC on 11th May, 2021. (Tracking sars-COV-2 variants,2021)

1.2 [Association between Countries and VOCs]

South Asia was one the first sub-continents to experience the exposure of SARS-CoV-2. The virus was considered to spread in this region through travelers from different countries back in January of 2020 (Bhutta, Z. A., 2021). Among the South Asian countries, we emphasized only on Bangladesh, India, Sri Lanka, Pakistan and Nepal. Between January 2020 to December of 2021, there had been a total of approximately 1,584,518 confirmed cases along with 28,063 deaths in Bangladesh (World Health Organization., n.d.). During the entire timeline of the pandemic, the country had witnessed high prevalence of the Alpha, Beta and Delta variants while the infectivity rate of the Gamma variant had been less evident. In India, the first confirmed case of COVID-19 was also identified in January of 2020. Since then, there had been a total 34,960,261 confirmed cases of SARS-CoV-2 infection with 482,017 deaths till December of 2021 (World Health Organization., n.d.). Among the Variants of Concern (VOCs), Delta variant was first identified in India and caused severe widespread infection. Besides this variant, Alpha, Beta and Gamma variants were also prevalent in India. In Sri Lanka, the total number of confirmed cases has been 588,300 along with 15,037 deaths in the timeline between January of 2020 to December of 2021. Among the Variants of Concern (VOCs), the Alpha and Delta variants were more common in India. On the contrary, the Beta and Gamma variants were relatively less prevalent. However, a unique variant of SARS-CoV-2 has been identified in Sri Lanka which is often referred to as the Sri Lankan variant. The Pango Lineage of this variant is B.1.411 and infection with this variant was widespread in the country within the months of October 2020 and April 2021 (Madushanka, T. T. et al., 2021). In Pakistan, within January 2020 and December 2021, the reported number of total confirmed cases and deaths were 1,297,235 and 28,943 (World Health Organization., n.d.). Among the SARS-CoV-2 Variants of concern (VOCs), the Alpha, Beta and Delta were more widespread. Although infection with Gamma variant was present in Pakistan, the number of infections has been comparatively lower than the other VOCs. Between the months of January 2020 and December 2021, there had been a total 829,632 confirmed cases of SARS-CoV-2 infection along with 11,601 deaths (World Health Organization., n.d.). Among the Variants of Concern (VOCs), the Delta variant caused widespread infection in Nepal. Prevalence of Alpha variant has also been present in the country. However, relevant information regarding spread of other VOCs is unavailable for Nepal (Paudel et al., 2021).

1.3 [Country Specific Waves]

Waves of a disease is the situation when a country is facing the highest rate of transmissibility by any disease causing agent. COVID-19 has impacted the world with different waves on different time frames. The severity of the waves was associated with different variants of concern of the virus. Countries like Bangladesh, India, Pakistan, Sri Lanka have faced the peak of the infectivity rate of the virus several times in the last two years by different strains of SARS-COV 2. Till now Bangladesh is dealt with 3 deadly waves of Coronavirus. The time frame of the First wave was between May, 2020 and November, 2020. Second and Third waves were from March 2021 to May 2021 and June 2021 to August 2021, respectively. In the case of India, the duration of the waves was longer but the number of waves was 2. Time frame of those waves was from July of 2020 to November of 2020 and April of 2021 to August of 2021, respectively. Some countries like Pakistan have already witnessed 4 waves with the time frame of May 2020 to July 2020, November 2020 to January 2021, March 2021 to May 2021 and July 2021 to Sep2021, respectively. Sri Lanka and Nepal were also affected with the peak of this deadly virus in different time periods. The duration of the 2 waves of Nepal was from September of 2020 to December of 2020 and between April of 2021 to August of 2021 (WHO coronavirus disease dashboard with vaccination data,2021). Sri Lanka witnessed three different waves from January of 2020 to October of 2020, October of 2020 to April of 2021 and April of 2021 to September of 2021, respectively (*COVID-19 Epidemiology, Sri Lanka* 2021).

1.4[Effects of the variants during different waves]

Spread of different variants of SARS-CoV-2 contributed to the waves in many countries. For instance, the second wave of the pandemic in India was caused due to the impact of the deadly Delta variant (Tareq et al., 2021). On the contrary, the first wave was caused by the Wuhan-like strains of Covid. Similarly, in the case of Bangladesh, the first wave of the pandemic was caused by Wuhan-like strains of SARS-CoV-2. The second and third waves in the country were however due to the effects of the Variants of Concern (VOCs), particularly due to Alpha, Beta and Delta variants (Saha et al., 2021). Pakistan however experienced four waves of the pandemic. Although the first wave was caused by Wuhan-like strains of SARS-CoV-2, the second, third and fourth waves were due to other variants such as Alpha, Beta, Gamma, Delta and Epsilon (COVID-19 Results Briefing, 2021). Sri Lanka also went through

four waves of the pandemic. The first wave was caused by Wuhan-like strain whereas the Sri Lanka variant (B.1.411) contributed to the second wave. Alpha and Delta variants mostly contributed to the third and fourth wave in the country. In Nepal, there were two major waves of the pandemic which were due to prevalence of Wuhan like strains and Delta variant respectively.

1.5[Aim of Our study]

The aim of this study is to find out the direct association between different waves and variant of concerns (VOC's) in some countries of South Asia like Bangladesh, India, Sri Lanka, Pakistan, Nepal and the scientific reason behind the less devastating effects of Delta Variant in Bangladesh.

After analyzing all the data given in the paper we assume that the reason behind the less severity of delta variant in Bangladesh is connected with the Pre- prevalence of Beta variant in our country. The explanation behind that is we have been given in the table (Result section), that there was high prevalence of Beta variant in Bangladesh before the Delta detected whereas this scenario was not seen in India, Nepal, Sri Lanka (Where the effects of Delta was deadly). (Who coronavirus disease (covid-19) dashboard with vaccination data,2021)

Chapter 2 [Methodology]

2.1[Search strategy and Data Source]

We have used Scopus and PubMed as the primary data source of this study. Google Scholar, a search engine was also used to find the original articles related to our title, "Wave-wise comparison of COVID 19 based on SARS-CoV-2 Variants of Concern (VOCs) in Bangladesh, India, Sri Lanka, Pakistan, Nepal and the probable reasons behind the less devastating effects of Delta variant in Bangladesh". This search was done independently by us from July,2020 to October 2021 (studies related to our topic published in this time period). To ensure the authenticity and inclusion of grey literature in the project we go through the news archives and reports connected to our topic from different newspapers of different

countries. We also used some information published in country specific health websites. Different international websites and databases (For example: https://www.who.int/ and Our World in Data) harboring the statistical information regarding the number of confirmed cases, death and timeline of the pandemic had been used to obtain adequate information for our graphs and tables.

In this study we have used some key terms for searching our articles. The key terms were related to our subject of interest. We have rearranged the position of key terms in our search method so that we can cover all the related articles for this study. For example, we have used the key terms like Alpha Variant of COVID in India, B.1.1.7 Variant of COVID in India, UK Variant of COVID in India (these key terms have been arranged by using the HO label, Pango Lineage and Country specific name of the variant).

2.2[Eligibility Criteria]

While working on this study, we mainly tried to find out the effects of different SARS-CoV-2 variants on the outbreak of the pandemic in our selected countries. The inclusion criteria were: 1) Articles highlighting the outbreak of the pandemic on our desired countries; 2) Articles highlighting on SARS-CoV-2 Variants and their mutations; 3) Studies associated with spread of different VOCs; 4) Government or international data on a particular country, 5) Studies highlighting transmission, confirmed cases and death rates in Bangladesh, India, Sri Lanka, Pakistan and Nepal; 5) and, original articles published between January 1st, 2021 to November 30, 2021.

Besides, the following exclusion criteria had been applied: 1) Articles regarding VOCs specifically focusing on countries outside our sub-continent; 2) Non-peer reviewed publications; 3) Incomplete publications such as letter to editors; 4) Studies published on languages other than English; 7) Studies that met our selected criteria but full text being inaccessible.

Tools used in this study:

The component of Microsoft Office, named Microsoft Word, Microsoft Excel was used in this study as the main tool of writing and preparing Graphs and Tables (In our result section). Mendeley reference manager (version 2.62.0) had been used in this study to organize and cite the articles. We have also used SmallSEO Tools, an online plagiarism checker for ensuring the authenticity of our writing.

2.3[Data extraction]

A summary table had been created at first to extract our desired data from the eligible studies. For each study, the table included the following sections: Title of the publication, country, name of first author, date of publication, study type and key information. The accuracy of our extracted data had been confirmed by revising the included articles. The data involving confirmed cases, number of deaths and timeline of the pandemic have been converted to per million count before working on our graphs. We used these data to prepare graphs according to the different waves. Data regarding prevalence of the different variants had been arranged in separate tables based on transmission rate, identification and spread on the selected countries. We later used these data for obtaining our desired results.

Chapter 3[Result]

3.1[Bangladesh]

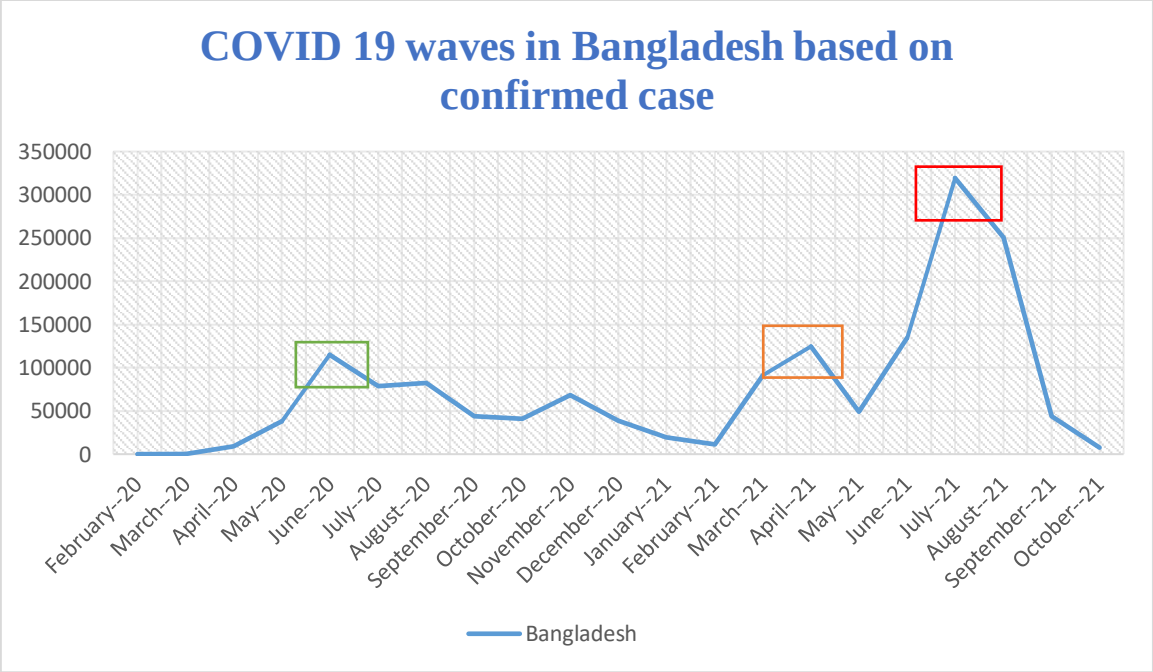

Figure 1**:** Line graph presenting different waves of the pandemic in Bangladesh on the basis of confirmed cases.

WHO Label	**Pango Lineage**	**First Outbreak**	**1st Detection date in world**	**Declared as variant of concern in world**	**Detection date in Bangladesh**	**Detection %**
Alpha	B.1.1.7	UK	20 Sep 2020	18 Dec 2020	Dec,2020 (CHRF) 6th Jan,2021	Jan21: **21%** Feb21: **16%** Mar21:**8%**
Beta	B.1.351	South Africa	May 2020	14 Jan 2021	Feb,2021	Feb21:**33%** March21:**77%** May21:**90%**
Gamma	P.1	Brazil	Nov 2020	15 Jan 2021	Feb 18,2021	No Specific Data was found
Delta	B.1.617.2	India	Oct 2020	6 May 2021	8th May,2021	May/June:**68%** July21:**90%**

						Sep21:**90%**

Table 1**:** Prevalence of the Variants of Concern (VOCs) in Bangladesh.

Bangladesh endured three waves of COVID 19 pandemic. The time period of the first wave lies between May and November of 2020. During this time, Wuhan-like strains were the main causative agent and VOCs were not even discovered in the country until December, 2020. The country went through the second wave during March to May of 2021. Beta variant was clearly dominant in Bangladesh during that time (Rahman et al., 2021). The third wave of the pandemic started in May, 2021 and lasted till August of 2021. The Delta variant was the most commonly found variant during that time.

3.2[India]

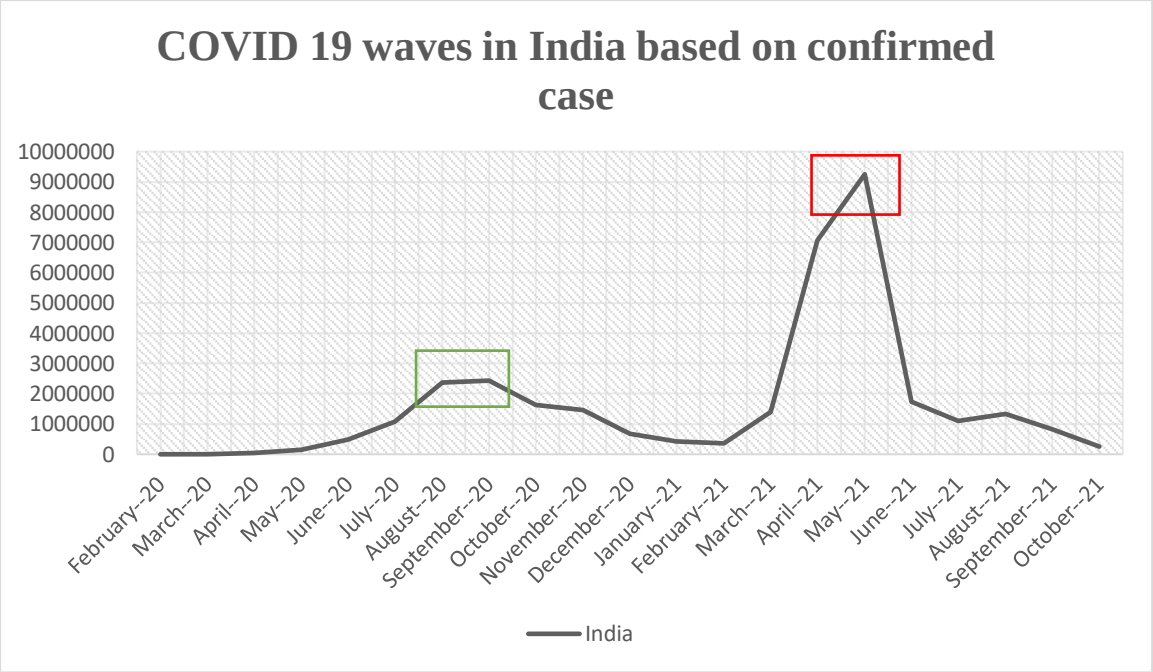

Figure 2**:** Line graph presenting different waves of the pandemic in India on the basis of confirmed cases.

WHO Label	Pango Lineage	First Outbreak	1st Detection date in world	Declared as variant of concern in world	Detection date in India	Detection %
Alpha	B.1.1.7	UK	20 Sep 2020	18 Dec 2020	29 Dec,2020	April 21:**12.1%**
Beta	B.1.351	South Africa	May 2020	14 Jan 2021	April	April: **33.9%(Combined)**
Gamma	P.1	Brazil	Nov 2020	15 Jan 2021	April	April: **33.9%(Combined)**
Delta	B.1.617.2	India	Oct 2020	6 May 2021	October 20	March 21**:1%** May21:**70%/81.6%** June21:**88.8%**
Epsilon	B.1.427 and B.1.429	USA	March 2021	**Not VOC**	April	April: **33.9%(Combined)**

Table 2**:** Prevalence of the SARS-CoV-2 Variants in India.

India went through two different waves of the pandemic. The first wave was between July and November of 2020. During this time, the VOCs were not prevalent. The second wave started during April of 2021 and lasted till August of that year. During this time, multiple VOCs of SARS-CoV-2 were prevalent with the Delta variant being the main factor behind increased severity.

3.3 [Pakistan]

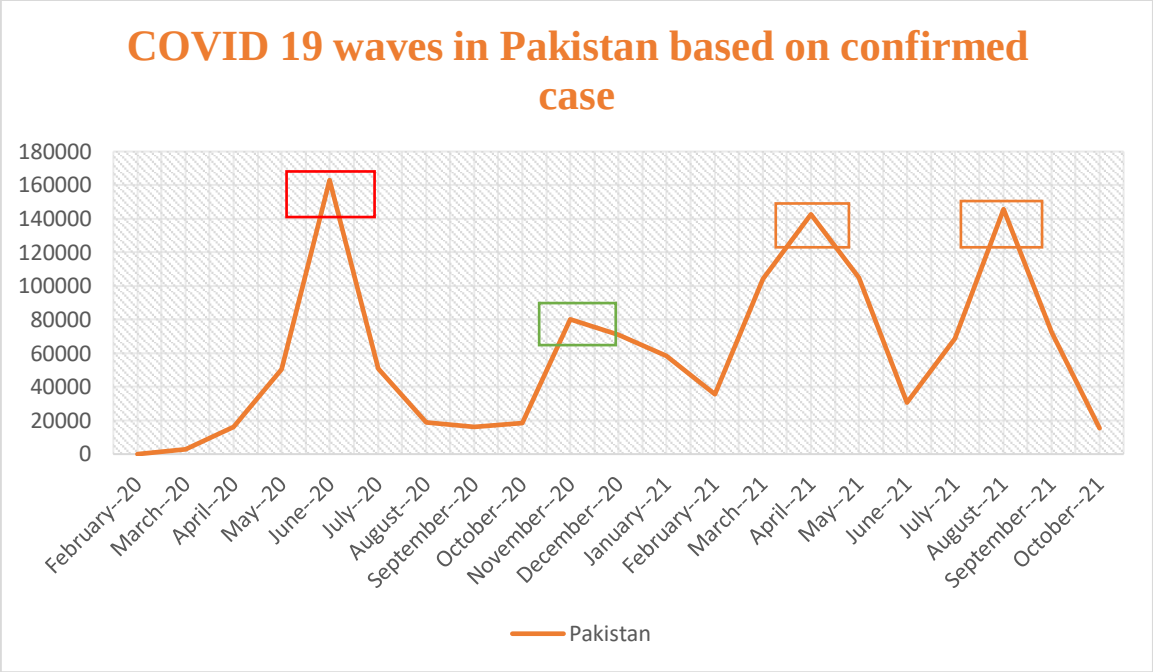

Figure 3**:** Line graph presenting four different waves of the pandemic in Pakistan on the basis of confirmed cases.

WHO Label	**Pango Lineage**	**First Outbreak**	**1st Detection date in world**	**Declared as variant of concern in world**	**Detection date in Pakistan**	**Detection %**
Alpha	B.1.1.7	UK	20 Sep 2020	18 Dec 2020	Jan27,2021	May21:**60-70%-** April – July:**37% out of 63%**
Beta	B.1.351	South Africa	May 2020	14 Jan 2021	April 30	June-**59%** July **1%**
Gamma	P.1	Brazil	Nov 2020	15 Jan 2021	April 30	April to July-**7%**
Delta	B.1.617.2	India	Oct 2020	6 May 2021	May 28,2021	July-**43%**
Epsilon	B.1.427 and B.1.429	USA	March 2021	**Not VOC**	July 2021	July-**21.7%**

Table 3**:** Prevalence of the SARS-CoV-2 Variants in Pakistan.

Pakistan went through four different waves (Hasan et al., 2021). During the first two waves, the VOCs had not been involved. The third wave lasted between March and May of 2021. During this time, the Alpha variant was the most prevalent. However, other variants such as Gamma and Beta also contributed to the increased cases and deaths during this time (Hasan et al., 2021). The fourth wave started in July of 2021 and lasted till October of 2021. Although the Delta variant mostly aided this wave, other variants such as Epsilon and Beta were also present.

3.4[Sri Lanka]

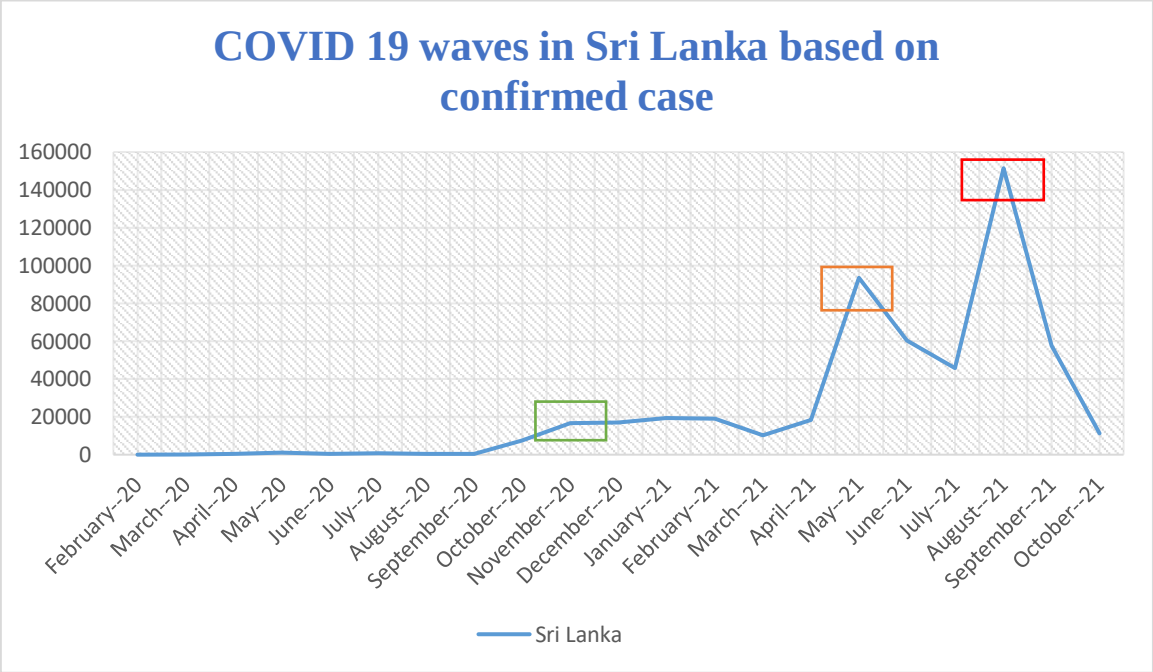

Figure 4**:** Line graph showing three different waves of the pandemic in Sri Lanka on the basis of confirmed cases.

WHO Label	**Pango Lineage**	**First Outbreak**	**1st Detection date in world**	**Declared as variant of concern in world**	**Detection date in Sri Lanka**	**Detection %**
Sri Lankan Variant	B.1.411	Sri Lanka	October 2020	-	October 2020	64%(Oct20-april2021)
Alpha	B.1.1.7	UK	20 Sep 2020	18 Dec 2020	Jan 2021	85%- 26th March to 30th April(2021

Beta	B.1.351	South Africa	May 2020	14 Jan 2021	March 21	No Specific Data was found.
Gamma	P.1	Brazil	Nov 2020	15 Jan 2021	No Specific Data was found.	No Specific Data was found.
Delta	B.1.617.2	India	Oct 2020	6 May 2021	May 2021	75%-July2021

Table 4**:** Prevalence of the SARS-CoV-2 Variants in Sri Lanka.

Total of three waves had been evident in Sri Lanka. The first wave lasted between January and October of 2020. The Sri Lankan Variant (B.1.411) aided in this wave. The second wave was evident during the months of October 2020 to April of 2021 and During this time the Alpha variant was widespread in the country. The third wave was in between the months of July and September of 2021. The Delta variant caused a drastic outcome in the country during the third wave.

3.5[Nepal]

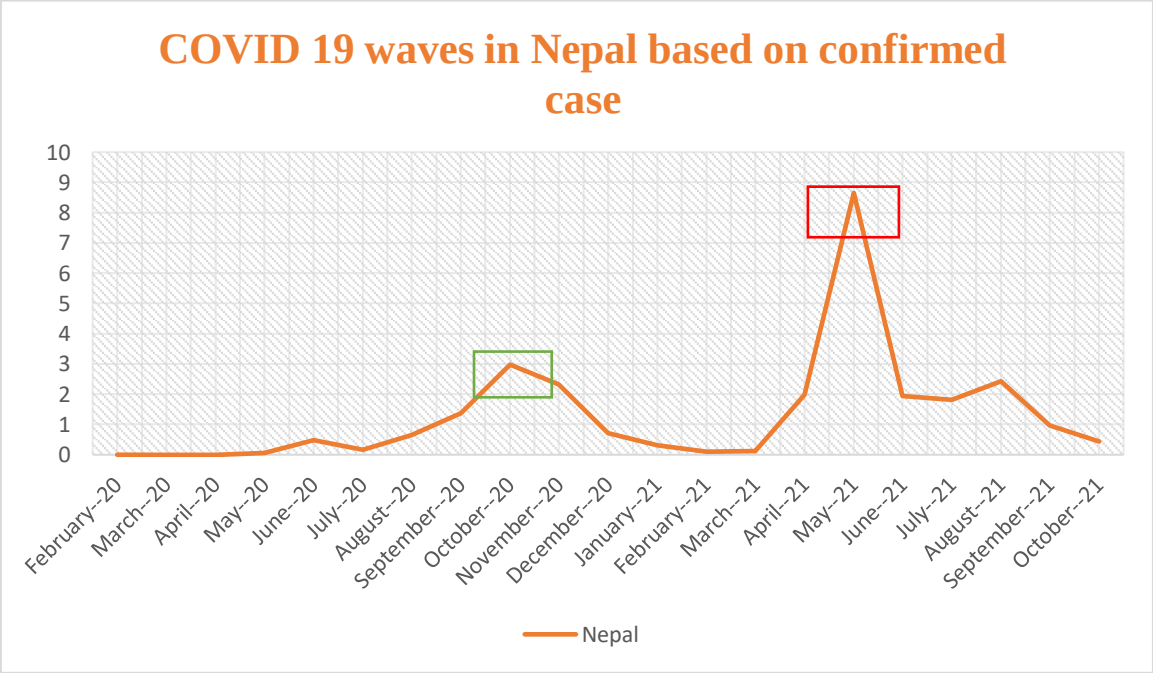

Figure 5**:** Line graph showing three different waves of the pandemic in Nepal on the basis of confirmed cases.

WHO Label	Pango Lineage	First Outbreak	1st Detection date in world	Declared as variant of concern in world	Detection date in Nepal	Detection %
Alpha	B.1.1.7	UK	20 Sep 2020	18 Dec 2020	June 2021	No Specific Data was found.
Beta	B.1.351	South Africa	May 2020	14 Jan 2021	No Specific Data was found.	No Specific Data was found.
Gamma	P.1	Brazil	Nov 2020	15 Jan 2021	No Specific Data was found.	No Specific Data was found.
Delta	B.1.617.2	India	Oct 2020	6 May 2021	May-July 2021	75%

Table 5: Prevalence of the Variants of Concern (VOCs) in Nepal.

The country went through two waves of the pandemic. The first wave lasted between the months of September and December of 2020 and the VOCs were not prevalent during this time (Paudel et al., 2021). However, the Delta variant was widespread in Nepal during the second wave which lasted between the months of April and August of 2021 (Paudel et al., 2021).

3.6[Combined Results]

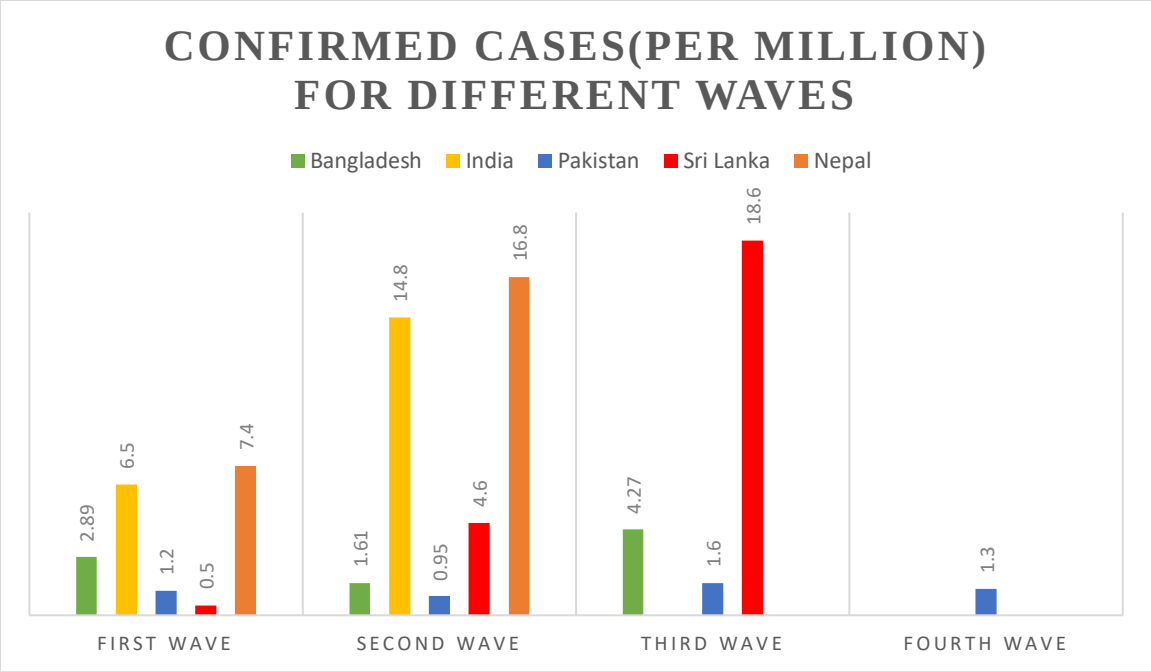

Figure 6: Analysis of **confirmed cases** based on different waves of COVID 19 infection. The values are represented as thousands **per million**.

Notes: For the third wave, data for the countries India, and Nepal were unavailable. Fourth wave is only relevant for Pakistan since this phenomenon did not take place in other countries.

Our findings suggest that, based on the overall populations, the confirmed cases were highest in India and Nepal (6.5 and 7.4 thousand per million respectively). During this wave, non-VOCs were the main causative agents of SARS-CoV-2 infections. In the case of the second wave, both of these countries again had the highest number of confirmed cases per million populations (approximately 14.8 thousand in India and 16.8 thousand in Nepal). The Delta variant was the most commonly found variant during this time for these two countries. The third wave of the pandemic was only prevalent in Bangladesh, Pakistan and Sri Lanka. On the basis of overall population to cases ratio, Sri Lanka witnessed the highest number of confirmed cases (18.6 thousands) per million due to the impact of the Delta variant. Finally, the fourth wave of the pandemic was only present in Pakistan.

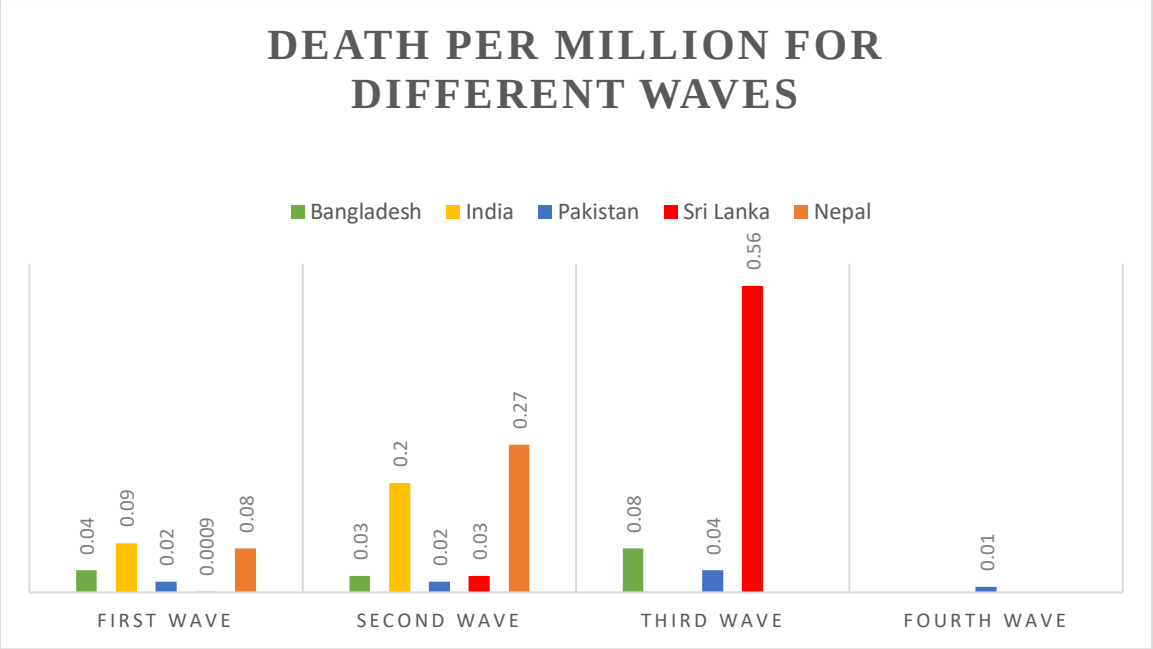

Figure 7**:** Analysis of number of **deaths** based on different waves of COVID 19 infection. The values are represented as thousands **per million.**

Notes: For the third wave, data for the countries India and Nepal were unavailable. Fourth wave is only relevant for Pakistan since this phenomenon did not take place in other countries.

In our wave-wise analysis for the number of deaths, we found a pattern similar to the confirmed cases. In the first wave, India and Nepal also had the highest number of deaths among our selected countries (0.09 thousand per million for India and 0.08 thousand per million populations in Nepal). In the case of the second wave, the death rate was again highest in the two countries (0.20 thousand per million in India and 0.27 thousand per million in Nepal) due to effects of the Delta variant. In the third wave, Sri Lanka had the highest number of deaths as the number rose approximately 0.56 thousand per million populations.

3.7[Vaccination]

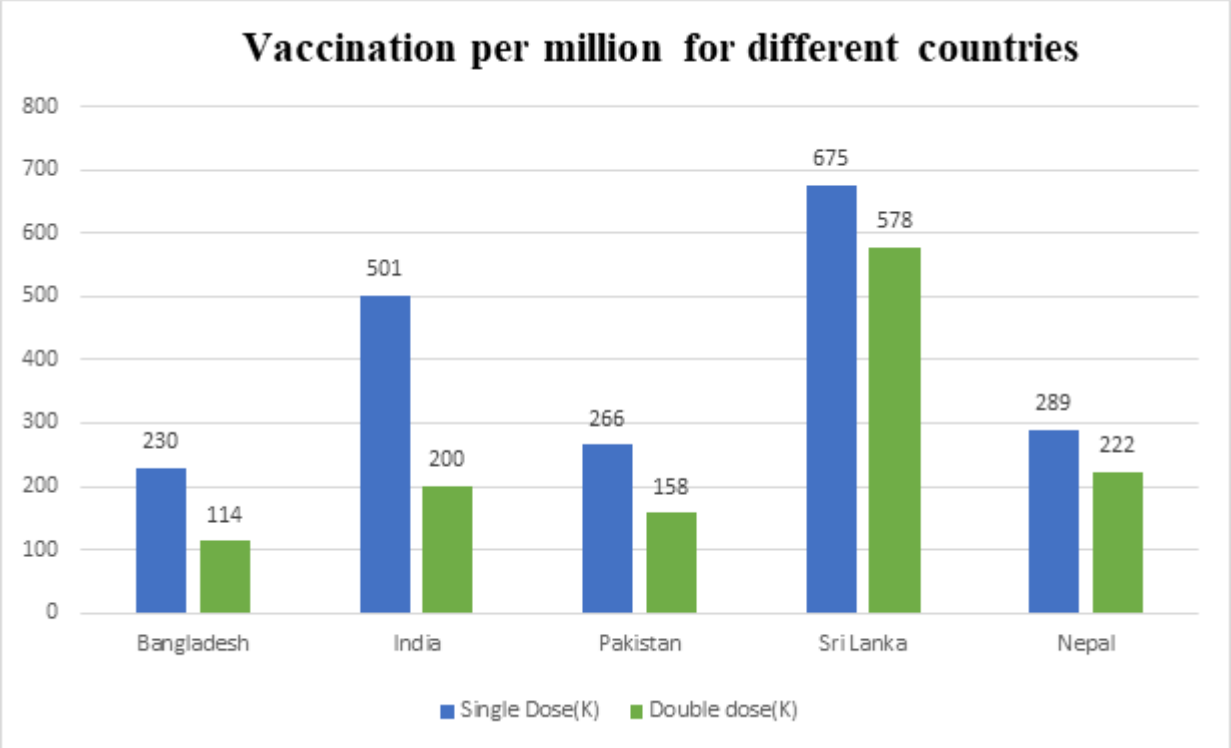

Figure 8**:** Single and Double dose vaccines administered per million populations. The data is presented as thousands per million.

Country	Doses given	Fully vaccinated	Percentage of population fully vaccinated
Bangladesh	56.1 M	18.7 M	11.3%
India	968 M	276M	20.0%
Pakistan	93.6M	34.8M	15.8%
Sri Lanka	27.4M	12.6M	57.5%
Nepal	14.9M	6.47M	22.1%

Table 6**:** Proportion of Vaccinations.

Among our selected countries, Sri Lanka had the highest proportion of vaccinations compared to the population till October 2021. 57.5% of their population were vaccinated which is much higher than the other four countries. On the other hand, Bangladesh had the lowest vaccination rate during the time period since only 11.3% of the population was fully vaccinated (Ritchie, H. 2021). In the other three countries (India, Pakistan and Nepal), around 20% of the population were fully vaccinated.

Chapter 4[Discussion]

The analysis of the data reveals that India has faced the most devastating impact of Delta Variant during the second wave (The prevalence of Delta Variant was 81.6% in May 2021 and was 88.8% in June 2021) among the five mentioned countries (Zaman, 2021). On the other hand, Delta affected least in Pakistan on their fourth wave (The prevalence of Delta Variant was 43% in July) among the stated countries (Hasan et al., 2021). The prevalence of Delta variant was also high in Bangladesh during the time period of May 2021 to September 2021 but it shows less devastating impact on the people of Bangladesh compared to other countries. One of the probable reasons behind the less severe effects of the Delta variant in spite of having high prevalence is that the effects of Beta variant immediately before the Delta variant had arrived (Saha et al., 2021). Beta variant caused relatively less severe effects and deaths compared to the Delta variant along with increased numbers of asymptomatic infections in healthy and young populations. Our findings suggest that mass spread of Beta variant in Bangladesh contributed to development of immune response in population which led to overall less infections and death when the Delta variant arrived.

Beta variant was prevalent in Bangladesh between the months of March 2021 and May 2021. The rate of confirmed cases in that time period was 77% and 90%, respectively (Saha et al., 2021). On the other hand, there was less prevalence of Beta in India before the Delta Variant outbreak. Moreover, the death rate was high compared to other times in Bangladesh during the time when the Beta variant was most abundant. Similarly, as we mentioned before that the destructive effects of Delta were also lower in Pakistan as well, there we can implement the same hypothesis that the high prevalence of Beta variant (59% in July of 2021) can be the factor which conferred protection in Pakistan (Umair et al., 2021).

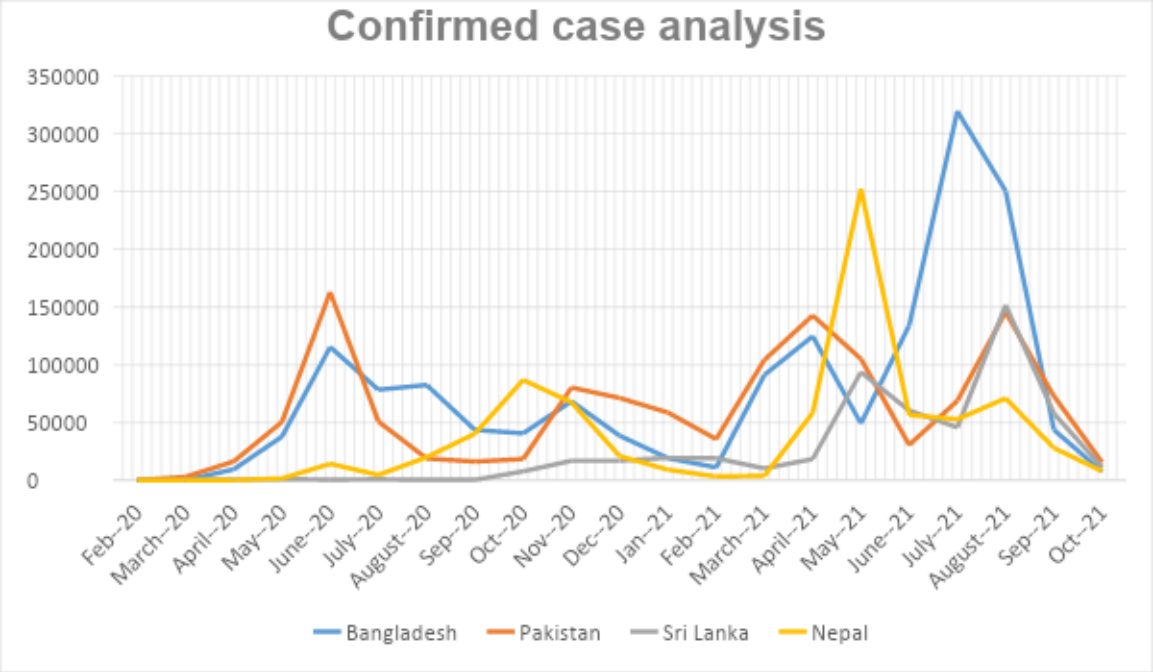

Figure 9**:** Analysis of **confirmed cases** per month for COVID 19 infection. The values are represented as thousands **per million.**

In addition to, after analyzing the data of Sri Lanka and Nepal, there was a clear scenario that Delta played its destructive effects on the countries where there was no impactful prevalence of other variants like Beta and Gamma or lower prevalence of those variants. In Sri Lanka, after the effects of alpha Variant from March 21 to April 2021, there was no highlighted data for Beta and Gamma. So Delta variant was found 75% in July and the death rate was highest in that particular time period in Sri Lanka (Kodikara, 2021). Similarly, Nepal shows the same prevalence and highest death rate in May-July 2021 where the rate of confirmed cases was approximately 75% (Paudel et al., 2021).

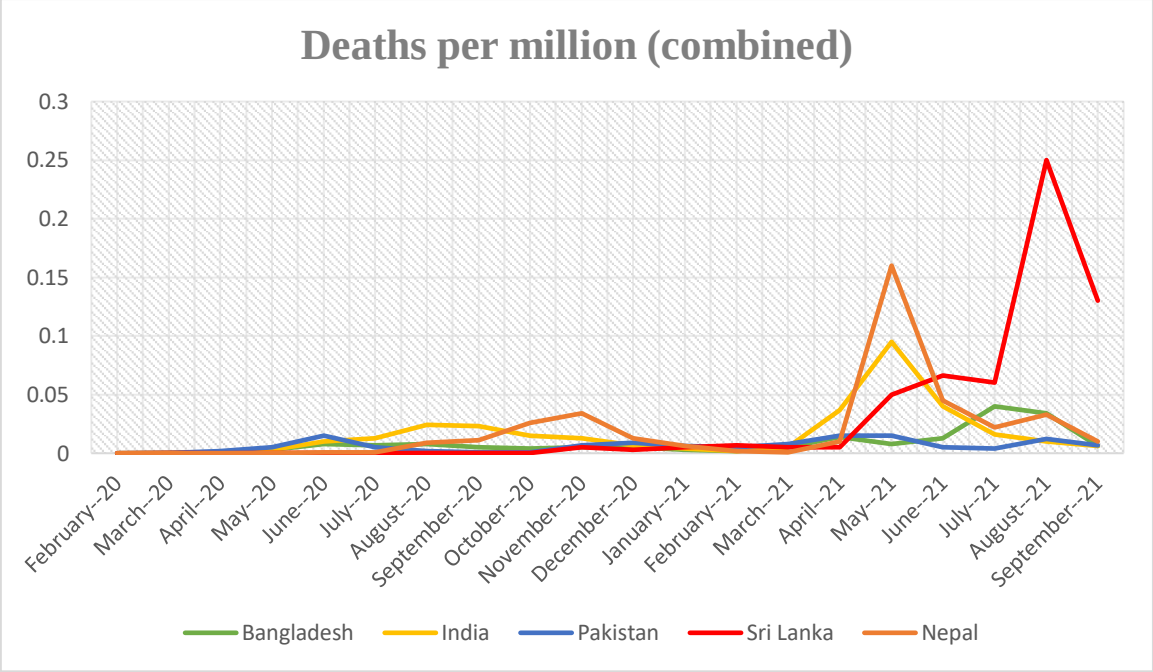

Figure 10**:** Analysis of monthly number of **deaths** for COVID 19 infection. The values are represented as thousands **per million.**

The reason behind less devastating effects of Delta variant in Bangladesh is supported by the provided statistical analysis and wave wise comparison with different variants is also evident with the provided information. So the hypothesis of this study is supported with enough authentic information and country specific data.

A number of factors contribute to the generation of viral mutations. Firstly, interventions by the human immune system can lead to mutations as many components of the immune system can interfere with the viral genome. Secondly, rapid transmission and quick host to host transmission rate can lead to mutations in a virus. Finally, RNA viruses are prone to rapid mutations as compared to DNA viruses due to their error prone replication mechanism. All these factors might have contributed to generation of rare mutations of the SARS-CoV-2 virus which finally resulted in various variants (Chakraborty et al., 2021).

Among the COVID 19 variants, the Alpha, Beta, Gamma and Delta are currently classified as the Variants of Concern (VOCs). A Variant of Concern (VOC) is considered to be more infectious along with increased likelihood of causing breakthroughs or re-infections in individuals who were previously infected or vaccinated. These variants cause comparatively more severe diseases and have the tendency to resist antiviral treatments or may evade diagnostic tests (*Covid variants: What you should know,* 2021).

The reasons behind increased transmission and or severity of a certain variant is mainly due to mutations. For example, ΔH69–V70 deletion mutations of the Alpha variant contributes to the characteristic of immune escape in case of immunocompromised patients. E484K is another notable mutation in a number of VOCs which also improves the ability of a virus to escape the host immune system by decreasing the binding with human monoclonal antibodies (mAbs). P681H mutation on the other hand allows the virus to survive in presence of neutralizing antibodies. P681R mutation in the furin cleavage site aided by increasing the rate of S1-S2 cleavage which ultimately resulted in better transmissibility (Harvey et al., 2021). Certain mutations such as K417N, N501Y, L452R, T478K and E484Q enhance the affinity for human ACE2 receptors which ultimately aids in higher infectivity of the virus (Umair et al., 2021). L452R mutation is unique for the Delta variant and it has a wide range of effects including increased stability of the spike protein, reinforced affinity towards ACE2 receptor, elevated infectivity and even promotes replication of the virus (Harvey et al., 2021). The infectivity and severity of the Variants of Concerned (VOCs) is mentioned in the following table:

WHO Label	**Pango Lineage**	**Notable mutations**	**Attributes**
Alpha	B.1.1.7	ΔH69–V70, N501Y, P681H, E484K (Total 18 mutations over the reference genomic sequence)	• Estimated 64% more deaths compared to Wuhan-like strains. • Transmissibility relative to previously circulating variants: Approximately 29%

Beta	B.1.351	K417N, E484K, N501Y	• Prevalence was higher among the young population without comorbidities. • In-hospital mortality was 20% higher relative to previously circulating variants. • CDC (Centers for Disease Control and Prevention) estimated the transmission rate to be 50% increased. • Expressed escape from neutralizing antibodies in 48% of serum samples obtained from previously infected patients.
Gamma	P.1	K417T, E484K, N501Y (Total 21 lineage defining mutations)	• The mutations found in Gamma have been associated with increased transmissibility, a higher viral load and propensity for immune evasion, and reinfection. • Transmissibility: 38% higher than that of non-VOCs, 10% higher than that of Alpha and 17% higher than that of Beta. • [Exact data for mortality is not found; Wikipedia: 50%]
Delta	B.1.617.2	L452R, T478K, P681R	• Reproduction number relative to non-VOC/VOI: 97%. • Transmission rate is between 40 and 60 percent more than the Alpha variant • compared to non-variant of concern strains, Delta showed approximately 120% greater risk of hospitalization along with 287% greater risk of ICU admission and 137% greater risk of death.

Table 7: General information regarding the SARS-CoV-2 Variants of Concern (VOCs).

The association between country specific waves and different variants of COVID19 varies from country to country. For example, Beta was prevalent in the second wave of Bangladesh (90% in May 21), whereas in the second wave of India the ruling variant was Delta (88.8% in June). Though the first wave of COVID19 in every country is associated with a Wuhan like

variant of the virus, other waves were associated with different strains and different time frames.

Chapter 5[Conclusion]

Our study states that the reason behind less severe effects of Delta variant in Bangladesh is the high prevalence of Beta variant before the Delta Outbreak. The prevalence of Beta among the population has boosted the immunity of the people so that the deadly delta variant impacted with less destruction compared to the neighboring countries. After analyzing all the collected data, we have supported our hypothesis with enough evidence but there are some limitations in this study. We cannot manage all the variant specific detection rate and death rate for each country due to lack of adequate information on these aspects (Umair et al., 2021). Alongside, we are trying to complete some other parameters like the detection method, sample collection technique and so on.

Apart from the variants, many other factors may also have contributed to such varying patterns of the pandemic in different countries. For example, differences in factors such as meteorological variables, demography, comorbidities, immunological aspects, healthcare and medication practices, previous vaccinations, sociocultural practices, economic condition of the population, COVID specific vaccination and government regulations might have greatly influenced the spread of virus and effects of the pandemic in our selected countries. We are also working with some of these factors to find out their effects on different countries such as spread and death due to the emerging variants.

Finally, we are optimistic that the result of the study will help us to take necessary steps for minimizing the effects of future pandemics. For example, the result of this study suggests that we can surely focus on the spread of different variants over different time periods and by this we can take precautionary steps to control the massive spread of any disease causing agent. If a new variant of the virus is detected anywhere in the world, the government authorities must analyze the characteristics of the variant and emphasize on ensuring that the spread of the new variant is prevented.

There are some suggestions for developing countries like ours. There should be a high amount of RT-PCR and whole genome sequencing opportunities throughout the countries so that a particular variant can be identified with ease and patients can be adequately treated based on their situation. Apart from this, the countries can adopt statistical based forecasting

models which would help to predict different aspects of the pandemic such as spread and deaths due to a new emerging variant (Kamran & Ali, 2021).

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Appendix A.

The results and the analysis of our study is based on some factors like different VOCs, waves and vaccination associated with the mentioned countries. There are some other factors that can enrich our hypothesis and update our results like meteorological variables, demography, comorbidities, previous vaccination, immunological aspects, socio-cultural practices, economic conditions and so on.