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P O Box 70587 Gaborone
enquaries@leaders-schools.com
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Dr Tumelo Tlhoiwe
VICE CHANCELLOR

Vice Chancellor's Message To DDT academics Family and the Nation at large During this COVID-19 Pandemic

The whole world has been affected by Coronavirus, economies have shrunk, loved ones lost but our good lord has sustained us. I encourage everyone to consider research as a priority in order to come up with solutions to fight this pandemic.

The struggle you are in today is developing the strength you need for tomorrow. Being challenged in life is inevitable, but you have the choice to decide how you will react to the situation. Especially now, in this time of covid-19 crisis and uncertainty, change the changeable and accept the unchangeable. We may not be able to see it in the moment, but everything happens for a reason. Use this time to make a difference in your life or in the lives of someone else. Work on all areas of personal growth, spend quality time with family, and focus on goals for the future.

Train yourself to find a blessing in everything, Someone once said these words to me, which have stayed in my mind throughout my life. I truly believe that we are not put into a situation that we cannot conquer. Seeing the light in the midst of darkness is a lesson we all should learn, not only during this difficult time, but all the time. Stay focused on the good and making it better. It can only go up from here.

It's tough to see the light in times of darkness. My advice for all researchers and students is to continue to be positive and never give up hope. It's when we start to lose hope that we begin to struggle mentally. Lend a listening ear to everyone; sometimes all someone needs is a person willing to listen. We all need to come together in this time and continue to check on loved ones, friends, teammates, roommates, and classmates. You never know the impact of what a simple 5 minute phone call could do for someone. Spread that love each and every day.

"Life throws you curves but you learn to swerve." No one is ever really prepared for God's greater plans, but we figure it out, taking it one day at a time. During my time at university, there were some unfortunate events, but we always came together as a community to get it through it as one. Now more than ever, we need to take care of each other. Luckily we live in a world we can talk with friends and family virtually. Take care of yourself and your loved ones. We'll all look back on this time and remember the ones who helped us through this challenging time.

"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less."

"A life lived in fear is a life half lived."

VC



Dr Derrick D. Tlhoiwe
CHANCELLOR

Chancellor's Message

To all academic fraternity of DDT College of medicine and beyond, I would like to thank every one of you for your contribution in building Our University college. Thank you for believing in our vision.

DDT continues with its vision as the top medical university in Botswana and draws inspiration from the government of Botswana which has encouraged every citizen to migrate from a minerals-led to a knowledge-based economy, DDT aspires to bring knowledge to Batswana by engaging in state of the art research work and bring solutions to challenging health problems such as the covid-19 pandemic.

Yes our journey has not been smooth, we all understand, "The size of your success is measured by the strength of your desire; the size of your dream; and how you handle disappointment along the way." Disappointments are just God's way to saying 'I've got something better'. Be patient, live life, have faith." We shall overcome every barrier ahead of us for ours is a noble task of improving the lives of Batswana.

I encourage everyone of you to commit to research work, Desire to face the challenge in solving the unsolved problems, concern over practical problems initiates research; Desire to get intellectual joy of doing some creative work; Desire to be of service to society; Desire to get respectability due to your creativity and innovation.

Covid-19 has ravaged many economies, I therefore encourage everyone of you to dedicate considerable amount of time in coming up with solutions to curb this pandemic.

DDT will set aside substantial amount of resources to go into each faculty research work. Your commitment to research will also build your promotion ladder to senior lecturer, assistant professor to full professor.

Last but not the least, I encourage you once again to remember that, The road to success and the road to failure are almost exactly the same it depends on the one you want embrace, Success is not final; failure is not fatal: Opportunities don't happen. You create them , It is the courage to continue that counts. It is better to fail in originality than to succeed in imitation. There are two types of people who will tell you that you cannot make a difference in this world: those who are afraid to try and those who are afraid you will succeed.

Chancellor

Contributors

Featured Contributors

Dr Derrick D. Tlhoiwe
Dr Tumelo Tlhoiwe
Ogorogile Mokate
Paul Moyo
Dr Carlos Alberto Justo Sedeno
Kabo O. Tshiamo
Raymond Chibvongodze
Dr Martinson Danquah
Dr Tapfuma Mudawarima
Suwilanji Chisenge
Dr Larry L. Mweetwa
DDT 2019 Final Year Students

Administrative Assistance

Gofaone R. Masake
Katlego V. Kenosi

Executive Editor

Dr Larry L. Mweetwa

Supporting Partner

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Dr Derrick D. Tlhoiwe
Chief Editor



Dr Tumelo Tlhoiwe
Deputy Chief Editor



Ogorogile Mokate
Managing Editor



Kabo O. Tshiamo
Senior Editor



Dr Carlos
Assistant Editor



Dr Larry L. Mweetwa
Executive Editor

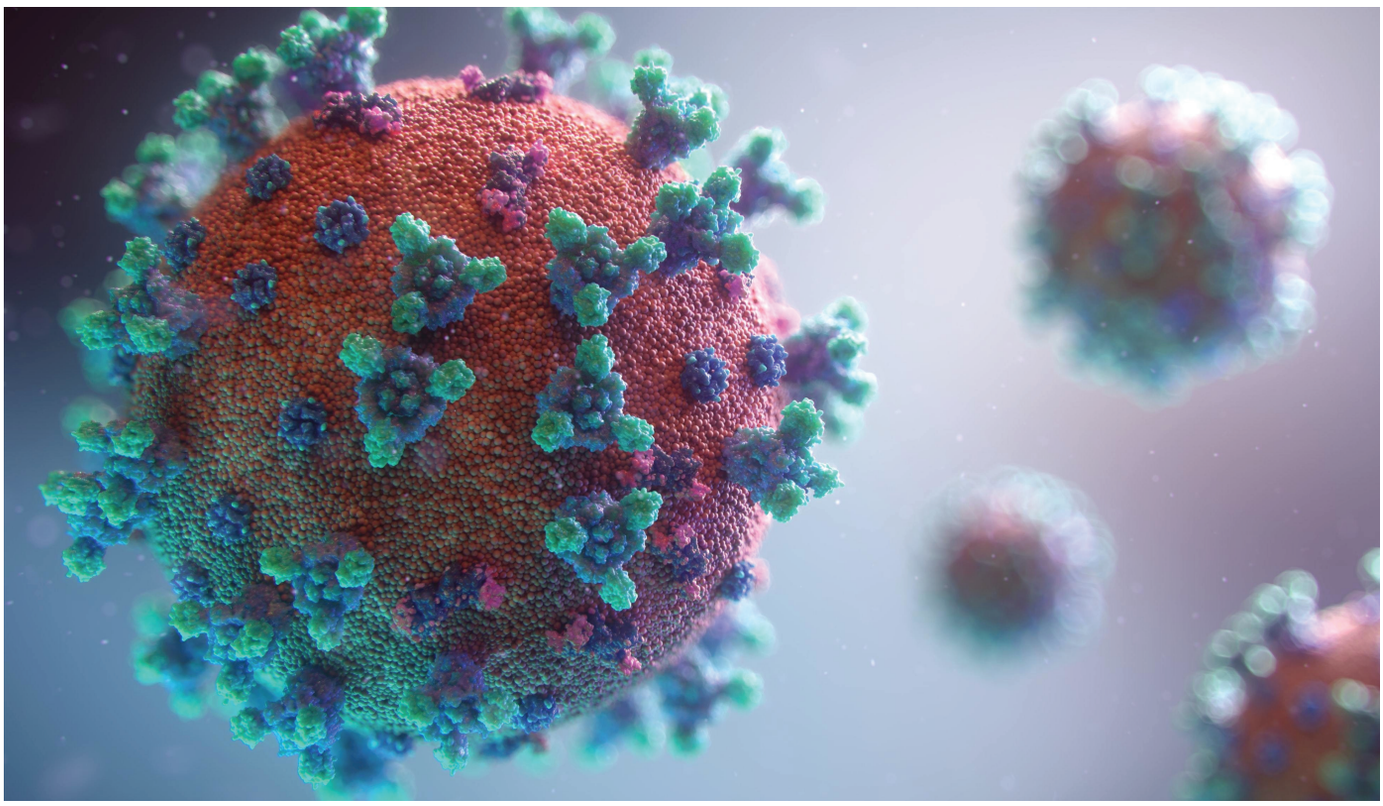
The Financial and Economic Implication of Emerging SARS-CoV-2 Variants: A Global Perspective

Author: *Dr. Larry Mweetwa*

1. Department of Pharmacy and Pharmaceutical Sciences

Corresponding Author *Dr. Larry Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract:

The Covid-19 pandemic, which initiated from Wuhan, China, spread like wildfire globally, disrupting both the demand and supply of the economies in a highly unprecedented manner. While the demand immensely suffered, the supply has also been severely affected due to restricted movement of the personnel, social distancing protocols implemented across the globe, and closure of the international borders hence disrupting the supply, reducing the production and accessibility of the raw materials.

Objectives:

The objective of this research is to critically examine the finance and the economic implications of the Emerging SARS-CoV-2 variant to analyze its global impact.

Key Findings:

No country was exempt from the negative implications of the pandemic irrespective of policies adopted to mitigate the effects as direct and indirect economic influences were felt throughout the globe. The graveness of the impact only relied on the structural economic integrity of the individual countries. At micro-level, the financial implementation of the businesses demanded credit for working capital requirement. With lockdowns in place, it became difficult for the businesses to meet short-term debt obligations resulting in bankruptcies of small-scale enterprises throughout the globe. Developing and underdeveloped countries also lagged behind on remittances as a direct result of increasing unemployment levels and a reduction in incomes. The highest decline was recorded in the Foreign Direct Investment globally in 2020, accounting for a 42% reduction. Yet, the developing economies, specifically within the Asian region, recorded a less drastic decline in the FDI as opposed to developed nations.

Conclusions:

The findings revealed that economic growth globally reduced by a staggering 4.5%, with many developing countries facing many severe consequences due to supply and demand disruption. However, with the development of vaccines, a sharp recovery in economic growth is expected in 2021 to overcome the losses of the previous year.

Keywords:

SARS-CoV-2 variant, COVID-19, omicron variant, delta variant, lambda variant, alpha variant, beta variant financial impact, economic impact.

1.0 Introduction

In December 2019, China reported an outbreak of pneumonia in Wuhan. The disease was referred to as coronavirus disease (COVID-19) or (SAR-COV-2), and the spread of the disease resulted in an ongoing pandemic across the globe (Chowdhury and Oommen, 2020). With the increment in the disease rate, the World Health Organization (WHO) provided recommendations for imposing the local, and national area lockdowns, restricting the business operations, and maintaining social distancing for limiting an interaction curtailing the spread of the virus. The pandemic situation has been resulting in unprecedented impacts on the health and well-being of countries' populations. The recent statistics revealed that 2,705,236 individuals had died from Covid-19, such that the situation has not improved since the outbreak of the virus (Worldometers, 2021). Along with a significant death loss, the spread of Covid-19 had imposed a significant financial and economic burden on the countries. According to Darab et al. (2021), from the economic perspective, the spread of Covid-19 and increment in the number of patients have been imposing a direct medical and an indirect cost on the patients, the health system, and the government.

The analysis of the economic burden of a direct medical cost revealed that the cost might vary with reference to the number of infected individuals, the severity of the disease, the length of hospital stay, and a range of other factors. A significant number of Covid-19 infected populations are reported to experience critical conditions and require special care services, which results in a significant increment in healthcare costs. The health emergency created due to the Covid-19 situation has only resulted in a significant burden on the healthcare cost; rather, it has been influencing almost all sectors of the economy. The report presented by the United Nations Office for Disaster Risk Reduction (UNODRR) revealed that the socioeconomic cost due to Covid-19 had exceeded the cost of the global financial crisis.

The health emergency caused by the covid pandemic has had a significant influence on the purchasing behaviours of the individuals due to restrictions associated with physical interaction among the individuals (Alexander and Karger 2020). Lockdown caused market friction to marketing and had a negative influence on the liquidity and transacted prices. The lockdown orders given for mitigating the Covid pandemic's effects characterised a negative demand shock, which restricted the buyers from conducting the research and bidding process. Thus, the contagion rate of Covid-19 and the subsequent shutdowns also had a negative influence on the residential markets (D'Lima, Lopez, and Pradhan, 2020).

The early estimates predicted that the virus pandemic would result in the loss of 2.4 % of the Gross Domestic Product (GDP) over the year 2020, resulting in a decline in global economic growth (Statista, 2021). The global stock markets had experienced a significant decline due to the Covid outbreak, such that the largest ever single-day fall was reported up to 3000 points, presenting that the Covid-19 pandemic had negatively influenced the financial and economic sector of the developed as well as developing countries of the world. This research aims to identify the financial and economic implications of Covid variants.

1.2 Covid- 19 Epidemiology

In December 2019, China reported a pneumonia outbreak of unknown causes in Wuhan. Most of the early cases of Covid- 19 were found to be associated with the Huanan seafood wholesale market. The next-generation sequencing of lower respiratory tract samples of the patients provided insight into the presence of beta coronavirus. The observation of the virus under the electron microscope revealed that the virus's diameter was 60 to 140 nm, whereas the characteristic spikes were 9 to 12 nm, which was similar to the Coronoviridae family (Chowdhury & Oommen, 2020). the novel coronavirus was reported to possess similarity to two of the bat-derived coronavirus strains, having approximately 88% similarity compared to the coronavirus infecting humans, such as SARS, having 79% similarity (Chowdhury & Oommen, 2020).

According to CDC (2020), the individuals infected with the Covid-19 virus develop antibodies in their bodies to fight the virus; therefore, serological tests can be carried out to detect the antibodies. According to WHO (2020), the global research on Covid-19 suggested that most of the transmission occurs from the asymptomatic individuals, as compared to the Covid-infected individuals having symptoms; therefore, taking personal protective measures, such as the use of masks and social distancing, are likely to contribute to controlling the transmission of Covid-19 infection.

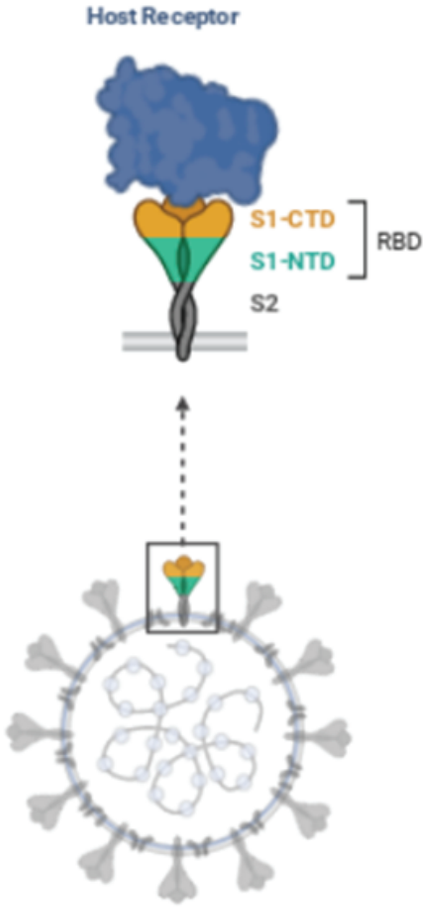
1.3 Mechanism of C-19 Mutation

The mechanism of C-19 mutation has been discussed with reference to the Receptor binding domain (RBD) modification and multiple spike protein switch in alignment.

1.3.1 Receptor binding domain (RBD) Modification

According to Tai et al. (2020), the Corona virus is comprised of four structural proteins, namely membrane (M), envelope (E), nucleocapsid (N), and spike (S) proteins. Among these proteins, the S-protein plays a significant role in viral attachment, fusion, and entry and is a target to develop antibodies, vaccines, and entry inhibitors (Du et al., 2017; Lu et al., 2014). The S-protein is responsible for mediating the virus's entry into the host cells by binding to the host receptor through the RBD within the S1 subunit and fusing the viral and host membrane through the S2 subunit. MERS-CoV and SARS-CoV RBDs are capable of recognising different receptors, such as MERS-CoV recognises dipeptidyl peptidase 4 (DPP4), whereas SARS-CoV is involved in recognition of angiotensin-converting enzyme 2 (ACE2) (figure 1). The SARS-CoV-2 also recognise ACE2 as a host receptor binding to the viral S protein. For this reason, it is crucial to define RBD in SARS-CoV-2 S protein because it is the main target to develop the virus attachment inhibitors, neutralise the antibodies, as well as vaccines.

Schematic of spike-receptor binding mechanism

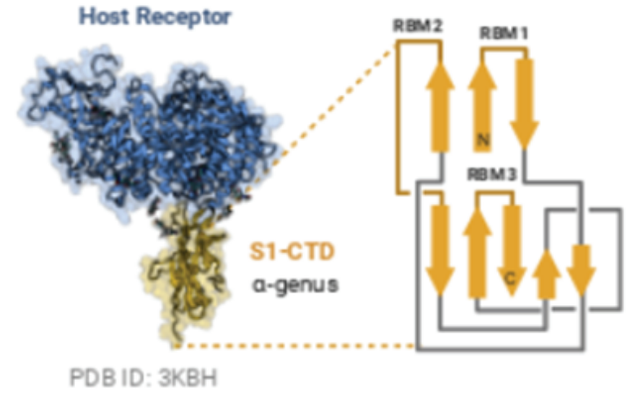


Receptor Binding Domain (RBD)



Receptor Binding Motifs (RBM)

Receptor binding motifs of S1-CTD bind to host receptor



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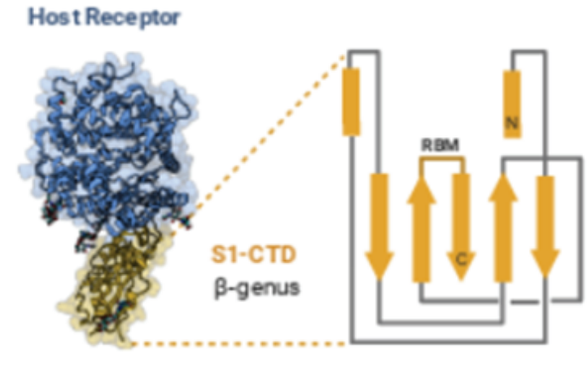

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Figure 1: RBD Modification

1.3.2 Multiple Spike protein switch in alignment

McCallum et al. (2020) mentioned that the first step of SARS-CoV-2 S refolding is SB's transition from a closed to an open conformation (figure 2). The arresting of the process of transitioning from a closed to an open conformation is likely to enhance the prefusion state's stability and might serve as a useful molecular tool. The structural fluctuations of the receptor binding the SB domain, which is referred to as RBD from the closed to open conformation, facilitate the Receptor-Binding Motif exposure (RBM). The RBM facilitates mediating the interaction with angiotensin-converting enzyme 2 (ACE2) for SARS-CoV and SARS-CoV-2 (Hoffmann et al., 2020; Letko, Marzi, and Munster, 2020). The RBM might also mediate the interaction of dipeptidyl-peptidase 4 for MERS-CoV (Raj et al., 2013; Wang et al., 2020).

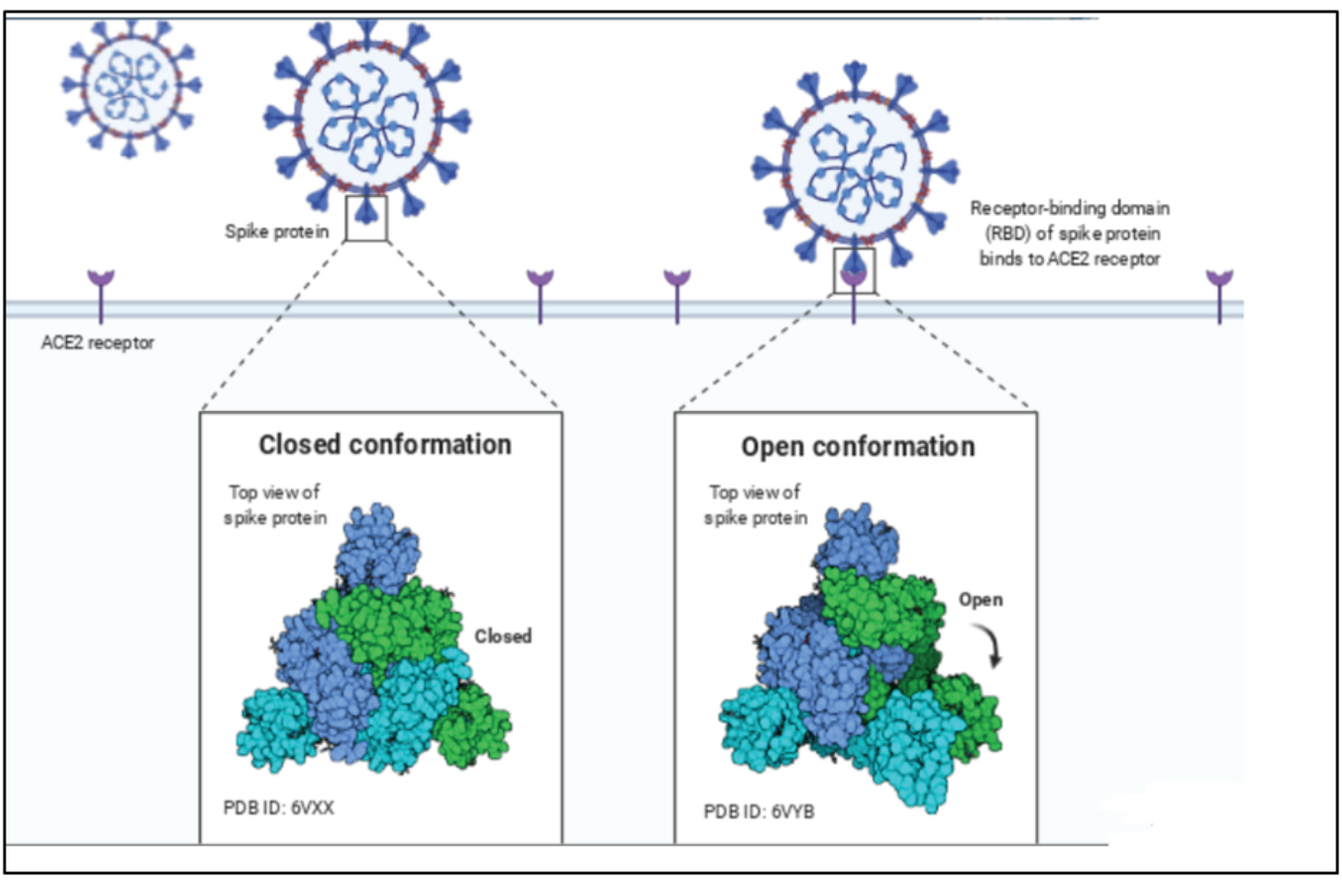

Figure 2: Multiple Spike protein switch in alignment

Presently selected Variants of Concern (VOCs) +: 29/11/2021

The recognized nomenclature and tracing SARS-CoV-2 genetic lineages by GISAID, Nextstrain and Pango are presently in use for easier scientific research as well assisting public discussions of variants as guided by WHO. The purpose behind this nomenclature is to prevent c –stigmatizing countries of origin of variants of concern (VOC) as well as variants of Interest (VOI) and the Greek Alphabet nomenclature was adopted (Tracking SARS-CoV-2 variants, 2021). The following are variants of concern:

1.4 SARS-CoV-2 Global variants Surveillance

1.4.1 Wuhan Chinese variant

With reference to the epidemiologists, the Chinese variant of SARS-CoV-2 came from the animals sold within the Wuhan market. The virus was referred to as coronaviruses, which caused an acute respiratory syndrome. Variant B.1.525 was found in China, which was then reported within the African countries. Another variant B.1.1.7 was also identified within the Chinese population, which was also reported in the US, and UK (Global Times, 2021).

1.4.2 South African variant [Beta variant]

The CDC's report revealed the emergence of B.1.351 variant, which was emerged independently of B.1.1.7. It was reported that B.1.351 possesses some of the properties similar to B.1.1.7. The variant was found to possess a range of mutations in the spike protein, including E484K, K417N, and N501Y. Contrary to the detection of B.1.1.7 lineage in the UK, B.1.351 variant was not reported to contain deletion at 69/70. According to CDC (2021a), there is currently no evidence suggesting that the variant influences the severity of the disease; however, there has been
evidence that the mutation of one of the spike protein E484K might influence neutralization by the monoclonal, as well as polyclonal antibodies.

1.4.3 Zambian SARS-CoV-2 Variant

The B.1.351 variant was found in the specimen collected in Zambia (CDC, 2020). The B.1.351 variant was reported to possess an association with the higher viral loads and was reported to include the spike protein mutation (E484K), which might hinder the antibody binding, and could blunt the naturally developed immunity or might cause hindrance in the antibody binding process (CDC, 2020). The predominance of this variant in Zambia revealed that it might have become the dominant lineage in Zambia.

1.4.4 UK variant [Alpha variant]

The report presented by CDC (2021a) reported that a new variant of SARS-CoV-2, which is also recognized as B.1.1.7, 20I/501Y.V1, or VOC 202012/01, had been found to emerge in the UK. The variant has been recognized for a large number of mutations. B.1.1.7 has been reported to have mutations within the receptor-binding domain (RBD) of the spike protein at position 501, at which the amino acid tyrosine (Y) replaces the amino acid asparagine (N). B.1.1.7 variant has been reported to be associated to an increased risk of death, in comparison to other variants. However, there is a requirement to conduct further studies for confirming the rates of mortality caused due to this variant.

1.4.5 Brazilian variant [Gamma variant]

The CDC (2021a) report revealed that in Brazil, a variant referred to as P.1 was first identified among the travelers during screening at the airport. The variant P.1 comprises a set of additional mutations, which might comprise the ability to recognise the antibodies. The CDC report presented that variant was found to have a moderate impact on neutralization by the EUA monoclonal antibodies' therapy. The variant was also recognised to have routine neutralisation by the post-vaccination and convalescent sera. The P.1 lineage comprises three large mutations, within N501Y, E484K, and K417T, which are the spike proteins receptor binding domains. With reference to the available evidence, some of the P.1 variant related mutations influence the transmissibility, as well as antigenic profile, which might have a significant influence on the capabilities of the antibodies generated via the previous natural infections, or via vaccinations performed to recognise, or neutralize the virus.

1.4.6 USA SARS-CoV-2 Variant [alpha variant]

According to the report presented by CDC (2021b), similar to the UK, in the US, several cases of B.1.1.7 have been detected, and it was found that the variant B.1.1.7 is more efficiently transmitted, as compared to other variants of SARS-CoV-2. The increased transmission of B.1.1.7 is anticipated to threaten the sustained healthcare resources and require an extended, however rigorous, implementation of the public health strategies.

1.4.7 INDIAN SARS-CoV-2 Variant [Delta variant]

The delta variant of SARS CoV-2 originally named B.1.617.2 was detected on 31st May 2021 which has a high transmissibility rate is the most common type of coronavirus presently globally. This variant was responsible for the second wave outcompeting the other variants (Mahase, E., 2021). The delta variant has continued to mutate to various new lineages such as AY.4.2 although with a minimal transmission capacity.

1.4.8 BOTSWANA SARS-CoV-2 Variant [Omicron variant]

The Nation of Botswana was first among several other countries to detect cases of the confirmed B.1.1.529 variant of the sample taken on 9th of November 2021 from four diplomats on a bilateral mission. First genomic sequencing of the virus and identification was conducted by South African Scientists. Instead applauding South Africa and Botswana for this remarkable work, European countries especially Britain and America punished the two nations with travel bans of its citizens. This variant has been identified as having numerous mutations that could pose a huge danger to society. Initial evidence put forward high risk of transmissibility, reinfection in comparison to other VOCs. WHO has intensified surveillance and several studies are underway and the Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE) experts will continue to monitoring this variant. This variant has been categorized as VOC and designated a Greek alphabet name Omicron (Tracking SARS-CoV-2 variants, 2021).

Currently designated Variants of Concern (VOCs)

In order for a SARS-CoV-2 variant to meet the classification under VOC as in the table below, it should demonstrate such association with one or more of the following levels of changes in respect to global public health consequence:

A. Raise in clinical disease burden or in virulence
B. Increased rate of transmissibility or undesirable changes in COVID-19 epidemiological data
C. Decreased in effectiveness of public health interventions such as social measures, diagnos tic approach or available therapeutics or vaccines.

Table 1| currently designated Variants of Concern (Tracking SARS-CoV-2 variants, 2021).

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Additional amino acid changes monitored°	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2	G/478K.V1	21A, 21I, 21J	+S:417N +S:484K	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021
Omicron*	B.1.1.529	GR/484A	21K	-	Multiple countries, Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov-2021

Variants of Interest (VOI)

In order for a SARS-CoV-2 variant to meet the classification under VOI as in the table below, it should demonstrate such association with one or more of the following levels of changes in respect to global public health consequence:

- Predictable genetic vicissitudes known to affect characteristics of the virus especially transmissibility, immune escape, disease severity, therapeutic escape or diagnostic.
- Multiple COVID-19 clusters with high risk of trans mission of global public health concern.

Table 2| currently designated Variants of Concern (Tracking SARS-CoV-2 variants, 2021).

WHO label	Pango lineage*	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan-2021	30-Aug-2021

1.5 Global Economic Implication

The pandemic, which started in China in early 2020 and spread like wildfire across the globe, hit the world in an unprecedented manner. The disruption caused by the pandemic has not only been limited to the private lives of the citizens but spilt over towards the commercial sector (Ahmed et al., 2020). Given the global nature of the pandemic, it also exacerbated the scale of the disruption and the impact that this had.

The economies of countries in general and the global economy, in particular, have been adversely impacted by the pandemic.The disruptions caused to both the demand and supply side of the economies have been unprecedented in global history, leaving little room for the policymakers to bank on a tried and tested strategy (Hevia and Neumeyer, 2020). Besides the magnitude of the impact of the pandemic, the nature of the impact has also been unprecedented. It has impacted economies both directly and indirectly.

While the supply side has shrunk globally as a result of the pandemic, the demand has suffered immensely as well (McKibbin and Fernando, 2020).

6. Uncovering Clinical Data

6.1 Johnson and Johnson

The efficacy and safety of the Janssen COVID-19 candidate vaccine for protection against moderate to severe COVID-19 was evaluated in a phase 3 clinical trial by considering co-primary endpoints of 14 and 28 days after vaccination [26]. It was found that the Janssen candidate was 66% effective for the prevention of moderate to severe COVID-19 at 28 days after vaccination. A single dose of the Johnson & Johnson vaccine showed a 66% percent effectiveness at preventing moderate to severe disease from COVID-19 and 85% at preventing severe disease. However, there were variations in efficacy in regional clinical trials when evaluated for moderate to severe COVID-19 with a 72% effectiveness in the United States, 57% in South Africa and 66% in Latin America reported. The vaccine also exhibited good results when multiple variants of COVID-19, such as B.1.351 variant found in South Africa were tested.

Johnson and Johnson [27] reported that the onset of protection was also observed as early as the 14th day of infection. The Janssen COVID-19 vaccine provided complete protection against COVID-related hospitalisation and death 28 days after vaccination. The vaccine was reported to have a clear effect on the number of COVID-19 cases requiring extracorporeal membrane oxygenation (ECMO), mechanical ventilation, or other medical interventions.

6.2 Gamaleya

The Sputnik V vaccine developed by Gamaleya is based on a human adenoviral vector platform and makes use of adenovirus 26 (Ad26) and 5 (Ad5) as vectors to express the genetic sequence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein [28]. Logunov et al. [28] reported the interim results from a phase 3 clinical trial of the Sputnik V COVID-19 vaccine and the results revealed that the vaccine provided strong protection in all age groups that participated [29]. The efficacy of the vaccine established by monitoring confirmed cases of COVID-19 from 21 days after vaccine administration revealed 91.6% efficacy (95% CI 85•6–95•2) [29] and was equally effective in individuals in all age groups.

6.3 Sinopharm

Sinopharm, a pharmaceutical company based in the Republic of China, have developed an inactivated SARS CoV-2 vaccine, which has been administered to approximately 1 million individuals [30]. Additional phase 3 trials of the vaccine are currently being undertaken in Indonesia and Turkey [30]. In Brazil, the vaccine has been administered intramuscularly to participants in two different doses provided at an interval of 14 days [30]. The Sinopharm vaccine has been reported to be 79% effective [31] however, efficacy trials on the same product have p roduced efficacy data of 50%, 65%, 78% and 91% [32].

7.Ethical Considerations Surrounding Vaccine Development and Production

A concerted application of science and technology is required to ensure that the research undertaken in respect of the COVID-19 outbreak includes risk assessment, management, vaccine development, and production whilst always promoting human rights. The development and production of an effective vaccine for dealing with the pandemic is y dependent on the outcomes of appropriately designed clinical and non-clinical trial outcomes performed in vitro, in animal and human subjects [33]. For this reason, there is a bioethical debate surrounding the trials conducted in respect of these vaccines developed during the pandemic. In respect of the COVID-19 situation, no vaccine has been proven to be effective for treatment of the disease and therefore an ethical dilemma when including healthy subjects for testing the efficacy of the vaccine exists [34]. The development and production of vaccines during pandemics is always likely to raise ethical concerns.

8. Challenges of Acquisition and Distribution of SARS-CoV-2 Vaccine in Middle- and Low-Income Developing Nations.

The rapid spread of the contagion crosses the globe and within less developed countries in Asia and Africa has resulted in a significant global health emergency. Countries require context-specific responses dependent on the prevailing situation such as number of COVID-19 cases ranging from none to a limited number or increased number of cases [32]. Decisive actions are required and effective physical (social) distancing, use of quarantine and/or lockdowns, implementation of widespread testing, contact tracing in a systematic manner are necessary to reduce the risk of further spread of the disease [32]. In combination with extensive testing the distribution of vaccines in low income developing counties is a significant challenge due to conflict, over population in rural and urban areas, and lack of accessibility to basic health services [30]. In developing countries, the most significant challenge includes the need for systematic decontamination measures and massive testing to reduce the risk of a devastating outbreak. The acquisition of COVID-19 vaccines requires an in-depth analysis of the changing epidemiology of the disease including the period of incubation between appearance and duration of symptoms [35].

The distribution of a vaccine is currently determined by considering an ability to develop and initiate testing and purchase vaccines [35]. A small number of multinational companies produce most of the vaccines globally and are also involved in negotiating with the private and public[36] sectors to sell their vaccines. In this respect developed countries of the

world attempt to purchase access to vaccine candidates well in advance whereas due to a lack of resources, developing countries are unlikely to have early access the vaccines [35]. Consequently there is likely to be inequitable access and an unethical allocation of vaccines, depending on the ability of countries to pay for vaccines and distributive justice is one of the fundamental considerations necessary when distributing vaccines during such a pandemic so as to ensure that the principles of distributive justice are met and the allocation of scarce resources are applied equally to all viz., local, national and global communities [35]. However, the limited supply of vaccines and the mass demand during pandemic situations is a challenge when aspiring to equal distribution of resources.

The lack of accessibility to vaccines and storage conditions required may result in failure to achieve desired clinical outcomes even if bulk distribution of vaccines to developing countries was successful [31]. The inadequate refrigerated cold chain network in many developing countries therefore poses a significant challenge. Consequently vaccine candidates for COVID-19 requires that require long term storage at -20 °C to -70°C are likely to result in the loss of vaccine particularly if inadequate refrigerated cold chain networks exist [32]. Therefore, the acquisition, distribution and successful clinical application of SARS-CoV-2 vaccine in low- and middle-income developing nations may be extremely challenging.

9. Conclusions

In light of the analysis and review of the vaccines that have been developed and approved for emergency use in many countries it is evident that grey areas exist and scientists are yet to establish conclusive solutions to ensure successful treatment strategies. Similar concerns are shared by the World Health Organization (WHO) in that assurance of long-term immunity or estimated time of immunity protection with the current vaccines are not yet known. In addition, there is no certainty of immune response or durability thereof. Evidence from the clinical trial data has revealed that the current vaccines have a e capability to protect some individuals against disease but are not conclusive in respect of an ability to prevent transmission and subsequent infection following exposure to the COVID-19 virus.

Furthermore, there is a dearth of evidence regarding the age-related use of these vaccines as, by way of example, the use of the vaccine in paediatric subjects has not yet been undertaken and efficacy established and as such these populations remain at risk to transmission and infection by the virus.

An additional concern relates to the availability of the sufficient vaccine doses to cater for entire communities and/or populations so as to ensure protection to a significant number and wide range of individuals, which may reduce confidence in the current intervention strategy and fight against COVID-19.

Consequently, it is recommended that adherence to COVID-19 protocols such as hand sanitization, physical distancing and wearing of masks is maintained despite the state of vaccination of an individual or population as the COVID-19 pandemic

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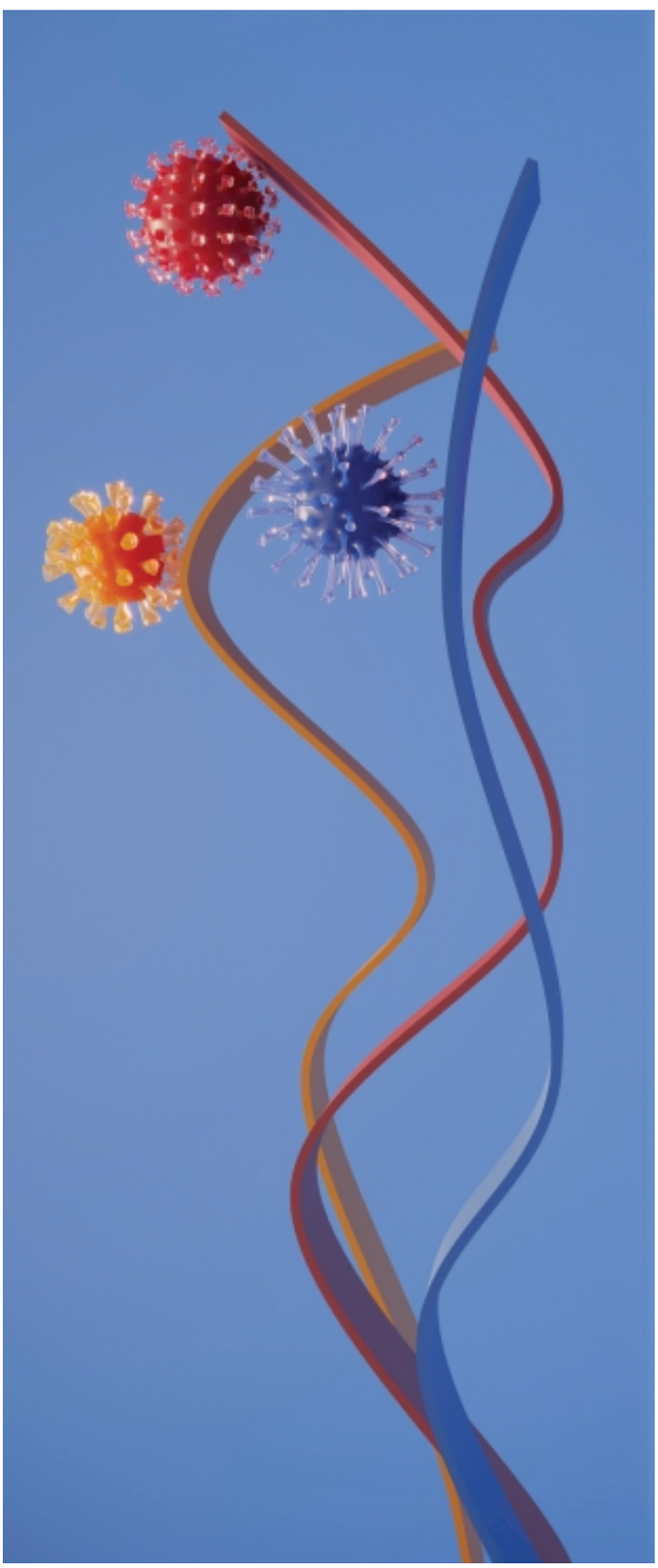
The Financial and Economic Implication of Emerging SARS-CoV-2 Variants: A global perspective

Author: *Dr. Larry Mweetwa*

1. Department of Pharmacy and Pharmaceutical Sciences

Corresponding Author *Dr. Larry Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract |

The Covid-19 pandemic, which initiated from Wuhan, China, spread like wildfire globally, disrupting both the demand and supply of the economies in a highly unprecedented manner. While the demand immensely suffered, the supply has also been severely affected due to restricted movement of the personnel, social distancing protocols implemented across the globe, and closure of the international borders hence disrupting the supply, reducing the production and accessibility of the raw materials.

Objectives: The objective of this research is to critically examine the finance and the economic implications of the Emerging SARS-CoV-2 variant to analyze its global impact.

Key Findings: No country was exempt from the negative implications of the pandemic irrespective of policies adopted to mitigate the effects as direct and indirect economic influences were felt throughout the globe. The graveness of the impact only relied on the structural economic integrity of the individual countries. At micro-level, the financial implementation of the businesses demanded credit for working capital requirement. With lockdowns in place, it became difficult for the businesses to meet short-term debt obligations resulting in bankruptcies of small-scale enterprises throughout the globe. Developing and underdeveloped countries also lagged behind on remittances as a direct result of increasing unemployment levels and a reduction in incomes. The highest decline was recorded in the Foreign Direct Investment globally in 2020, accounting for a 42% reduction. Yet, the developing economies, specifically within the Asian region, recorded a less drastic decline in the FDI as opposed to developed nations.

Conclusions: The findings revealed that economic growth globally reduced by a staggering 4.5%, with many developing countries facing many severe consequences due to supply and demand disruption. However, with the development of vaccines, a sharp recovery in economic growth is expected in 2021 to overcome the losses of the previous year.

Keywords: SARS-CoV-2 variant, financial impact, economic impact.

1.0 Introduction

In December 2019, China reported an outbreak of pneumonia in Wuhan. The disease was referred to as coronavirus disease (COVID-19) or (SAR-COV-2), and the spread of the disease resulted in an ongoing pandemic across the globe (Chowdhury and Oommen, 2020). With the increment in the disease rate, the World Health Organization (WHO) provided recommendations for imposing the local, and national area lockdowns, restricting the business operations, and maintaining social distancing for limiting an interaction curtailing the spread of the virus. The pandemic situation has been resulting in unprecedented impacts on the health and well-being of countries' populations. The recent statistics revealed that 2,705,236 individuals had died from Covid-19, such that the situation has not improved since the outbreak of the virus (Worldometers, 2021). Along with a significant death loss, the spread of Covid-19 had imposed a significant financial and economic burden on the countries.

According to Darab et al. (2021), from the economic perspective, the spread of Covid-19 and increment in the number of patients have been imposing a direct medical and an indirect cost on the patients, the health system, and the government. The analysis of the economic burden of a direct medical cost revealed that the cost might vary with reference to the number of infected individuals, the severity of the disease, the length of hospital stay, and a range of other factors.

A significant number of Covid-19 infected populations are reported to experience critical conditions and require special care services, which results in a significant increment in healthcare costs. The health emergency created due to the Covid-19 situation has only resulted in a significant burden on the healthcare cost; rather, it has been influencing almost all sectors of the economy. The report presented by the United Nations Office for Disaster Risk Reduction (UNODRR) revealed that the socioeconomic cost due to Covid-19 had exceeded the cost of the global financial crisis.

The health emergency caused by the covid pandemic has had a significant influence on the purchasing behaviours of the individuals due to restrictions associated with physical interaction among the individuals (Alexander and Karger 2020). Lockdown caused market friction to marketing and had a negative influence on the liquidity and transacted prices. The lockdown orders given for mitigating the Covid pandemic's effects characterised a negative demand shock, which restricted the buyers from conducting the research and bidding process. Thus, the contagion rate of Covid-19 and the subsequent shutdowns also had a negative influence on the residential markets (D'Lima, Lopez, and Pradhan, 2020). The early estimates predicted that the virus pandemic would result in the loss of 2.4 % of the Gross Domestic Product (GDP) over the year 2020, resulting in a decline in global economic growth (Statista, 2021). The global stock markets had experienced a significant decline due to the Covid outbreak, such that the largest ever single-day fall was reported up to 3000 points, presenting that the Covid-19 pandemic had negatively influenced the financial and economic sector of the developed as well as developing countries of the world. This research aims to identify the financial and economic implications of Covid variants.

1.2 Covid- 19 Epidemiology

In December 2019, China reported a pneumonia outbreak of unknown causes in Wuhan. Most of the early cases of Covid- 19 were found to be associated with the Huanan seafood wholesale market. The next-generation sequencing of lower respiratory tract samples of the patients provided insight into the presence of beta coronavirus. The observation of the virus under the electron microscope revealed that the virus's diameter was 60 to 140 nm, whereas the characteristic spikes were 9 to 12 nm, which was similar to the Coronoviridae family (Chowdhury & Oommen, 2020). the novel coronavirus was reported to possess similarity to two of the bat-derived coronavirus strains, having approximately 88% similarity compared to the coronavirus infecting humans, such as SARS, having 79% similarity (Chowdhury & Oommen, 2020).

According to CDC (2020), the individuals infected with the Covid-19 virus develop antibodies in their bodies to fight the virus; therefore, serological tests can be carried out to detect the antibodies. According to WHO (2020), the global research on Covid-19 suggested that most of the transmission occurs from the asymptomatic individuals, as compared to the Covid-infected individuals having symptoms; therefore, taking personal protective measures, such as the use of masks and social distancing, are likely to contribute to controlling the transmission of Covid-19 infection.

1.3 Mechanism of C-19 Mutation

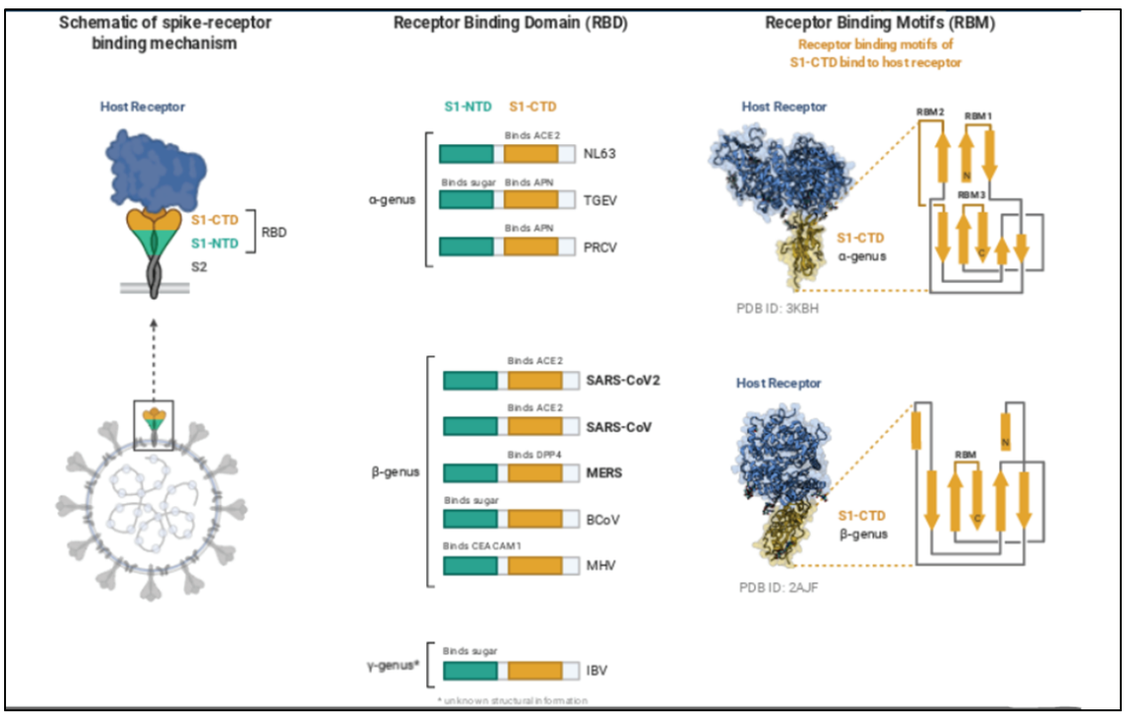
The mechanism of C-19 mutation has been discussed with reference to the Receptor binding domain (RBD) modification and multiple spike protein switch in alignment.

1.3.1 Receptor binding domain (RBD) Modification

According to Tai et al. (2020), the Corona virus is comprised of four structural proteins, namely membrane (M), envelope (E), nucleocapsid (N), and spike (S) proteins. Among these proteins, the S-protein plays a significant role in viral attachment, fusion, and entry and is a target to develop antibodies, vaccines, and entry inhibitors (Du et al., 2017; Lu et al., 2014). The S-protein is responsible for mediating the virus's entry into the host cells by binding to the host receptor through the RBD within the S1 subunit and fusing the viral and host membrane through the S2 subunit. MERS-CoV and SARS-CoV RBDs are capable of recognising different receptors, such as MERS-CoV recognises dipeptidyl peptidase 4 (DPP4), whereas SARS-CoV is involved in recognition of angiotensin-converting enzyme 2 (ACE2) (figure 1).

The SARS-CoV-2 also recognise ACE2 as a host receptor binding to the viral S protein. For this reason, it is crucial to define RBD in SARS-CoV-2 S protein because it is the main target to develop the virus attachment inhibitors, neutralise the antibodies, as well as vaccines.

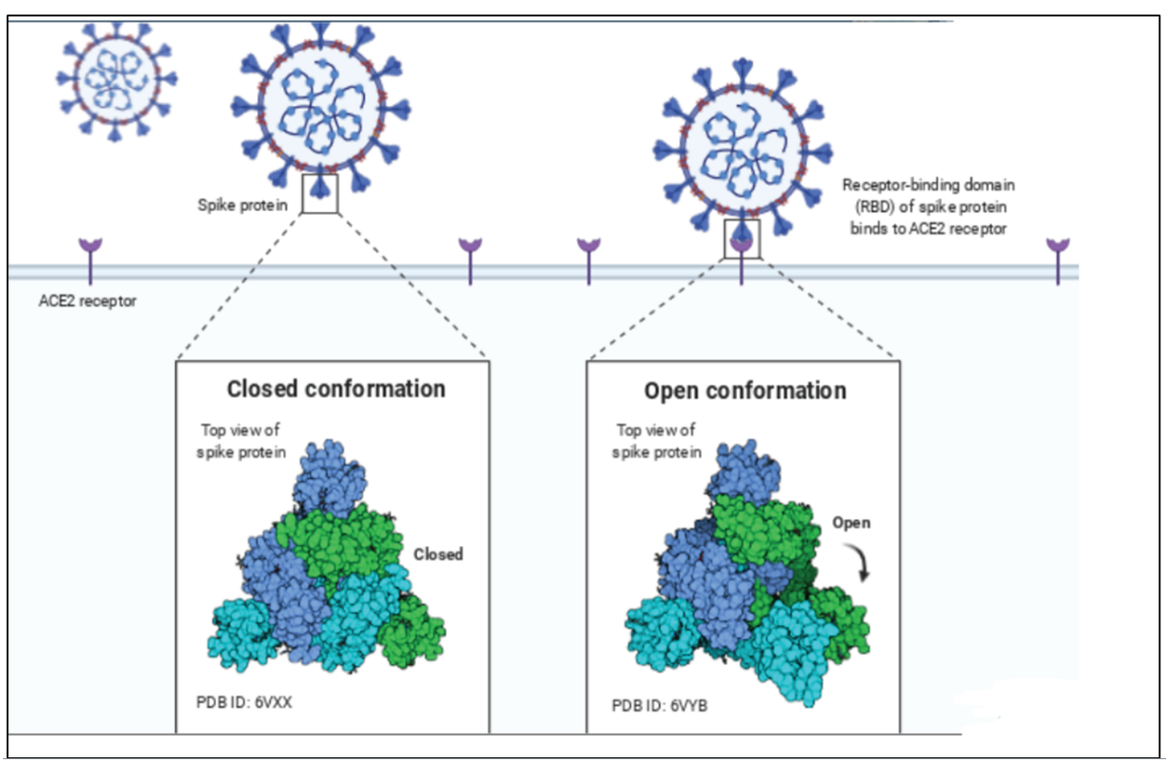
Figure 1: RBD Modification



1.3.2 Multiple Spike protein switch in alignment

McCallum et al. (2020) mentioned that the first step of SARS-CoV-2 S refolding is SB's transition from a closed to an open conformation (figure 2). The arresting of the process of transitioning from a closed to an open conformation is likely to enhance the prefusion state's stability and might serve as a useful molecular tool. The structural fluctuations of the receptor binding the SB domain, which is referred to as RBD from the closed to open conformation, facilitate the Receptor-Binding Motif exposure (RBM). The RBM facilitates mediating the interaction with angiotensin-converting enzyme 2 (ACE2) for SARS-CoV and SARS-CoV-2 (Hoffmann et al., 2020; Letko, Marzi, and Munster, 2020). The RBM might also mediate the interaction of dipeptidyl-peptidase 4 for MERS-CoV (Raj et al., 2013; Wang et al., 2020).

Figure 2: Multiple Spike protein switch in alignment



1.4 SARS-CoV-2 Global variants Surveillance

1.4.1 Wuhan Chinese variant

With reference to the epidemiologists, the Chinese variant of SARS-CoV-2 came from the animals sold within the Wuhan market. The virus was referred to as coronaviruses, which caused an acute respiratory syndrome. Variant B.1.525 was found in China, which was then reported within the African countries. Another variant B.1.1.7 was also identified within the Chinese population, which was also reported in the US, and UK (Global Times, 2021).

1.4.2 South African variant

The CDC's report revealed the emergence of B.1.351 variant, which was emerged independently of B.1.1.7. It was reported that B.1.351 possesses some of the properties similar to B.1.1.7. The variant was found to possess a range of mutations in the spike protein, including E484K, K417N, and N501Y. Contrary to the detection of B.1.1.7 lineage in the UK, B.1.351 variant was not reported to contain deletion at 69/70. According to CDC (2021a), there is currently no evidence suggesting that the variant influences the severity of the disease; however, there has been evidence that the mutation of one of the spike protein E484K might influence neutralization by the monoclonal, as well as polyclonal antibodies.

1.4.3 Zambian SARS-CoV-2 Variant

The B.1.351 variant was found in the specimen collected in Zambia (CDC, 2020). The B.1.351 variant was reported to possess an association with the higher viral loads and was reported to include the spike protein mutation (E484K), which might hinder the antibody binding, and could blunt the naturally developed immunity or might cause hindrance in the antibody binding process (CDC, 2020). The predominance of this variant in Zambia revealed that it might have become the dominant lineage in Zambia.

1.4.4 UK variant

The report presented by CDC (2021a) reported that a new variant of SARS-CoV-2, which is also recognized as B.1.1.7, 20I/501Y.V1, or VOC 202012/01, had been found to emerge in the UK. The variant has been recognized for a large number of mutations. B.1.1.7 has been reported to have mutations within the receptor-binding domain (RBD) of the spike protein at position 501, at which the amino acid tyrosine (Y) replaces the amino acid asparagine (N). B.1.1.7 variant has been reported to be associated to an increased risk of death, in comparison to other variants. However, there is a requirement to conduct further studies for confirming the rates of mortality caused due to this variant.

1.4.5 Brazilian variant

The CDC (2021a) report revealed that in Brazil, a variant referred to as P.1 was first identified among the travelers during screening at the airport. The variant P.1 comprises a set of additional mutations, which might comprise the ability to recognise the antibodies. The CDC report presented that variant was found to have a moderate impact on neutralization by the EUA monoclonal antibodies' therapy.



The variant was also recognised to have routine neutralisation by the post-vaccination and convalescent sera. The P.1 lineage comprises three large mutations, within N501Y, E484K, and K417T, which are the spike proteins receptor binding domains. With reference to the available evidence, some of the P.1 variant related mutations influence the transmissibility, as well as antigenic profile, which might have a significant influence on the capabilities of the antibodies generated via the previous natural infections, or via vaccinations performed to recognise, or neutralize the virus.

1.4.6 USA SARS-CoV-2 Variants

According to the report presented by CDC (2021b), similar to the UK, in the US, several cases of B.1.1.7 have been detected, and it was found that the variant B.1.1.7 is more efficiently transmitted, as compared to other variants of SARS-CoV-2. The increased transmission of B.1.1.7 is anticipated to threaten the sustained healthcare resources and require an extended, however rigorous, implementation of the public health strategies.

New strains will continue emerging as we have seen with delta and lamba variants.

1.5 Global Economic Implication

The pandemic, which started in China in early 2020 and spread like wildfire across the globe, hit the world in an unprecedented manner. The disruption caused by the pandemic has not only been limited to the private lives of the citizens but spilt over towards the commercial sector (Ahmed et al., 2020). Given the global nature of the pandemic, it also exacerbated the scale of the disruption and the impact that this had.

The economies of countries in general and the global economy, in particular, have been adversely impacted by the pandemic. The disruptions caused to both the demand and supply side of the economies have been unprecedented in global history, leaving little room for the policymakers to bank on a tried and tested strategy (Hevia and Neumeyer, 2020). Besides the magnitude of the impact of the pandemic, the nature of the impact has also been unprecedented. It has impacted economies both directly and indirectly.

While the supply side has shrunk globally as a result of the pandemic, the demand has suffered immensely as well (McKibbin and Fernando, 2020). The restricted movement of individuals, the social distancing protocols in place across the globe, and the closing down of international borders were some of the main reasons because of which supply was disrupted, production levels dropped, and raw material access was limited for the manufacturers (Ashraf, 2020). Similarly, on the demand side, the demand for goods and services dropped as businesses closed down, and the unemployment rate soared across the globe. Unemployment and pay cuts meant that the purchasing power of individuals went down, which, in turn, led to a drastic reduction in demand across the globe (Maital and Barzani, 2020). This further deteriorated as development activities undertaken by the government across the globe, further fuelling a downtrend in aggregate demand.

In the last one year since the pandemic started to grip the whole globe, a number of researchers have tried to study and quantify the impact that the pandemic has had on the global economy (McKibbin and Fernando, 2020; Ashraf, 2020, Ahmed et al., 2020). While those investigations have taken different methodologies, the focus has been to study the heterogeneous, non-linear impacts that the covid-19 pandemic has had on the macroeconomic level. Such studies have focused on either the stock market as the representative of the economic outlook of the country or have employed multi-sectoral studies to deep dive into the impact that the pandemic had on the economies in various regions of the world.

Among the studies which have been undertaken to study the macroeconomic impact of the pandemic, a paper by Chudik et al. (2020) has been an important one taking a unique and boarder approach, where they have departed from undertaking a single country analysis and focused on developing a multi-country model which aimed to better study the macroeconomic impacts of Covid. The advantage of focusing on the multilateral model was that it helped to mitigate any spillover effects and overestimation as a result of correlation among markets. To render more accuracy to the reported results, the model incorporated not only developing countries but emerging markets as well to ensure input from various economic conditions.

In the case of the ongoing pandemic, the study reported that excessive global volatility caused by pandemic was one of the main reasons which impacted the economic growth in various regions. From the money market side, the main contributor towards this lower economic growth is the increase in precautionary savings on the end of consumers (Mogaji, 2020). Given that the consumers faced an unprecedented situation in the face of a pandemic, it was concluded that the saving level among individuals rose (Chudik et al., 2020). Similarly, investment delays were also observed as the businesses and individuals anticipated suppressed demand and low aggregate demand within economies (Chudik et al., 2020).

A major contributor towards stalled economic growth during the pandemic was observed to be the higher cost of capital across the countries that were studied. The lag in policy changes and policy response in most economies in the world meant that economic activity suffered, leading to reduced economic growth and lower productivity levels (Chudik et al., 2020). The global volatility plotted against economic growth based on time series data is presented below.

internationally hence gives the whole world an assignment to devise relevant measures to monitor antimicrobial agent's usage as misuse of this agents lead to the development of antimicrobial resistance (Wutzke, S.E.2005).

Based on the findings of Chopra, I. and Roberts, M., 2001 it is highly possible that a single antibiotic may not only select resistance to just one particular drug. This means resistance can occur with other drugs of similar structure and related compounds of the same class. For example, resistance to tetracycline may result resistance to oxytetracycline, chlortetracycline, doxycycline, and minocycline.

In 2014 World Health Organization (WHO) cautioned that the antibiotic resistance dilemma is reaching epic proportions and also MDR bacteria have been confirmed to be a significant danger to public health and national security by the IDSA and the Institute of Medicine, as well as the federal Interagency Task Force on Antimicrobial Resistance (Golkar, Z et al., 2014).

There is need for sensitization and education of healthcare sector and public on irrational use of antibiotics and their impact on antibiotic resistance and the ways to alleviate the problem, more especially in our country Botswana since limited studies have been conducted in this topic.

RESEARCH AIM

The aim of the study is to evaluate the effects of irrational use of antibiotics and its impact on antibiotic resistance which is a global crisis

GENERAL OBJECTIVE

The general objective of the research is to establish key factors that bring about the irrational use of antibiotics, and its effect on antibiotic resistance.

SPECIFIC OBJECTIVES

1. To explore actions that are being used to counteract the antibiotic resistance crisis globally.
2. To explore those actions being used in Botswana to address antibiotic resistance.
3. To determine possible implementations to alleviate the problem of antibiotic resistance

METHODOLOGY

In order to answer the aims and objectives of the research topic, secondary data was systematically reviewed. Data was collected from academically reputable data bases like PubMed and Google scholar the utilization of the multiple databases presented the opportunity to gain accurate and reliable information. Studies were selected using the PRISMA tool approach for inclusion and exclusion. Five articles were selected in the final analysis of the findings.

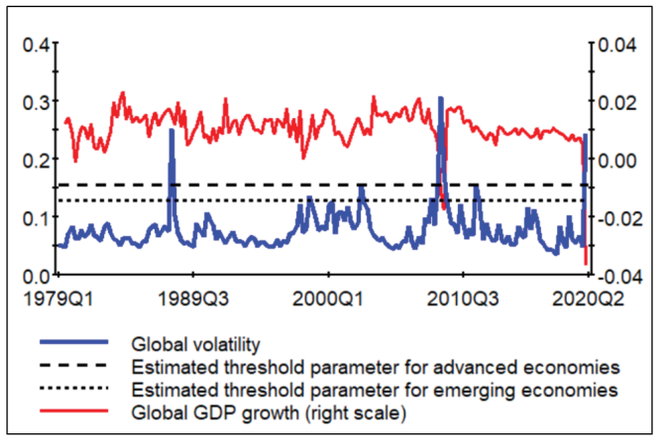


Figure 3: Global Volatility & GDP Growth (Source: Chudik et al., 2020)

As represented above, the spike in volatility caused by the pandemic was almost of the same magnitude as the one which was caused by the sub-prime mortgage led financial crisis of 2007 (Chudik et al., 2020). The dotted horizontal lines on the graph represent the threshold level of various economies to sustain volatility. As depicted, the threshold level for advanced economies is significantly higher as compared to emerging economies (Chudik et al., 2020).

However, given the sharp rise in the volatility, it is visible that the threshold level of economies across the board was breached, leading to an impact on economic growth and a sharp decline in economic activity.

The results presented show that volatility is detrimental to economic activity across all economies. While advanced economics are able to sustain the shock of volatility better than emerging economies, they are adversely impacted in case the shock is of a sizeable magnitude. However, it was also noted that the impact in the case of advanced economies was smaller in magnitude as compared to the emerging economies, which had a lower threshold level and hence were hence more adversely impacted by the adverse shock (Chudik et al., 2020).

These results of threshold analysis for both advanced economies and emerging economies are depicted below. As the graph shows, in the case of emerging economies, the threshold effect was significantly negative for all the emerging economies which were included in the analysis except Turkey, Thailand, Peru, and Mexico (Chudik et al., 2020). This is representative of the structural strength of these economies and the fact that these economies are self-sufficient in most of the economic sectors, with limited reliance on imports for sustaining economic growth.

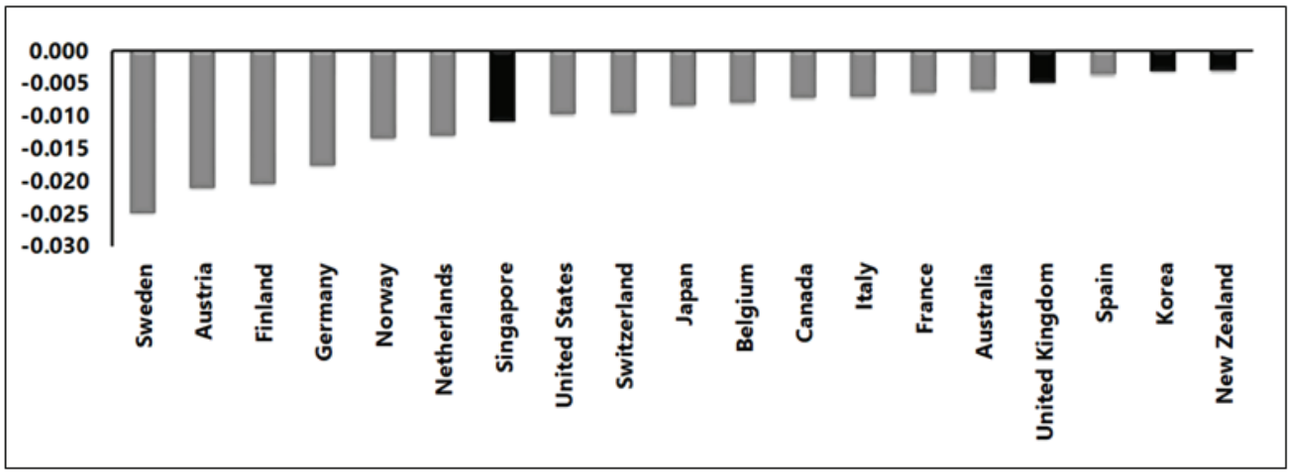


Figure 4: Threshold Effect for Advanced Economies (Source: Chudik et al., 2020)

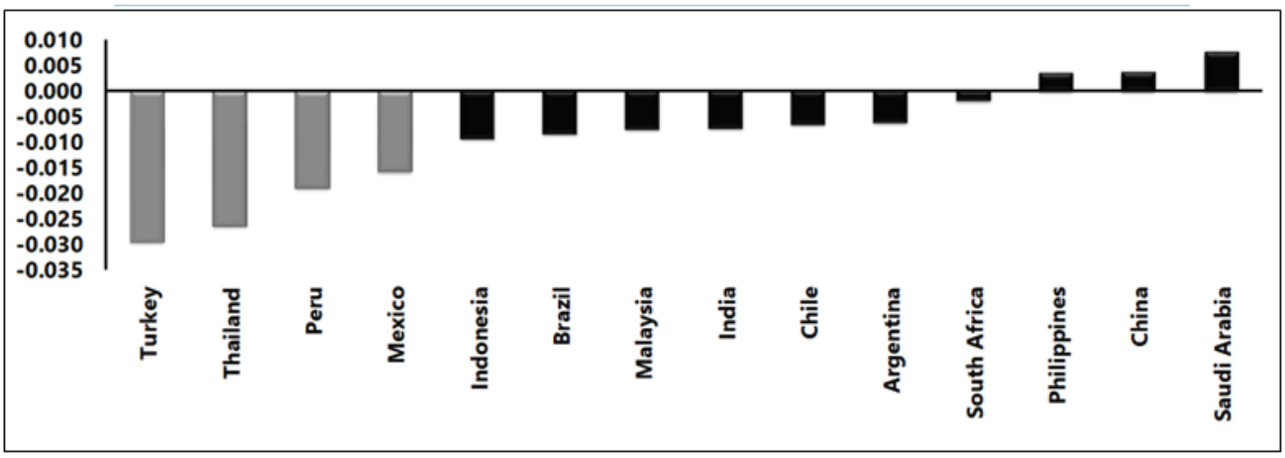


Figure 5: Threshold Effect for Emerging Economies (Source: Chudik et al., 2020)

To further strengthen the analysis, the TGVAR model was employed to study the impact of the pandemic on the economic growth of these countries. The application of the model enabled to study of all of the economies in isolation to better understand their prospects in the post-pandemic world (Chudik et al., 2020). Through the application of the model, it has been estimated that roughly 3 percentage points would be knocked off the global GDP growth, compared to the projections which were made before the start of the pandemic.

The impact of the shock is only made evident when the past projections of economic growth in the absence of a pandemic are compared with economic growth projections, which incorporate the impact of the pandemic (Chudik et al., 2020). However, it is critical to note that all such analysis assumes that the reduction in the GDP growth rate, which has been witnessed post-pandemic, is caused solely by the direct and indirect impacts of the pandemic.

The application of the TGVAR model on the individual economies helped to arrive at wide-ranging results. The results have been summarized in graphical form below. The application of the model has highlighted that among the developed economies, the US and UK will suffer from longer-lasting impacts due to the pandemic (Chudik et al., 2020). The forecasted sluggish recovery of the two countries can be attributed to the unstable macroeconomic environment of the two countries. While the UK was struggling with macroeconomic challenges caused by the decision of Brexit, the US economy was suffering from similar challenges as it revised its trade deals with other countries and tried imposing protectionist policies (Bareket-Bojmel, Shahar, and Margalit, 2020).

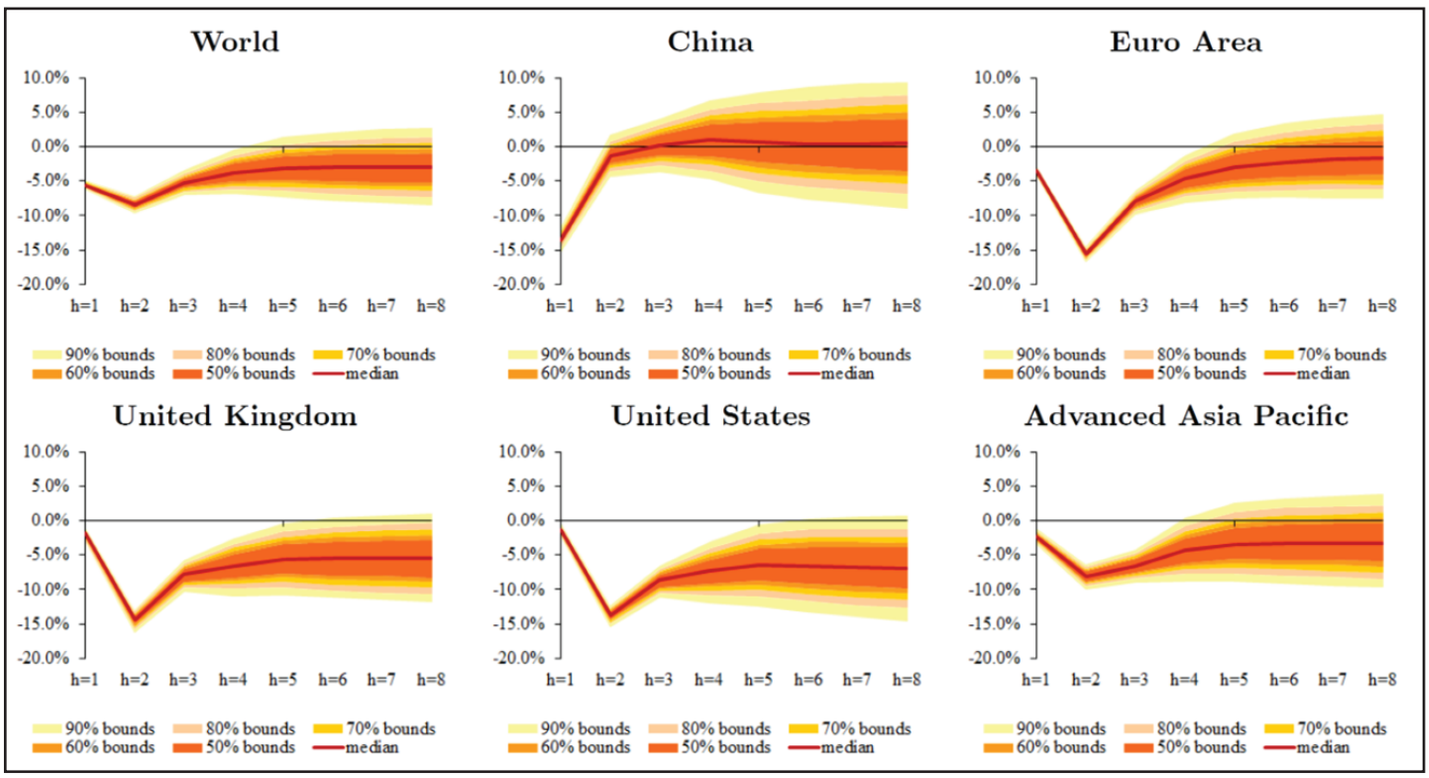


Figure 6: TGVAR Model Implementation (Source: Chudik et al., 2020)

As the graphs suggest, among the developing economies, China has the best probability of rebounding and recovering from the adverse impacts of the pandemic. This probability for China is so significant that it has enabled to improve the future performance prospects of the whole group of emerging economies (Liu, Yue, and Tchounwou, 2020). While the emerging economies are expected to fare better in the aftermath of the pandemic, because of strong structural factors and the higher growth potential, some of the emerging economies like Turkey, South Africa, and Saudi Arabia are expected to suffer from worse consequences of the pandemic, which will also take longer to subside (Topcu and Gulal, 2020). It is estimated through the model that the aftermath of the pandemic, in terms of economic growth, might last as much as eight quarters for these countries (Chudik et al., 2020).

Another key finding of the study undertaken by Chudik et al. (2020) was the relevance of spillover effects in terms of the pandemic. In this context, the study of Sweden was undertaken. Within the European region,Sweden took a drastically different approach towards the pandemic compared to its neighbors. While other countries in the region-imposed lockdowns and mandated social distancing protocols, in the case of Sweden, no lockdown was imposed (Jonung, 2020).

However, citizens were required to ensure self-imposed social distancing. This provided a good opportunity to study if economies like Sweden were also impacted by the pandemic even though they did not undergo any lockdown. The comparison showed that there was a significant spillover impact in the case of Sweden (Chudik et al., 2020).

As other economies went into lockdown, both the imports and the exports of the country were impacted, which, in turn, impacted various segments of the economy, reducing the growth rate of the country. This main spillover was caused by the impact on industrial production. As imports and exports of the country were hampered, the supply lines were adversely impacted, which, in turn, had an adverse impact on the production within the economy. Similarly, as the trade across borders was reduced to almost zero, the commodity prices were also adversely impacted, which, in turn, further led to a negative strain on the economy (Chudik et al., 2020).

This analysis showed that no country across the globe was left untouched from the negative impacts of the pandemic. Despite the policy options that a country may have opted for, the direct and indirect adverse economic impacts of the pandemic were felt across the globe. The severity of the impact only depended on the structural strengths of the economies of the individual countries.

1.6 Global Financial Implication

While the economic impacts of the pandemic have been studied at length in the previous section, the financial implications need a thorough study as well, as the financial implications can also lead to long term macroeconomic impacts on the countries. The financial impacts from the pandemic were seen across the micro and the macro level as well (Zhang et al., 2020). From countries to individuals, everyone has impacted, which, in turn, resulted in a snowball effect, leading to financial implications on a global level.

On the micro-level, the key financial implication was on the businesses which needed credit for meeting their working capital requirements (Poole et al., 2020). While credit comes at the expense of interest, as the economies shut own and business activity contracted, it became difficult for businesses to meet their short-term debt obligations. This resulted in defaults and bankruptcies for small to medium enterprises (Adam and Henstridge, 2020). While bailout packages were announced in order to support such businesses, the lag in policy formulation and implementation meant that in most of the cases, it was already too late.

The borrowing and national debt also presented a financial complication in the face of the pandemic (Bulow et al., 2020). As GDP growth rates nose-dived across the board, most countries faced difficulties in meeting their debt obligations (Berglöf, 2020). Reduction in commercial activity meant that the receipts for governments based on tax collection were significantly reduced, which put pressure on the funds that were available to the government (Cespedes et al., 2020). The foreign exchange reserves also faced critical pressure. The sources of foreign borrowing shrunk considerably during this period, which meant that countries across the board were under financial duress, increasing the financial risks which were being faced across economies.

Additionally, the debt crisis for countries was also exacerbated because of the reduced access to international capital markets (Faria-e-Castro, 2021). The shutdown of commercial activity and hindrance in international travel limited access to capital markets. In the local landscape, the utilization of domestic borrowings to fund the budget deficit was expected to fuel inflation level within the economy, reducing the capacity of the government to utilize domestic borrowing.

A key mitigating factor for developing and underdeveloped countries was the fact that most of the advanced economies announced relief in terms of deferment of the short-term debt obligations during the pandemic (Truman, 2020). IMF and World Bank also took similar steps, which helped to ensure that the impact of short-term debt obligations is mitigated, enabling the countries to better tackle the financial stress created by the interest and repayment obligations.

Another key financial implication of the pandemic was the impact that it had on the remittances across developing and underdeveloped countries (Choudhary, 2020). Remittances are a key source of capital inflow for both developing and underdeveloped countries as their citizens working in developed economies send back money for either investment purposes or supporting their families (Diao and Mahrt, 2020). However, as economic activity declined in the face of the pandemic, employment levels fell down, and incomes were reduced, the remittance inflow was severely impacted for both developing and underdeveloped countries. The graph below highlights a sample of countries to reinforce the cut back of remittances across countries.

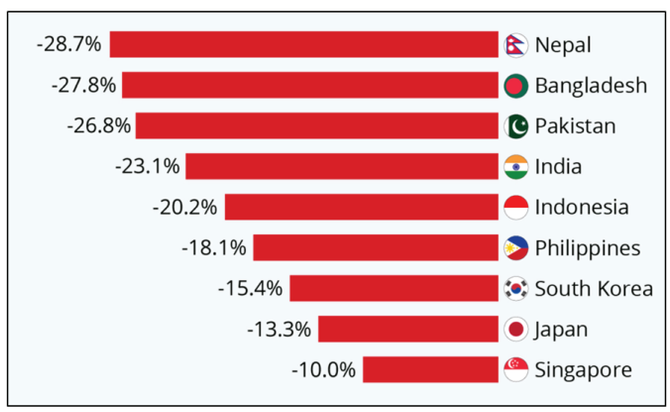


Figure 7: Remittance Decline during Pandemic (Source: Statista, 2020)

As the graph shows, across the spectrum, a substantial reduction in capital inflows was recorded during the pandemic. The degree of impact on remittance level was different for all countries (Statista, 2020). The key factor in this context was the source of such remittances. The countries for which the key source of remittances were the developed countries saw a bigger reduction in remittances as these countries were the ones that saw stricter lockdown and considerably higher reduction in economic activity (Diao and Mahrt, 2020). On the other hand, the countries for which developing countries contributed more towards remittance flow saw a lower impact on the level of remittance reduction.

For most of the developing and under-developed countries, remittance is a critical contributor towards economic growth as they help to plug the gap between cash inflows and outflows caused by the discrepancy between imports and exports (Chami et al., 2008). These inflows help to ensure that the balance of payments remains in check. Hence, the disruption to these remittances caused by the pandemic left a critical financial impact across global economies.

Foreign direct investment is also a key financial indicator that helps sustain growth in economies. The FDI was also a key factor that was impacted during the ongoing pandemic (Strange, 2020). The graph below highlights the FDI reduction, which was observed across various blocks globally (Statista, 2020).

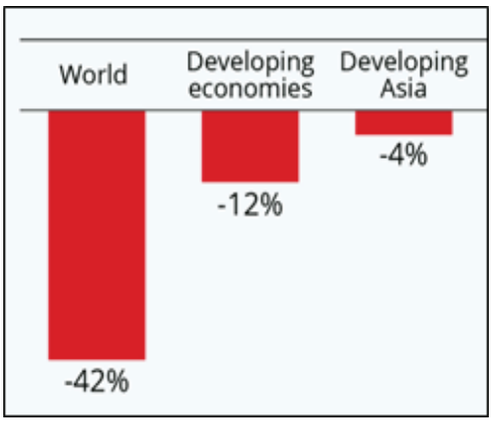


Figure 8: FDI across Globe during Pandemic (Source: Statista, 2020)

As the graph depicts, the highest reduction was observed in FDI globally during 2020, amounting to a 42% reduction (Statista, 2020). This was mainly caused by the fact that investment opportunities were limited during the pandemic. Additionally, given the uncertainty, which was caused by the pandemic, investors were wary of undertaking new investments.

Precautionary saving levels also increased, delivering a blow to aggregate demand across the globe, which, in turn, reduced the need for investment. However, the developing economies and specifically the economies in the Asia region saw a less drastic reduction in FDI (Statista, 2020). This anomaly in the trend is caused by a few Asia countries, including China, India, and the Philippines, which actually saw a jump in FDI during the pandemic (OECD, 2020).

The growth in the FDI for these countries is depicted below. As the investment opportunities shrink across the globe during the pandemic, these countries, which have been showing good growth over the recent past, became a hub for foreign investors. In the face of falling interest rates and declined commercial activity, these countries were able to attract international investors who were looking to earn a good return on their investments.

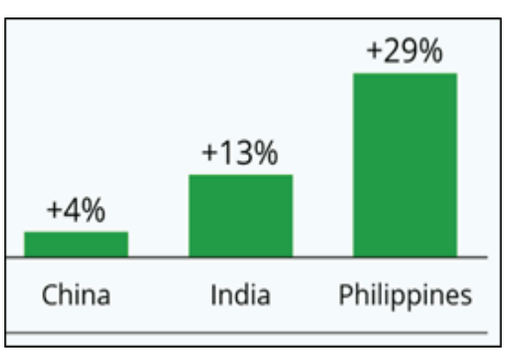


Figure 9: FDI during Pandemic (Source: Statista, 2020)(Source: Statista, 2020)

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Contact Information & Map

Tel: +267 5441716 | Mobile (with Whatsapp): +267 73176799 | Fax: +267 544 1698
Email;kgogomodumolodge@gmail.com | Address: 1258 Sepojane Kanye
GPS Coodinates: Lat;24'57'31.6S Lon;25'20'38.8E

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The flight of financial capital was also observed during the pandemic from the developed economies towards the developing and fast-growing economies of the Asian region (Nicola et al., 2020). This trend was representative of the desire of these investors to make capital gains in the face of a devaluation of currencies and to mitigate the impact of inflation on their capital.

1.7 Future Outlook

While the impacts of the pandemic have been felt across various sectors of the economy, it is believed that the disruptions were either caused by 'supply shocks' or 'demand shock'. The supply shock curtails the ability of an economy to ensure the production of goods and supply, whereas a demand shock curtails the ability and willingness of consumers to consumer goods and supply (Altig et al., 2020). The fact that the pandemic disrupted both supply and demand sides was the main reason that it led to such severe economic and financial impacts across countries (Statista, 2020a). However, as the economies recover, the spread of the virus slows down, and the rollout of vaccines increase, the economies are expected to bounce back sharply.

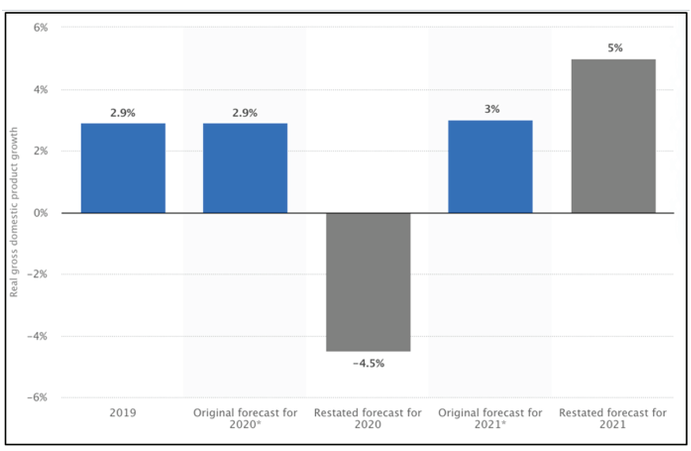

Figure 10: Forecasted Real GDP Growth (Source: Statista, 2021a)

The graph above highlights the projected economic recovery expected in the wake of the coronavirus. As the graph shows, in 2020, the global economy was expected to grow at a rate of 2.9% originally (Statista, 2020a). This forecast did not take into consideration the pandemic and post-pandemic economic realities. However, the restated forecast, incorporating Covid pandemic effects, led to a growth rate projection of 4.5% (Statista, 2020a). This means that during 2020, the global economy contracted by 4.5% as a result of the pandemic and the supply and demand shocks that it caused.

Given the extremity of nose-dive of the global economic growth, it is forecasted that the rebound will be equally strong as economies recover (Albu et al., 2020). The forecasted global GDP growth rate in 2021 is 5% (Statista, 2020b). This strong rebound forecast is based on the various measures that governments have undertaken in the previous year to support their economies. From stimulus packages to lower interest rate, waving off of rental obligations and tax rebates, these measures will not only enable businesses to better coup with the impact of the pandemic but at the same time also enable them to attain a higher level of sustainability (Statista, 2020b).

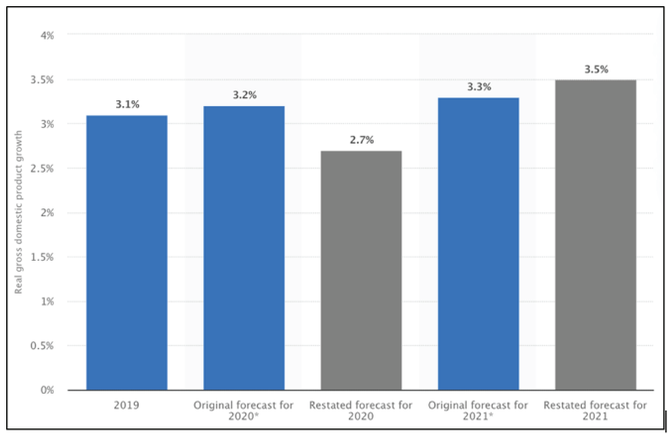

Figure 11: Forecasted GDP Growth in G8 Countries (Source: Statista, 2021b)

The graph above presents a similar forecast for the G20 countries. As the graph depicts, while the restated forecast for G20 countries was only 0.5% lower than the original one, the rebound expected is a strong one (Statista, 2020b). The reason for a lower economic impact on the G20 countries is that they have strong economies, which are structurally resilient and hence were able to better stand the stress because of the pandemic. The G20 economies also rely less on external financing, as a result of which the financial implications for these countries were limited, allowing them to better weather the storm post-pandemic.

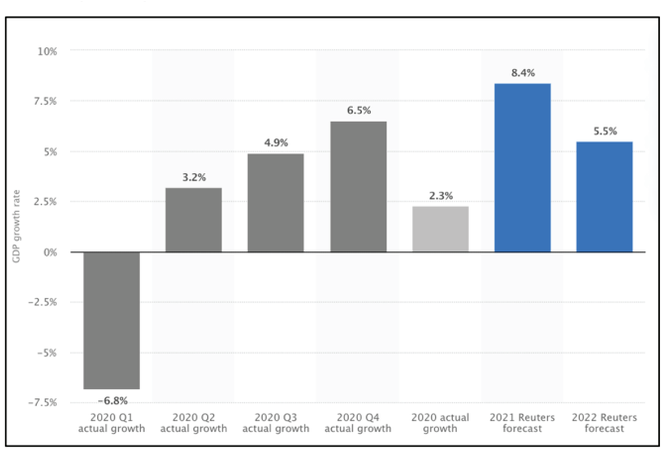

Figure 12: China GDP Growth during Pandemic (Source: Statista, 2021c)

China was among the first countries which were hit by the coronavirus and were also the most severely hit as well as a result of the extreme lockdowns which were imposed by the government in the country. The graph above shows the quarterly recovery path for China over the last year and the forecast for 2021 (Statista, 2020c). As shown, the economic growth was severely hampered in the first quarter for the country, with a slow recovery made with each passing quarter.

The actual growth experienced by the country despite the pandemic was 2.3%, which is significantly lower than in previous years. This subdued growth can be attributed to the pandemic and the measures taken to stem its spread.

However, the Chinese economy is expected to rebound strongly in 2021 as the country starts rollout of the vaccine in an attempt to rein in the pandemic and stop the spread of the virus. The forecasted growth rate for the Chinese economy is 8.4%, backed by key monetary policy loosening initiatives of the government and the opening up of international trade (Gill, 2020). These measures are expected to drive the demand up in the global economy, which, in turn, will help in instigating economic recovery in the country.

1.8 Conclusion

The Covid-19 pandemic, which initiated in China and spread rapidly across the globe, has impacted national health, economic activity, and future prospects of countries across the globe. The rapid spread of the virus and the ensuing lockdowns in various countries and regions resulted in supply and demand shocks. While on the one hand, production and manufacturing activity was hampered as a result of lockdowns and limited movement of goods and services; on the other hand, the demand dwindled as uncertainty and panic gripped the public. In this context, economic growth was impacted by growth. It is estimated that during 2020, the global economy shrunk by a staggering 4.5%, with a lot of countries faring even worse. However, as the spread of the virus is curtailed, vaccine rollout improves, it is estimated that in 2021, the global economies will post a sharp recovery to cover the losses of the previous year.

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COVID-19 PATHOGENESIS AND ITS PHARMACOTHERAPEUTIC BASIS

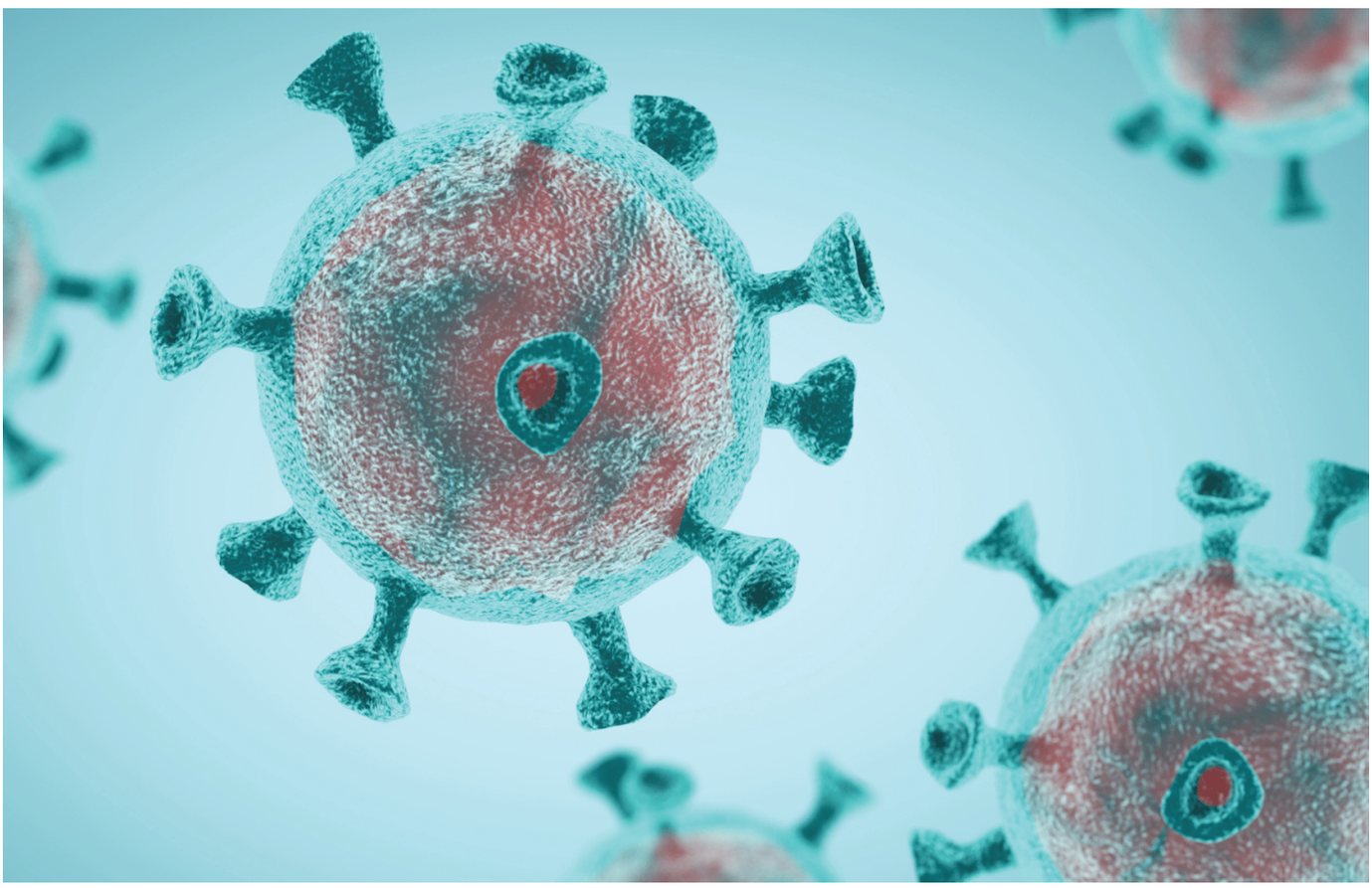
Author: : Pelotshweu R Nyambe and Bokang Y Mothofela

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Corresponding Author *Dr Derrick D.Tlhoiwe, Dr Tumelo Tlhoiwe, Larry.L. Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract

Towards the end of 2019, a sudden acute atypical respiratory disease was identified in the Wuhan province of China with most of its initial cases identified to have been exposed at the Huanan seafood market at which the sale of dead seafood and live animals occurred. The Chinese government notified the World Health Organization (WHO) and closed the Huanan seafood market in January 2020. A drastic increase in the number of cases has been observed subsequently including persons who had not been exposed to the seafood market directly which confirmed human to human transmission of the causative organism (Bwalya, A.W., et al 2020). The first fatality was reported on 11th January. This turned out to be an epidemic, initially spreading to other countries like Thailand, South Korea, and Japan as there was massive Chinese migration due to Chinese New Year's Eve (Pandey, A., et al 2020).

The pathogen was ultimately identified as a novel enveloped RNA β coronavirus that was subsequently named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the SARS-CoV-2 tag was assigned due to the virus exhibiting approximately 80% homology to the SARS-CoV, which caused acute respiratory distress syndrome (ARDS) with associated high mortality during the early 2000 s. In February 2020, WHO referred to the disease caused by this virus Coronavirus disease 19 or COVID-19, and a pandemic was declared in March 2020, the impact of which has been widespread with >200 countries and territories being affected (Bwalya, A.W., et al 2020).

Key words | Covid-19, coronavirus, Acute respiratory distress syndrome(ARDS)

Background

The outbreak of emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) in China has been brought to global attention and declared a pandemic by the World Health Organization (WHO) on March 11 2020. Scientific advancements since the pandemic of severe acute respiratory syndrome (SARS) in 2002-2003 and Middle East respiratory syndrome (MERS) in 2012 have accelerated our understanding of the epidemiology and pathogenesis of SARS-CoV-2 and the development of therapeutics to treat viral infection. As no specific therapeutics are available for disease control, COVID-19 is posing a great threat for global public health.

RESEARCH AIMS

1. The aim of this research was to conduct a systematic review to better comprehend the disease Covid-19 and come up with ways to combat it
2. The aim of this research was to conduct a systematic review to better comprehend ways to maximize public awareness about Covid-19 to reduce its spread

OBJECTIVES

The general objective of this study was to evaluate and understand Covid-19 pathophysiology and its potential therapeutics.

SPECIFIC OBJECTIVES

1. To understand the structure and lifecycle of coronavirus
2. To evaluate the clinical manifestations of Covid-19
3. To come up with Covid-19 potential therapies

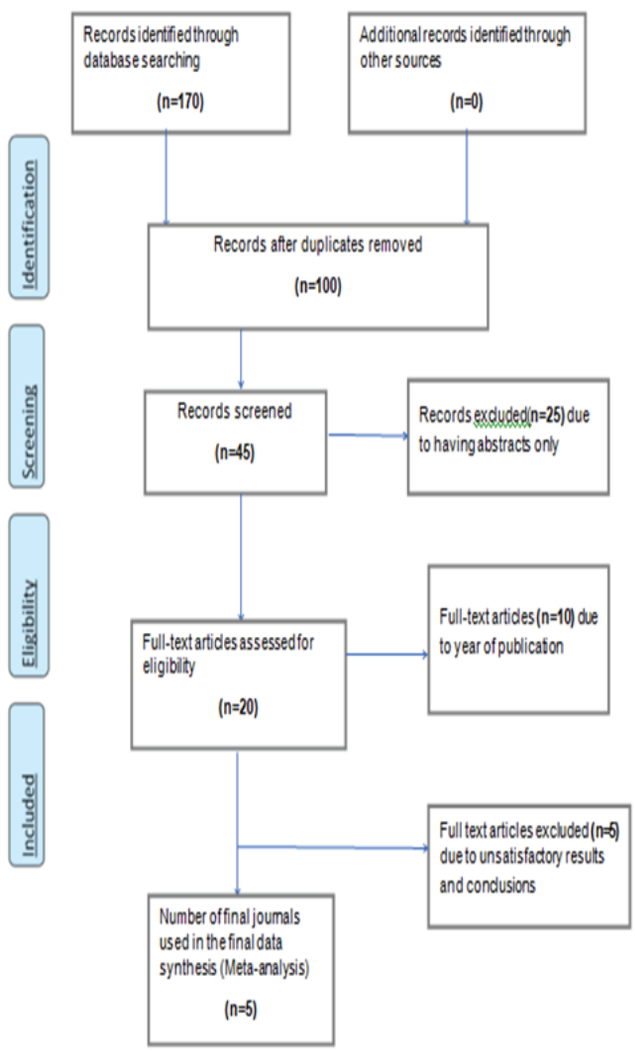
METHODOLOGY

We searched 3 databases; Google Scholar, Pub-med and NCBI from (2011-2021) for qualitative studies on patients and health care providers with free text "COVID-19 and PHARMACOTHERAPEUTICS or TREATMENT". Study quality was predetermined and extracted independently on to a form. 190 articles were screened and we selected 5 articles that met the per-specified inclusion criteria.

In present research work, the case studies were excluded because some were duplicated, some had abstracts only and some were out of date. Furthermore, the studies that deviate from the current subject were also not considered. Since the study intends to discuss the Covid-19 pathogenesis and its pharmacotherapeutic basis, the case studies with no related or specific content in regard to the Covid-19 pathophysiology and treatment were also rejected. Language, year of publication as well as abstracts only publications formed exclusion criterion.

The thesis provides an overview of qualitative evidence derived from this multiple international studies. We identified 6 major themes across studies; convalescent plasma, fusion, blocking endocytosis, viral enzyme inhibition, ACE-2/S-protein receptor domain binding interactions and suppression of excessive inflammatory response. The findings of this study are limited by the quality of the included studies.

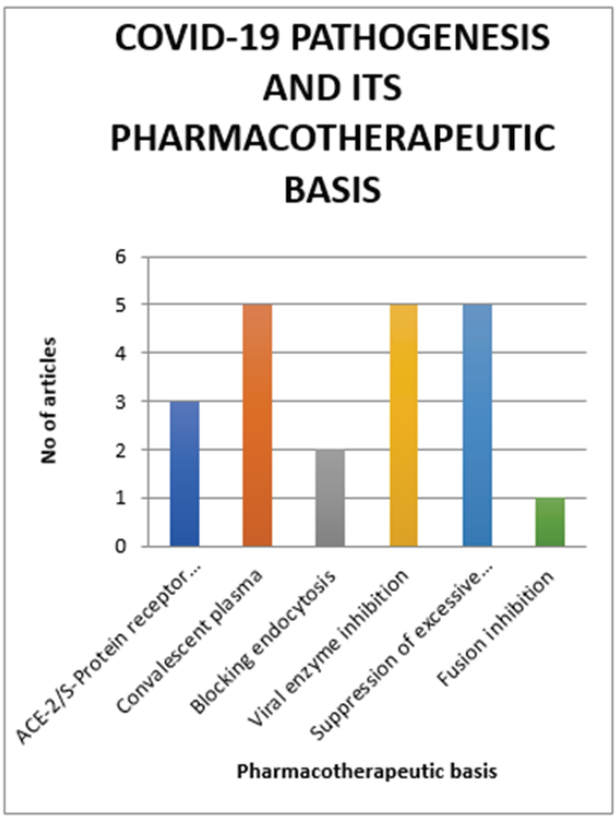
Fig 1.0 | Prisma Flow Chart



RESULTS

A round up from all the journals, 100% of the journals stresses that convalescent plasma, viral enzyme inhibition and suppression of excessive inflammatory response are pharmacotherapeutic basis of Covid-19, 60% that is 3 of the 5 journals agrees to ACE-2/S-protein receptor domain binding interactions, blocking endocytosis ratio is confirmed by 2 of the 5 journals being 40% and fusion inhibition is accounted by 20%.

Fig 1.2 | KEY RESULTS AND DISCUSSION



DATA ANALYSIS AND INTERPRETATION

ACE-2/S-Protein receptor domain binding interactions

Human angiotensin-converting enzyme 2 (ACE2) is a functional receptor hijacked by SARS-CoV-2 for cell entry. ACE2 is a type I membrane protein expressed in lung, heart, kidney, and intestine mainly associated with cardiovascular diseases. The full-length ACE2 consists of an N-terminal peptidase domain (PD) and a C terminal Collectrin-like domain (CLD) that ends with a single transmembrane helix and an~40-residue intracellular segment. In addition to cleavage of angiotensin (Ang) I to produce Ang-(1-9), ACE2 also provides a direct binding site for the S proteins of SARS-CoV-2 (Yuefei, J., et al 2020). The S protein of CoVs exists in a metastable pre-fusion conformation that undergoes a dramatic structural rearrangement to fuse the viral membrane with the host cell membrane.

This process is triggered by the S1 subunit and a host–cell receptor binding, which destabilizes the pre-fusion trimer, resulting in the S1 subunit shedding and the S2 subunit transition to a highly stable post-fusion conformation (De Wilde, A.H., et al 2018). This interaction between the spike proteins and ACE-2 receptors are a potential pharmacological target for treatment of infections. Engaging the ACE-2 receptor with recombinant human derived ACE-2 is an approach that can be explored, as the delivery of excess soluble ACE-2 may neutralize the virus through competitive binding to the SARS-CoV-2 envelope (Khattabi, L., 2020).

In addition, viral entry into cells may be blocked by proteins, peptides, or small molecule compounds that bind to the S protein of the virus, thereby preventing interaction of the virus with the host cell membrane. Since SARS-CoV-2 enters the host cell by binding to ACE-2 at the S protein receptor-binding domain (RBD), inhibition of SARS-CoV-2 RBD/ACE2 protein–protein interaction (PPI) is potentially a very important therapeutic target. The first-in-class peptide binder, 23-mer peptide binder (SBP1), was found to potentially restrict the entry process of SARS-CoV-2 into human cells through binding to the SARS-CoV-2-RBD, suggesting this is a potential approach to treatment (Bwalya, A.W., et al 2020).

4.1.2 Fusion

The entry of the SARS-CoV-2 organism to host cells is facilitated primarily by two host proteases, viz., serine protease TMPRSS2 on the surface of the cell surface, and/or cysteine proteases cathepsin B and L (CatB/L) in endosomes. Transmembrane protease serine type 2 (TMPRSS2), a protease belonging to the type II transmembrane serine protease family, cleaves the coronavirus spike protein, making it a potential therapeutic target for coronavirus infections (Iwata-Yoshikawa, N., et al 2019). The development of protease inhibitors could be useful to target these proteases as treatment options for COVID-19. Camostat mesylate, aTMPRSS2 serine protease inhibitor and a cathepsin L inhibitor, are novel agents which may be used to inhibit COVID-19 entry into host cells. The cathepsin L inhibitor in particular has exhibited good results in reducing infections in human lung cell lines when administered concomitantly with camostat mesylate. Nafamostat mesylate has also been shown to prevent TMPRSS2-triggered SARS-CoV-2 membrane fusion and has been licensed for use in Japan (Bwalya, A.W., et al 2020).

Blocking endocytosis

Chloroquine and hydroxychloroquine have been evaluated for their ability to inhibit viral progression of SARS-CoV-2 as they raise the pH of lysosomes and endosome thus preventing the virus fusion mechanism with host cells and corresponding replication. When HCQ enters antigen-presenting cells (APCs) it inhibits the development of antigen and the autoantigen exposure to T cells controlled by major histocompatibility complex (MHC) class II. It represses subsequent stimulation of T cells and CD154 expression and other cytokines. Furthermore HCQ disrupts DNA / RNA's interaction with toll-like receptors (TLRs) and the cGAS nucleic acid detector and thus the expression of pro-inflammatory genes cannot be triggered and consequently CQ and HCQ administration is not only expected to alleviate COVID-19's extreme development by preventing its replication and invasion but it also reduces the risk of cytokine storm by blocking T cell stimulation (Pandey, A., et al 2020).

Viral enzyme inhibition

Viral infection is sensed by RIG-I (RIG-I-like helicase) and MDA-5 (melanoma differentiation-associated protein 5) in recognition of viral RNA. Recruitment of adaptor proteins MAVS transduces signals to the downstream kinase complex which activates the transcription factor IRF-3 which coordinates the expression of type 1 interferons. Type 1 interferons induces the activation of STAT transcription factors resulting in the expression of IFN-stimulated genes and the establishment of an antiviral state in surrounding cells. PLpro can act on different branches of these pathways by interacting with or recognizing and deubiquitinating proteins within these pathways. The net effect of these is to help SARS-CoV evade the host antiviral response therefore targeting PLpro with antiviral drugs may have an advantage in not only inhibiting viral replication but also inhibiting the dysregulation of signaling cascades in infected cells that may lead to cell death in surrounding, uninfected cells (Yahira, M., et al 2015).

Suppression of excessive inflammatory response

Baricitinib is an immunosuppressant approved by the FDA for the treatment of moderate to severe rheumatoid arthritis. It is a janus kinase (JAK) inhibitor which acts by selectively and reversibly binding to JAK receptors there by inhibiting JAK1 and JAK2. This inhibition leads in halting the signal transduction from growth receptors or cytokines leading to reduction in immune cell function and haematopoiesis. Baricitinib also prevents the formation of viral particles and intracellular passage of viral cells by binding to associated protein kinase 1 (AAK1) (Lu, R., et al 2019).

Convalescent plasma

Convalescent plasma (CP) therapy has been proposed as a potential treatment strategy for COVID-19 infection. The plasma from a donor who has recovered from an infection is transfused in an attempt to develop passive humoral immunity against SARS-CoV-2-infections in patients. Currently the FDA only advises the use of COVID-19 CP under emergency use authorization (EUA) or investigational CP under an investigational new drug (IND) during a public health emergency (Bwalya, A.W., et al 2020) Additional protective antibodies including immunoglobulin G (IgG) and immunoglobulin M (IgM), are found in plasma in addition to neutralizing antibodies (NAbs) which might show antiviral effect. IgG and IgM are the key isotypes although immunoglobulin A (IgA) can also be important especially for viral mucosal infections. Non-NAbs which bind to the virus but do not affect its ability to replicate could contribute to prophylaxis and/or improvement in recovery. The humoral immune response targets mainly spike (S) protein thus preventing complement cascade (Pandey, A.,et al 2020).

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THE PATHOGENESIS, PREVENTION STRATEGIES AND DRUG THERAPEUTIC OPTIONS FOR COVID-19: A SYSTEMATIC REVIEW

Author: : Palesa Chilukwa and Dr Issa Bondo

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Corresponding Author *Dr Derrick D.Tlhoiwe, Dr Tumelo Tlhoiwe, Larry.L. Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract |

The Coronavirus disease of 2019 has affected the world in many ways since its discovery. Putting the world on edge as it was an unknown illness with little or no data available about it. It was for these reasons that relevant stakeholders and the public came together to work hand in hand and battle this new disease. Health organizations like the WHO and CDC along with other government bodies worked to get her to come up with drugs that could help their citizens fight this global pandemic while the citizens themselves worked with the government to adhere to new regulations that were used as prevention measures to control and stop the spread of this disease.

Keywords: COVID-19, prevention strategy, drug therapeutic option, pathogenesis.

Background

Towards the end of 2019, a sudden acute atypical respiratory disease was identified in the Wuhan province of China, with most initial cases identified to have been exposed at the Huanan seafood market at which the sale of dead seafood and live animals occurred (Pandey, A., et.al 2020). The Chinese government notified the World Health Organization (WHO) and closed the Huanan seafood market in January 2020. A drastic increase in the number of cases has been observed subsequently, including persons who had not been exposed to the seafood market directly, which confirmed human to human transmission (Huang, C., et.al 2019).The disease initially spread to Thailand, South Korea, and Japan as a consequence of massive Chinese migration due to celebration of the Chinese New Year. An epidemic caused by a novel coronavirus, with the first fatality reported on 11 January 2020, had commenced (Pandey, A., et.al 2020). The pathogen was ultimately identified as a novel enveloped RNA β coronavirus that was subsequently named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Huang, C., et.al 2019), and the SARS-CoV-2 tag was assigned due to the virus exhibiting approximately 80% homology to the SARS-CoV, which caused acute respiratory distress syndrome (ARDS) with associated high mortality during the early 2000 s (Ksiazek ,T.G., et.al 2020). In February 2020, WHO referred to the disease caused by this virus Coronavirus disease 19 or COVID-19, and a pandemic was declared in March 2020, the impact of which has been widespread, with >200 countries and territories being affected (Zhang ,J., et.al 2020),(Knoll ,M.D., et.al 2021).

As of 5 November 2020, over 47 million cases have been recorded worldwide resulting in more than 1.2 million deaths. Of the over 36 million cases that have had an outcome, 97% have been reported as recoveries (Knoll, M.D., et.al 2021). The primary site of infection of the SARS-CoV-2 virus has been reported as the respiratory system possibly due to the vast surface area of the lungs that makes them highly susceptible to the virus, if inhaled (Zhang,H.,et.al 2020), and subsequent

pathology involves broad systemic infection. The symptoms associated with COVID-19 include lower respiratory tract infection and related symptoms such as dry cough, dyspnoea, ARDS, and pulmonary fibrosis in addition to more general symptoms such as fever, headache, dizziness, generalized weakness, vomiting, and diarrhoea (Shi, H., et.al 2020). In some instances, patients may experience fulminant and fatal hyper-cytokinemia associated with multi-organ failure (MOF) as a result of cytokine storm syndrome (Coperchini, F., et.al 2020). In addition, patients with COVID-19 may also experience cardiac, hepatic, renal, central nervous system, or thrombotic disease (Galea, M.D., et.al 2021).

Current medical management of COVID-19 infection is largely supportive with no specific therapy available. Several drugs, including antimalarials such as chloroquine and hydroxychloroquine (Boulware, D.R., et.al 2020), (Schlagenhauf, P., et.al 2020), (Cavalcanti, A.B., et.al 2020), the anti-retroviral combination lopinavir/ritonavir (Cao,B., et.al 2020) , an investigational nucleotide analogue with broad-spectrum antiviral activity initially intended to treat hepatitis C and Ebola, viz., remdesivir (Beigel,J.H., et.al 2020), and the macrolide antibiotic azithromycin (Schlagenhauf, P., et.al 2020), (Cavalcanti, A.B., et.al 2020) , have been tested in clinical trials as potential treatment for the virus. However, it is worth noting that none of these approaches are a definitive cure or are suitable for prophylaxis.

COVID- 19 Epidemiology

In December 2019, China reported a pneumonia outbreak of unknown causes in Wuhan. Most of the early cases of COVID- 19 were found to be associated with the Huanan seafood wholesale market. The next-generation sequencing of lower respiratory tract samples of the patients brought forth knowledge about the presence of beta coronavirus. The virus was observed under electron microscope revealing that the virus's diameter was 60 to 140 nm, whereas the characteristic spikes were 9 to 12 nm, which was similar to the Coronoviridae family (Chowdhury & Oommen, 2020). The novel coronavirus was noted to possess similarity to two of the bat-derived coronavirus strains, having an approximated value of 88% similarity compared to the coronavirus infecting humans, such as SARS, having 79% similarity (Chowdhury & Oommen, 2020).

According to CDC (2020), the individuals infected with the Covid-19 virus develop antibodies in their bodies to fight the virus; therefore, serological tests can be carried out to detect the antibodies. According to WHO (2020), the global research on Covid-19 suggested that most of the transmission occurs from the asymptomatic individuals, as compared to the COVID-infected individuals having symptoms; leading to the conclusion that taking personal protective measures, such as the use of masks and social distancing, are likely to contribute to controlling the transmission of Covid-19 infection.

This virus was declared a world pandemic in March 2020 as it had already spread to more than 200 countries and territories. As of 5 November 2020, over 47 million cases were recorded worldwide leading to more than 1.2 million deaths. Of the over 36 million cases that have had an outcome, 97% have been reported as recoveries (Witika, B.A., et al 2020).

Other researches showed that on April 17 2020, this disease had affected 210 countries worldwide. Around the same time 142 229 death in 213 countries, areas and or territories were confirmed. The most affected countries with more than 300 000 confirmed cases of corona virus disease were United States of America, Spain, Italy, Germany, France, the United Kingdom, China, Iran, Turkey, Belgium, the Russian Federation, Canada and Brazil (Lone, S.A. and Ahmad, A., 2020).

RESEARCH AIM

To evaluate prevention strategies and drug therapeutic options of COVID-19.

OBJECTIVES

1. To assess the effectiveness of COVID-19 prevention strategies
2. To evaluate different drug therapeutic options in relation to the pathogenesis of the COVID-19.

METHODOLOGY

As a means of answering the aims and objectives of the research topic, secondary data was systematically reviewed. Among the databases used for attaining the information included were PubMed, Google scholar. The utilization of the multiple databases presented the opportunity to gain accurate and reliable information that signified the primary aspects of the study. Also, the research study used the PRISMA tool for screening the research resources.

RESULTS

Identified studies were uploaded into endnote (Thomas Reuters) and duplicates were removed. 4 reviewers vetted through the study based on the topic and abstracts that met the inclusion criteria. Studies selected after the first screening were further screened through a detailed full text browsing, to further exclude studies that had some of the exclusion criteria. Out of 64 studies identified, 34 were excluded due to having abstracts only, 15 were further excluded due to their year of publication. Of the remaining 15, 10 were excluded due to unsatisfactory results and conclusions. Only 5 were finally used.

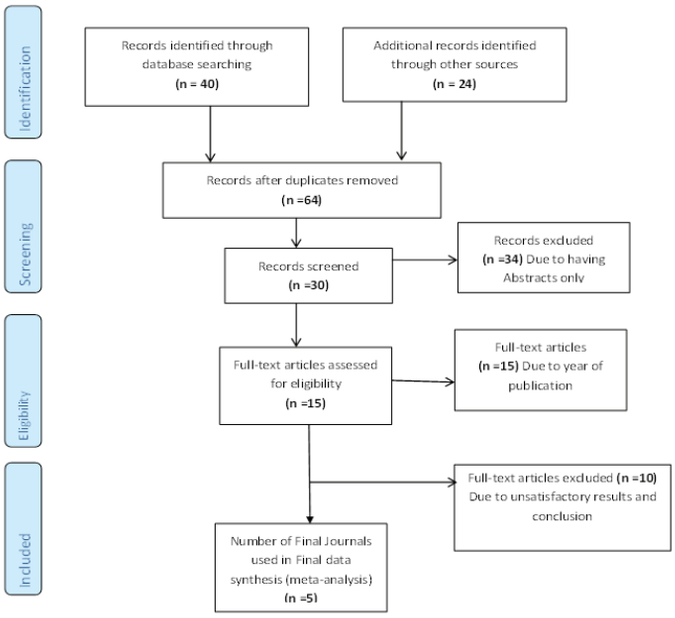

figure 1 PRISMA FLOW CHART

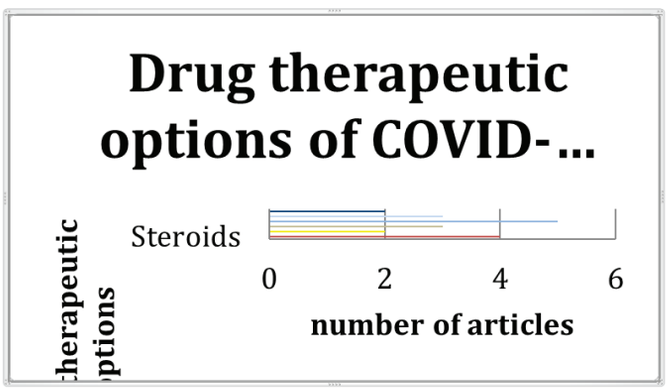

Fig 1.1| KEY RESULTS AND DISCUSSION

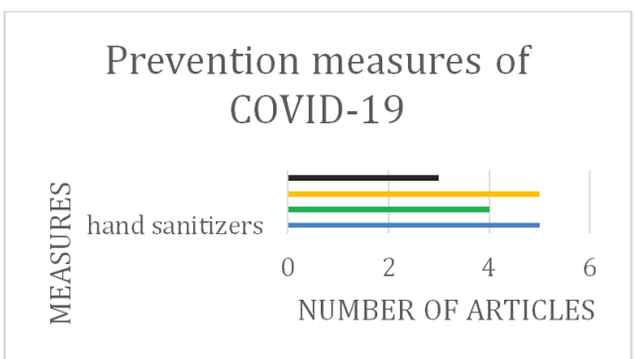

Fig 1.2 KEY RESULS AND DISCUSSION

DATA ANALYSIS AND INTERPRETATION

Drug therapeutic options

Antivirals

Few benefits have been noted with the use of antivirals as drug therapeutic options for COVID-19 as data from randomized trials proved them to have no benefit. An example would be the open label randomised controlled trial with 199 patients with confirmed SARS-CoV-2 infections; the effectiveness of a combination protease inhibitor therapy was tested where there was no benefit noted in the lopinavir-ritonavir group for treatment of COVID-19(Cao, B., et.al 2020).

However, there are some antivirals that have proven their efficacy against this virus such as remdesivir. Remdesivir, which is a nucleotide analogue, is a broad-spectrum antiviral agent. Remdesivir has been noted to have promising in vitro and in vivo activity in animal models especially against the MERS and SARS viral pathogens. (Alvi, M.M., et.al 2020) Once inside the cell, its active analogue inhibits viral RNA-dependent RNA polymerase (RdRp) stopping viral replication (Ferner, R.E. et.al 2020) proving effective against other coronaviruses including SARS-CoV and MERS-CoV in non-clinical animal models Favipiravir, an RNA polymerase antiviral agent, is another antiviral drug being investigated in a randomised Italy. Known for previously being used in Japan for influenza including some phase 3 trials in the US and several phase 3 trials in other parts of the world, it targets the RNA-dependent RNA polymerase, which is a protein important for the maturation, packaging, and subsequent reinfection of other cells. This feature highlights the importance of the medication being given to the patients at an early stage of the infection. Favipiravir in this case may only be suitable for milder infections or in combination with other therapies.

Chloroquinolone

The effectiveness of chloroquine was tested in a randomised double-blind study in the 1960s and the conclusion was noted as its antiviral effects being minimally beneficial (Updike, S.J. et.al 1967). However a number of in vitro studies have shown efficacy of chloroquine and hydroxychloroquine by affecting the ACE2 receptors necessary for viral entry, and increasing endosomal pH in host cells, hindering the lysosomal activation of the virus (Salata, C., eth.al 2017),(Vincent, M.J., et.al 2005).With randomized clinical trials proving minimal efficacy and invitro studies showing the benefit of the aminoquinolones much attention has been directed to them with their conflicting data, both, advocating and discouraging its use for treatment of patients with the SARS-CoV-2 virus (Alvi, M.M., et.al 2020)..

Vaccines

The success of a vaccine is based on its ability to generate a therapeutic antibody response. To successfully develop a vaccine there has to be preclinical animal studies, phase I-III studies showing safety, capacity to stimulate antibody in humans and then protective efficacy followed by large-scale of production of vaccine needs to be implemented. Both the private and public sector have been working hand in hand to produce the SARS-CoV-2 vaccine. WHO stated that, as of April 2020, an approximate number of 71 vaccines for SARS-CoV-2 are currently under consideration (WHO 2020).With a live attenuated virus vaccine, a mutation is introduced into the viral protein to attenuate the virulence of the SARS-CoV-2 virus.

This type of vaccine generates excellent T and B cell responses but is generally not suitable for immuno-compromised individuals. The viral DNA is briefly modified to encode for the desired antigen, with the expressed glycoproteins generating the desired immune response (Milligan, I.D., et.al 2016).Since a live virus is confronted by the patient's immune system, such vaccines result in lifelong immunity. On the other hand, patients with a compromised immune system may not be eligible to receive this type of vaccine placing limitations to achieve worldwide immunity from the SARS-CoV-2 virus.

Additionally, the virus has to stay in its alive form' until injected into the patients, requiring refrigeration, which may be a logistical issue when the vaccine will have to be delivered to remote areas of the world. Other vaccines such as the DNA based vaccine, mRNA-based vaccines, Protein based vaccine, and Virus-like particle vaccines are also being investigated to determine their efficacy as drug therapeutic options in the fight against the SARS-CoV- 2 virus. (Alvi, M.M., et.al 2020)

Steroids

Dexamethasone, a long acting corticosteroid that decreases neutrophil migration and production of inflammatory mediators is used as an anti-inflammatory and immunosuppressant agent in the treatment of acute asthma exacerbation, allergic response, autoimmune disease, cerebral oedema, and as an antiemetic in chemotherapy regimen].

In studies conducted on the efficacy of dexamethasone on reducing the mortality of COVID-19 patients data showed the survival rate was highest among the dexamethasone-treated participants who required invasive mechanical ventilation at randomisation. Dexamethasone, a low-cost agent, provided an efficient treatment for the highly sick COVID-19 patients requiring oxygen ventilation (Richardson, P.G., et.al 2005).

Dexamethasone use is not recommended in patients who are at risk for an adrenal crisis, or patients with known adrenal insufficiency. Moreover, the drug's use has also been associated with fluid retention and myocardial rupture. With many reports suggesting critically ill COVID-19 patients to have pre-existing cardiovascular diseases, the use of dexamethasone as a viable treatment is questionable. (Alvi, M.M., et.al 2020) Although, positive mortality outcomes warrant the use of dexamethasone for the treatment of severely sick COVID-19 patients requiring oxygenation, evaluation of potential adverse effects and careful consideration in patient populations eligible to receive the treatment `must be considered.

Ivermectin

Ivermectin, the drug known for its wide range of bioactivity is being considered as a possible drug therapeutic option for COVID-19.This drug is being considered based on its invitro study showing its inhibition of SARS –CoV-2 replication(Caly,L., et.al 2020).Studies show ivermectin has the ability to significantly bind to SARS-CoV-2 protein although contraindicated with pharmacokinetic reports stating that the routine antiparasitic dose concentrations are unobtainable in humans (Momekov, G., et.al 2020).



Monoclonal Antibodies

Drugs such as Bamlanivimab, a neutralizing monoclonal antibody derived from plasma of a patient recovering from COVID-19 has shown its ability to reduce viral replication and neutralize SARS-CoV-2 in non-human primates(Spinner, C.D.,et.al 2020). It does so by targeting the RBD of the spike protein of SARS-CoV-2.Bamlanivimab is to be used in junction with etesevimab as the combination is associated with significant reduction in SARS-CoV-2 viral load compared to placebo (Gottlieb, R.L., et.al 2021).Other monoclonal antibodies such as Anti-IL-6 receptor monoclonal antibody are considered the key factors in slowing down the inflammation process of COVID 19(Conti, P., et.al 2020). This assumption is based on the known fact that interleukin-6 is a proinflammatory cytokine considered as the key driver in the inflammatory state of associated with COVID -19(Michot, J.M., et.al 2020)

Prevention Strategies
Contact tracing

With the instructions published by WHO on laboratory testing guidance for SARS-CoV-2, for effective collection, packaging and shipment of specimens (WHO 2020),Several researchers have pointed out the applications of pooled testing strategy as this might lessen the burden on laboratories (Gollier, C.,et.al 2020)(Noriega, R., et.al 2020). This approach might be highly useful in densely populated areas or highly infected areas. As SARS-CoV-2 spreads through close contact and respiratory droplets, a number of countries have utilized contact tracing combined with testing as a way to manage the spread of infection.

If an individual is exposed they are tested and, if the test is positive, they are advised to self-quarantine for 14 days. This is done to contain the spread of the virus by quarantining those who may not be showing symptoms but are infected with the virus. Countries like South Korea which were successful with implementing this measure through easily accessible tests at drive-through stations, followed by intense tracing of the contacts of confirmed cases were able to control the spread of the infection (Salathé, M.,et.al 2020)(Lee, V.J., et.al 2020).

In contrast, Italy which did not employ such methods during the early phase saw a wider outbreak proving that this method is useful in curbing the spread of COVID-19 pandemic. This is also showcased by data from different transmission models (Hellewell, J., et.al 2020). It is important to note the weaknesses of this method of curbing the infection such as how time consuming and laborious it may be if done traditionally instead of digitally. Digital apps which allow countries to trace contacts with inbuilt GPS tracking has raised issues of privacy. None the less this method has proven efficient in the prevention of COVID-19.

PPE (masks)

With current evidence suggesting human-to-human transmission of this virus through close contact and respiratory droplets, several precautions can help decrease the spread of the virus, those in the Health care sector are increasingly exposed to the virus and therefore required to strictly adhere to the protocols, and use the WHO recommended Personal Protective Equipment (PPE) (WHO 2020).
The Centre for Disease Control and Prevention in the US, has suggested the use of non-medical masks to the public (Adams, J., 2020), however the latest WHO guidelines, as of 6 April 2020 have indicated the lack of evidence of the effectiveness of such masks
(WHO 2020).The effectiveness of personal protective equipment such as masks is lowered considerably if not used appropriately as evidenced during the outbreak of SARS-CoV-1 infection, when many Canadian health care workers were infected as a result of lack of understanding of PPE removal procedure (Puro, V.,et.al 2004). PPE plays a crucial role in managing the spread of infection.
Healthcare workers and others with possible exposure to SARS-CoV-2 must use proper PPE along with implementing personal hygiene to decrease the risk of infection. As scarcity of PPE is a major worry, future research must focus on fabricating reusable, yet efficient PPEs. Reusable PPEs will not only tackle the high demand in a pandemic such as COVID-19, but will also be environmentally friendly, an aspect that is currently being overlooked.

Social Distancing

Ever Since the World Health Organisation declared COVID-19 a global pandemic in early March 2020; many countries have implemented social distancing as their primary strategy to control the spread of the virus. Social distancing has been most successful in reducing the viral spread via asymptomatic carriers of SARS-CoV-2 that may otherwise be difficult to identify and isolate. Examples of Social distancing measures across the world include closure of schools, working from home, cancelling public gatherings and restrictions on unnecessary movement outside one's residence. Social distancing has been employed as a measure because of how successful it was previously with the influenza outbreak (Hatchett, R.J., et.al 2020).

A study from Imperial College London (Ainslie, K.E., et.al 2020) used correlation statistics to examine the effect of restricted movements in various cities in China and Hong Kong, on transmissibility with data depicting a strong positive correlation between movement and RT in the most affected regions of China initially. As transmissibility declined due to strict lockdown measures, the correlation also decreased rapidly (Alvi, M.M., et.al 2020).

Even as within-city movements began increasing post lockdown, Rt did not increase indicating the success of strict social distancing measures in China. Unlike China, Hong Kong neither had a complete restriction on mobility, nor did it show any correlation between mobility and Rt. Hong Kong was successfully able to contain the disease with minimal restrictions. Others various studies have also proven social distancing to be an effective method of preventing the spread of COVID-19 with data showing the correlation between the number of newly transmitted cases in countries with lockdown restrictions and those without. (Alvi, M.M., et.al 2020)Italy was the earliest country after China, to be severely affected by the COVID-19 pandemic. Lockdown measures were not implemented until the end of February 2020, a failure that is thought to have been largely responsible for the remarkably high death toll in that country. He et al. calculated that strict social distancing measures might have reduced the number of reported cases as of 29 March 2020 by >90 %(He, J., et.al 2020).

Hand sanitizers

For the disinfection of the hand, world health organization recommends alcohol-based hand rub or soap with water (WHO 2020). The alcohol-based hand rubs are mainly formulated with ethanol, propan-2-ol or propan-1-ol. Some of the hand sanitizers also contain additional chemicals such as triclosan, chlorhexidine digluconate, benzalkonium chloride, polyhexanide, hydrogen peroxide, DDAC, peracetic acid, and/or octenidine dihydrochloride (Kampf 2018). Alcohol based hand rubs inactivate the virus (Kratzel et al. 2020). Hand wash containing 62–70% alcohol has been found to be effective in inactivating avian flu influenza A H5NI virus (Bondi, C.A.M., et al. 2007). (Pradhan, D., et.al 2020) suggests some commercially available sanitizers and provides details about their chemical constituents.

CONCLUSION

The aim of this study was to study the pathos genesis of COVID-19 along with the prevention strategies and drug therapeutic options available. Specific objectives were to evaluate the different drug therapeutic options for COVID-19 in relation to the pathogenesis of COVID-19 and to assess the effectiveness of different COVID-19 prevention strategies available.

COVID-19 is an acute atypical respiratory disease which was identified in the Wuhan province of China, with most initial cases identified to have been exposed at the Huanan seafood market at which the sale of dead seafood and live animals occurred (Pandey, A., et.al 2020). In light of these occurrences stakeholders globally came up with prevention measures and worked together to develop drug therapy options to combat this pandemic. The drug therapeutic options available were antivirals of which Remdesivir was noted to have promising in vitro and in vivo activity in animal models especially against the MERS and SARS viral pathogens. Its active analogue inhibits viral RNA-dependent RNA polymerase (RdRp) stopping viral replication (Ferner, R.E. et.al 2020) proving effective against other coronaviruses including SARS-CoV and MERS-CoV in non-clinical animal models.

(Alvi, M.M., et.al 2020) Few benefits have been noted with the use of other antivirals as drug therapeutic options for COVID-19 as data from randomized trials proved them to have no benefit. Another drug therapeutic option chloroquine noted for its ability to affect the ACE2 receptors necessary for viral entry, and increasing endosomal pH in host cells, hindering the lysosomal activation of the virus (Salata, C., eth.al 2017),(Vincent, M.J., et.al 2005)

Vaccines were also included as a drug therapy option for COVID-19 for their ability to generate a therapeutic antibody response. Vaccines such as the DNA based vaccine, mRNA-based vaccines, Protein based vaccine and Virus-like particle vaccines are also being investigated to determine their efficacy as drug therapeutic options in the fight against the SARS-CoV- 2 virus (Alvi, M.M., et.al 2020).With a live attenuated virus vaccine, a mutation is introduced into the viral protein to attenuate the virulence of the SARS-CoV-2 virus. This type of vaccine generates excellent T and B cell responses.

Another drug therapeutic option was steroids, most prominently dexamethasone. Steroid medications such as dexamethasone and prednisone are anti-inflammatory and suppress the immune system which has proven to help reduce the mortality rate of COVID-19 patients. Dexamethasone has proven effective for the highly sick COVID-19 patients requiring oxygen ventilation (Richardson, P.G., et.al 2005).
Ivermectin is also a drug therapeutic option for COVID-19 because of its invitro ability to inhibit SARS-CoV-2 viral replication although dose concentrations are yet to be determined for humans. The drug is currently not indicated for COVID-19 treatment of patients (Cascella, M., et.al 2021)

Various types of monoclonal antibodies including anti-IL-6 receptor monoclonal antibodies and potent anti-spike monoclonal antibodies are included as drug therapeutic options (Cascella, M., et.al 2021).Anti-IL-6 receptor monoclonal antibodies combat the COVID-19 virus disease by slowing down the process of inflammation associated with the disease and anti-spike monoclonal antibodies neutralize SARS-CoV-2 and reduce its viral replication

There were various prevention strategies that were put in place, one of them being The use of hand sanitizers of which Alcohol based hand rub or soap was recommended (WHO 2020). This strategy was put forth to combat issues of contamination and has proven effective. Another prevention strategy was contact tracing which had helped many countries fight the spread of the infection as opposed to those who didn't implement it (Salathé, M.,et.al 2020)(Lee, V.J., et.al 2020).

With increasing evidence of person to person transmission through close contact and respiratory droplets (WHO 2020) PPEs have been noted to a play a crucial role in managing the spread of infection. Because of how useful it was against the influenza pandemic, social distancing has also been put toward as a prevention strategy (Hatchett, R.J.,et.al 2020).It has since then proven effective as a prevention strategy against the spread of COVID-19 pandemic. However the effectiveness of most of not all these prevention strategies relies mostly on proper adherence to guidelines.

Limitations

- Limited time to complete study
- Limited research on the topic of research
- COVID-19 protocols prohibiting researcher from gathering information

Recommendations

Various researches, studies and surveys have been carried out and as evidence would have it COVID-19 is a proven global pandemic. However extensive research on its many subtopics in places like African and especially SADC countries is still lacking, therefore more research in this regard would be recommended to shed more light on curbing this global pandemic. A recommendation of more information to be published and more topics to be discussed in regards to the prevention strategies and drug therapeutic options available is necessary. Increased awareness to the general public of the magnitude of this pandemic is also key.

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THE GLOBAL IMPACT OF COVID-19 PANDEMIC ON REFFERAL HOSPITALS: A SYSTEMATIC REVIEW

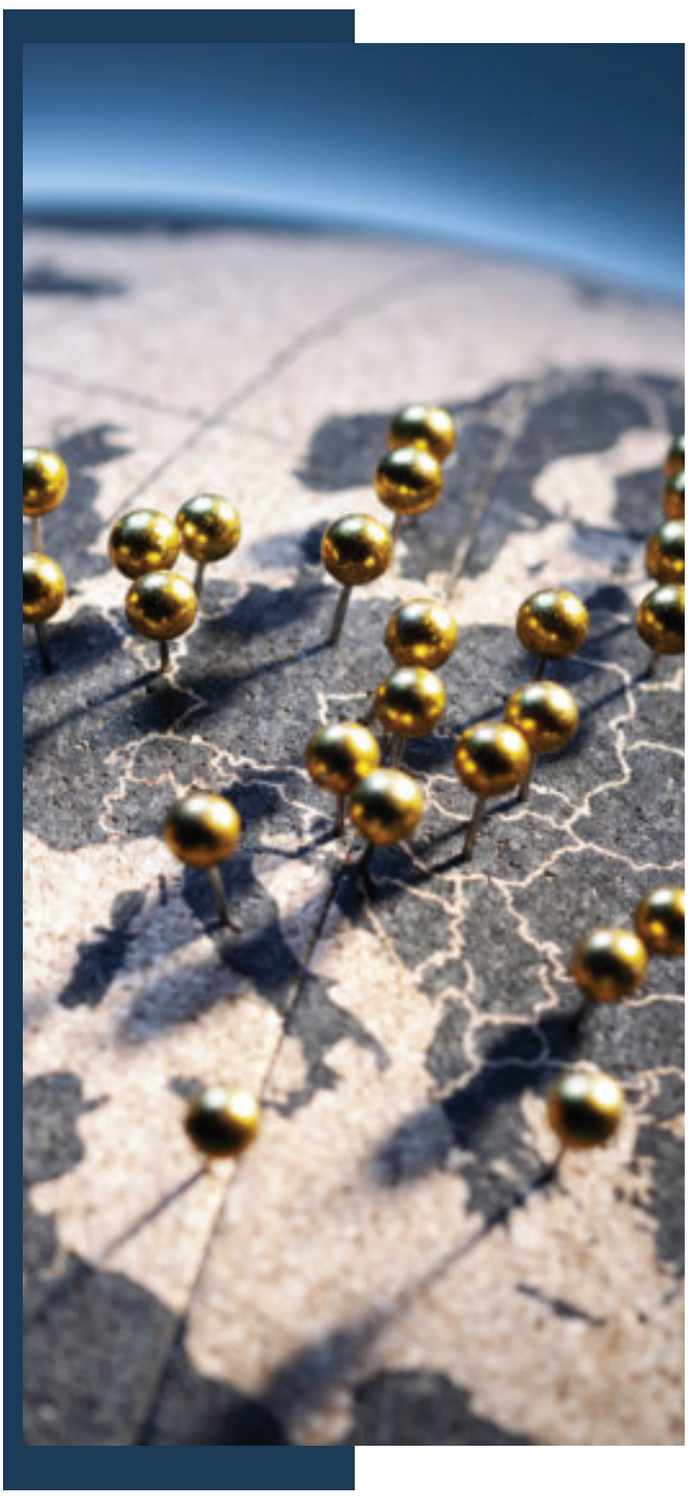
Author : Pearl Metlha Selebogo , Dr Issa Bondo

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Corresponding Author *Dr Derrick D.Tlhoiwe, Dr Tumelo Tlhoiwe, Larry.L. Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract

Covid- 19 pandemic had a great impact on the globe at large on each an every sector. There have been dramatic reductions in essential public health and clinical interventions; data from India's National Health Mission indicate that there was a 69% reduction in measles, mumps, and rubella vaccination in children, a 21% reduction in institutional deliveries, a 50% reduction in clinic attendance for acute cardiac events and, surprisingly, a 32% fall in inpatient care for pulmonary conditions in March, 2020, compared with March, 2019 Similar reports are emerging from other countries (Patel V. et al). Covid-19 pandemic has affected the health system in every possible way especially in the referral hospitals. From the care giver to the supply chain of medical necessities as well as the care receiver or patients.

Keywords: Covid-19, pandemic, health system, refferal hospitals, patients, institutional deliveries.

Background

In January 2020, the Chinese government informed the World Health Organization (WHO) and the Huanan seafood market was shut down. (Huang, C. et al 2020).This virus was named Coronavirus disease or COVID-19 by the WHO in February 2020 and the public was notified in March 2020, over 200 countries and territories affected then (Zhang, J. et al 2020; Ksiazek, T.G. et al 2020). It has been reported that the primary site of this SARS-CoV virus is the respiratory system which might be due to its vast surface area of the lungs which makes them highly susceptible to the virus, when inhaled (Zhang, H. ey al 2020), and this virus behaves like most pathologies involving the respiratory system making it a bit harder to distinguish at an early stage. The symptoms associated with COVID-19 include lower respiratory tract infection and related symptoms, viz., dry cough, dyspnoea, ARDS, and pulmonary fibrosis in addition to more general symptoms such as fever, headache, dizziness, generalized weakness, vomiting, and diarrhoea (Shi, H. et al 2020). Just like any other disease patients tend experience some specific signs and symptoms for instance some may also come presenting with fulminant and fatal hyper- cytokinesis associated with multi-organ failure (MOF) due to cytokine storm syndrome (Coperchini, F. et al 2020). COVID-19 is majorly affecting many countries all over the world, whereas Africa is the last continent to be hit by the pandemic.

However, Africa is expected to be the most vulnerable continent where COVID-19 spreading will have a major impact (Moore. M et al 2020). The continent confirmed its first case of COVID-19 in Egypt on 14th of February, 2020, and from sub-Saharan Africa the first case was reported in Nigeria on 27th of February, in an Italian patient who flew to Nigeria from Italy on 25th of February, 2020 (WHO. 2020; NCDC. 2020). Covid-19 pandemic had a great impact in the health sector globally in different departments found in the hospital including the health care workers themselves as well as the patient up to different sectors found in the hospital setting.

Impact of covid-19 pandemic on Health care workers
Health professionals experienced a temporary layoff initially with closure of academic institutions and private clinics, and disruption of hospital OPDs, elective procedures. However, their roles and responsibilities increased over the period of time (Ahmed .S et al 2020). Health professionals must deal with multiple Roles include administrative, clinical, and Educational role 9 During the COVID-19 pandemic, New online and clinical education Responsibility can have an impact. little Previous medical history, evidence base, and lack of vaccine Containing this new virus can also cause panic (Waris .A et al 2020).

Impact of covid-19 pandemic on patients of different commodities.

Effects of lockdown and subsequent wave of COVID-19 in patients with non-communicable diseases. The latest estimates from the International Diabetes Federation (IDF), "Diabetes Atlas" (9th edition), 2019, almost worldwide 463 million adults between the ages of 20 and 79 have diabetes, of which Almost 80% of them live in low- or middle-income countries, Almost 60% of them are Asian (International diabetes federation Aug. 2020). The estimate also found that one-tenth Adults have diabetes and one in five diabetics All parts of the world come from Southeast Asia, and in the United States, 1 in 6 adults has diabetes. The world comes from India (International diabetes federation Aug. 2020).These large numbers constitute important Responding to the challenge of diabetes during the COVID-19 pandemic. As expected, the condition of a large proportion of diabetic patients has increased Snacks\/carbohydrate intake and reduced physical activity during obstruction, leading to weight gain and unstable blood sugar control, which may lead to weight gain Complications associated with diabetes (Ghosh .A et al 2020). In addition, according to one estimate, weight gain during childbirth may increase the risk of diabetes decrease by 7% (Ghosal .S et al 2020).

Impact of covid-19 pandemic on the Psychiatric department

COVID-19 pandemic has affected the administration of psychiatric drugs care around the world. In China, the authors described the challenges this disease emerges in their psychiatric services (Cui et al., 2020). In Italy, the head of one of the largest psychiatric services in Lombardy has described the changes to their system (Percudani et al., 2020).
inside In the United States, we have seen the impact on access to care, quality and how the care itself is provided. Even legal theories and privacy rules exist failed to provide care in a completely different setting. the Mental care provision has changed depending on the context Psychiatrist is at work. To help doctors understand Many changes in care delivery, American Psychiatric Association National guidelines for COVID-19 practice were issued, (APA website, 2020).

Impact of covid-19 on the Intensive Care Unit Department

For the first time At the start of a pandemic, detailed hospital-level data on hospital capacity can be obtained using the following methods. This opens up the following possibilities: As there can be now understanding of how stressful the ICU is and may be, the being reason why some hospitals are more anxious than others (Li. R et al 2020). "I have reason to believe it will be different, some types of hospitals are unable to delay elective surgery, so there is a greater risk of using an intensive care unit." Said Tsai. Other organizations may be mainly vulnerable people, people susceptible to infections and diseases. Henceforth it have shown that some institutions are more likely to experience pressure on ICU capabilities. According to empirical data on these issues. Of which they were of great help. Using the recently released hospital-level ICU capacity data, few policy issues questions were answered including (Goyal. P ey al 2020)

Impact of covid-19 pandemic on the Laboratory department

In America , the majority of the laboratories that responded to the survey which was carried out August 2020 (135 of 167 laboratories; 80.8%) reported: The area where the lab is located Strictly restrictive measures have been implemented. Limit patient access to medical services (World Health Organization 2020). After experiencing severe SARS and MERS, several Asian countries, including Taiwan, Singapore, and South Korea, took timely action. Effective measures and successfully slowed down the spread. And prevent the outbreak (Guarner .J et al 2020). At the same time, those countries still Maintain high-quality patients and healthcare services Medical personnel were not treated inappropriately hence health risks (Tabish .S.A et al 2020). If there is no vaccine or effective treatment against COVID-19, restrictive measures Effectively promote disease control (Rodler .S ey al 2020). Current Research Findings also showed that a similar amount of medical care The institutions have implemented internal restrictions that limit the accessibility of medical services. Between All restrictive measures used, the most common Participants have discontinued electives Procedure and surgery (Hakim .A.A et al 2020).

RESEARCH AIM

The aim of this research is to evaluate the global impact of covid-19 pandemic on referral hospitals.

OBJECTIVES

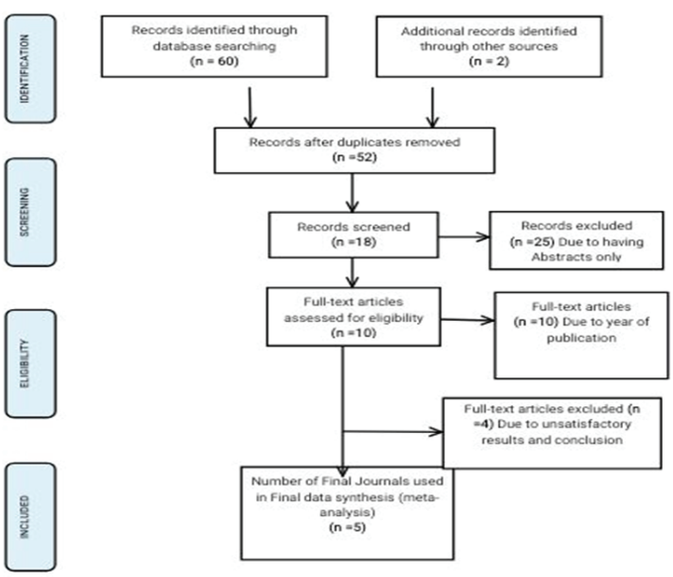
1. To assess how the outbreak of covid 19 pandemic affected the hospital setting at a global view.
2. To explore measures that can be implemented to reduce the covid-19 burden on the referral hospitals.

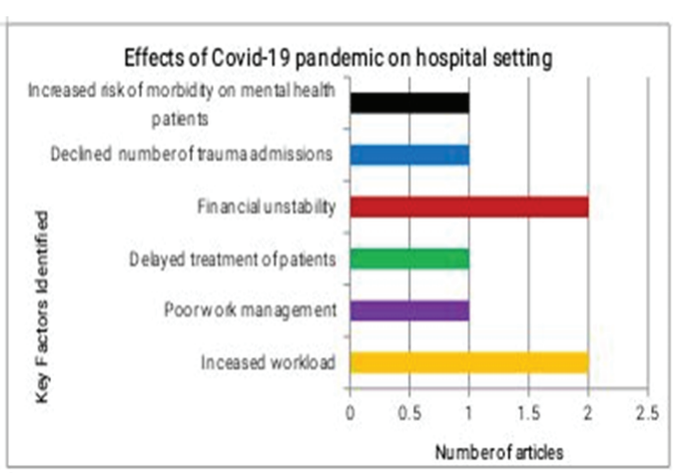
METHODOLOGY

What I present here is a secondary or systematic review approach with no primary collection of data. In order to answer the aims and objectives of the research topic, articles on this topic were reviewed, google scholar and pubmed was searched using the terms "COVID-19" AND "global mpact of covid-19 Pandemic on hospitals". An about forty-two articles resulted from different articles about different departments about global impact of covid-19 pandemic in their hospital setting and all were fully reviewed for relevance. Also, the research study used the PRISMA tool for screening the research resources.

RESULTS

Five authors were selected according to Prisma research tool guidelines in order to identify key factors coming out of the reviewed journals which build this discussion and as summarised in Figure 1.0





DATA ANALYSIS AND INTERPRRTATION

Due to the pandemic some institutions have imposed a pay cut. Of which is disheartening, even though health care providers are also working from home in 24/7 working shifts. In private facilities some health care workers were restrained home following the covid-19 protocols of reducing crowding and social distancing, some clinics also closed due to inability to meet covid-19 protocols yet workers were still payed regardless hence strain in the private health sector (Lai C.C, et al 2020).

There has never been a recession in the radiology field exacerbated by the simultaneous need to restrict the amount of imaging provided. This combination of events will severely stress the financial health of radiology groups throughout the country. Many practices will need to make short-term changes to survive this period, and permanent changes to the radiology practice environment are likely in the long term anecdotal evidence suggests that the duration of public policy–level and practice-level responses will last a minimum of 3–4 months. During this time, radiology practices should expect imaging volumes to decrease anywhere from 50% to 70%. Practices centered around outpatient imaging will be the hardest hit

Increased workload

In a survey carried out by (Bilal Ahmed Sethiey al 2020) heath care workers reported it is much difficult to teach or deliver lectures at workplace so working from home and online. They are engaged 24/7 while fighting against COVID-19. Social and family life is too much affected, emergency duties in the hospital as well as in the field.

Difficulties managing work, home and family

Similar to other reports of healthcare workers' responses to caring for patients with COVID-19 in China (Wu et al 2020 ; Lai et al 2020), psychiatric physicians in the US also experience stress, anxiety, and fear, based on survey results of colleagues across the country. These responses can stem from either events happening in one's own life (e.g., a family member being diagnosed with COVID-19, or fear of losing a lo moved one), one's work environment (new protocols to follow, ever-changing and unclear guidance on personal protective equipment), or the interplay of both (being exposed to a patient with COVID-19 at work, and then having to quarantine and isolate oneself from family for 14 days). In general, the need for psychiatric treatment by psychiatrists is increasing, and they are finding work hours becoming longer, and much needed vacation time being cancelled by their places of employment in some instances.

Delayed treatment of patients

During COVID-19 outbreak, many health care systems are facing challenges due to the high demand on pharmaceutical, equipment, and medical supplies that resulted in critical shortages which can force the clinicians to take tough decisions to restrict using advanced therapeutic options including mechanical ventilators to selected patients based on many factors including age, comorbidities or the expected clinical outcomes. Such difficult scenarios may raise ethical considerations regarding the allocation and use of the current limited resources to treat the most critically ill patients with complications or severe conditions. During this crisis, covid-19 protocols were introduced which included social distancing and avoiding crowding, healthcare providers numbers were reduced in facilities to avoid crowding hence delaying in process of delivering treatment. Delaying of treatment can come with various side effects including Oncologic emergencies (spinal cord compression, Hypercalcemia, etc.), High-grade sarcoma, Low grade lymphomas, large mass, Acute leukemias and aggressive lymphomas.

Increased in psychiatric visits

Providing care for patients in the inpatient psychiatric setting has changed in part to maintain CDC-guided social distancing protocols. In a recent paper, Li describes how one could address certain challenges in inpatient psychiatric units relating to the COVID-19 pandemic (Li 2020). Admittedly, implementing prevention measures in such units can be a challenge, especially when part of treatment traditionally includes close contact, for example frequent safety monitoring, group therapy sessions, and eating meals together. Furthermore, there are logistical factors to consider, such as shared bathrooms and sleeping rooms. Elements to contingency planning include (Li 2020): a) Disease precautions (screening, re-screening, personal protective equipment, use of designated clothing, cleaning of surfaces, and disinfection); b) restriction of visitors and minimization of non-essential contacts (e.g. medical students (Moszkowicz et al, 2020) ; c) physician workforce considerations (creating back-up pools, job reassignment) ; d) operational adjustments (creating isolation rooms in psychiatry inpatient units, tightening criteria for psychiatric admission); and e) group therapy changes (limiting number of participants, utilizing physical distancing).

As reported elsewhere and from experience, it is crucially important to have organized leadership, clear communication, and involvement of all disciplines in decision making (Li 2020) In Massachusetts, an increased need for psychiatric beds is emerging. At various hospitals, psychiatric units have opened to provide acute inpatient care for psychiatric patients presently infected with the novel coronavirus, but not medically ill enough to be hospitalized on an infectious disease unit. Infection Control subsections have been at the forefront with respect to collaboration, design and planning for the COVID-19 units

Increased risk of covid-19 morbidity and mortality on patients with serious mental illnesses

Patients with serious mental illness (SMI) are believed to be at increased risk of COVID-19 morbidity and mortality given their medical risk factors, lack of good hygienic habits, homelessness, and often congregate living situation which can facilitate viral transmission (Bartels et al., 2020). Psychiatrists working with this patient population have seen the need to adjust the way they deliver care. In New York, State-supported community behavioral health organizations, and programs of assertive community treatment (PACT) have developed COVID-19 responses protocols for various settings, including in shelters, mental health group home residences, clinics, and home visits, all including a component of screening questions or screening temperature, isolation pending on the response to the screen, providing the person in question with a mask or utilizing social distancing of 6-feet space, making use of help from a medical director or the state COVID hotline, and further reviewing symptoms and epidemiological risk factors to determine COVID-19 testing and disposition. For home visits, patients can be screened prior to the visit, and if symptomatic, staff can refrain from entering the home.

Declined number of trauma admissions

In a study carried out in the United States there was evidences showing that the pandemic and the related stay-at home order affected so uniquely both the volume of hospitalized trauma patients and the mechanisms of injuries that were not seen even during a natura disaster such as Hurricane Sandy (Curran .T et al 2020). Nevertheless, the reduced trauma volume is in line with a paper from New Zealand as well as a study from England that documented a 25% fall in emergency department visits (Christey G et al 2020). In Italy, fewer trauma hospitalizations were noted; however, these exhibited more severe injuries (Fojut R. 2020).

A concerning finding is that the COVID-19 era group had 2 self-inflicted injuries while the control cohort had none. Although these numbers cannot provide a statistically significant conclusion, this observation is still worth noting. It could be explained by increased psychological stress felt during the lockdown, as public health emergencies can negatively impact the behavioral health of the affected population (Brooks S.K et al 2020).

CONCLUSIONS

The aim of the study was to evaluate the global impact of covid-19 pandemic on referral hospitals. The specific objectives were to assess how the outbreak of covid 19 pandemic affected the hospital setting at a global view and to explore measures that can be implemented to reduce the covid-19 burden on the

referral hospitals. Covid-19 pandemic have caused a shake in the world at large including the hospital setting itself. It is evident from this study that the pandemic have a great impact on the hospitals starting from the patient, to the care giver or health care professional going to different departments of the hospital.

Patients are challenged in the sense that there is delay seeking and receiving care due to the covid-19 pandemic restrictions on the other hand worsening of health conditions hence increased morbidity and mortality rates worldwide. This reported to be due primarily and secondarily to the pandemic as researches show. The health professionals are anxious, overworked and financially unstable. Despite the challenges, they are working, planning, creating and caring for others and their families. Their heroism, dedication and selflessness offers reassurance that we will be able to overcome this virus.

We need to give them all the support they need to do their jobs, be safe and stay alive. Future research should explore the fears and coping strategies of health professionals as frontline soldiers during pandemics. From staining workloads which have both resulted in physical and mental strains. This being due to unusual working conditions during the pandemic. Researches shown there was marked change in working conditions in hospitals hence workers had to adapt to the new normal in a short space of time. From coping with their personal lives to their work life as they are referred to as soldiers during pandemics.

Different departments in the hospital have also experienced challenges during the pandemic. In the Psychiatric department there was a marked increase in the number of psychiatrist visits during the pandemic as indicated by research. Existing psychiatric patients and all others in the community are being faced with isolation, loneliness, sudden bereavement without being able to bury the dead, losing their livelihood, and fear of ultimately and suddenly losing their lives. All psychiatric care settings are impacted by this pandemic, and its services for people who suffer the mental consequences of having lived through this experience will be needed for years to come. While it is uncertain what this pandemic will fully mean for psychiatric care long-term going forward, we share our research and experience to facilitate dialogue, increase knowledge among psychiatric clinicians, and to inform healthcare policy makers and health care systems about the challenges and continued needs of financial and administrative support for psychiatric clinicians and mental health systems across the globe.

The radiology department have experienced a great financial instability as especially in the private sector where workers were still issued salaries even when some workers were home due to the covid-19 pandemic. In the department of trauma and acute care surgery there was evident decline in number of trauma admissions. The stay-at home order by government as a way of stopping the spreading of the covid-19 virus have uniquely impacted the trauma and acute surgery department as there is a decrease number of patients admitted in the hospitals on this area.

Global education communities about the covid-19 pandemic as well as restriction protocols to preventive measures remain the greatest weapon in battling with the virus. Introduction of online service so that patients may be consulted at the comfort of their home an avoid crowding will also help cope with the situation of delayed receiving treatment of patients.

Providing free special counselling to essential workers including the healthcare workers though they also offer counselling to others, as a way of dealing with their emotional strains. A healthy diet should also be encouraged especially in inpatients in the hospitals.

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ASSESSMENT OF THE IMPACT OF COVID-19 DISEASE ON ADULTS WITH PRE EXISTING PSYCHATRIC CONDITIONS.

Author : Shatho Jackson

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Corresponding Author *Dr Derrick D.Tlhoiwe, Dr Tumelo Tlhoiwe, Larry.L. Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract |

An ongoing bio threat, the covid-19 disease has devastatingly shook the entire globe, causing consequential effect on the physical wellbeing and the economy. Additionally to the fatal cardiopulmonary effects, it has dire effects on the mental wellbeing of all individuals due to distress of constantly losing a loved one and anxiety of probably being the next. Changes brought upon people as a response to mitigate the fastest spreading virus have in turn increased the prevalence of psychiatric symptoms of the general population, dramatically affecting a special subpopulation group that is often overlooked and given less priority as compared to other co-morbidities of; adults with pre-existing psychiatric conditions. This study is aimed at assessing the impact of covid-19 disease on adults with pre-existing psychiatric conditions and involves review of secondary data where articles and journals were systematically reviewed with the use of a PRISMA tool approach for inclusion and exclusion criteria to decompose the impact of the disease in relation to; the effect on mental health, risk

of infectivity and mortality and lastly socioeconomic wellbeing. As perceived, adults with pre-existing psychiatric conditions relapsed during the pandemic, various researches reported increased prevalence of exacerbation of psychiatric symptoms in this population and resorted to coping mechanisms that further compromised their mental health. It was also noted that adults with pre-existing psychiatric conditions were more prone to contacting the SARS-Cov-2 virus as compared to the general population and are at an increased mortal risk. This is a cause of concern because there is reduced availability of care at a time they need it the most. Lastly this socioeconomically disadvantaged group's livelihood is tremendously affected due to economic strain of countries globally.

Keywords: Covid-19, mental health, pre- existing, psychiatric conditions, risk, mortality, impact, prevalence and healthcare.

Background

The latest threat to global health is an ongoing respiratory disease pandemic known as Corona virus disease 2019 (Covid-19, previously known as 2019- nCoV), epicentred in Hubei Province of the republic of China (Velavan, M.C., et al 2020). This was caused by the novel corona virus SARS-CoV-2 which is structurally similar to a virus that causes Severe Acute Respiratory Syndrome (SARS) and was declared a global emergency on 30 January 2020 by WHO emergency committee based on the daily rise in cases reported in China and internationally (Fauci, L.H., et al 2020).

Coronaviruses are enveloped, positive- single stranded RNA viruses that infect not only humans but a wide range of animals. First cultivated from patients with common cold in 1966 and were termed corona virus based on their morphology that resembles a solar corona (a Latin name that means crown) (Velavan, M.C., et al 2020). Coronaviruses have four subfamilies; alpha, beta, gamma and delta where alpha and beta originate from bats and the latter from pigs and birds. Among all these SARS-CoV-2 belongs to the B lineage of Beta corona viruses and may cause severe disease and complications compared to the alpha coronaviruses (Fauci, L.H., et al 2020).

The SARS-Cov-2 virus was transmitted to humans at the Huanan seafood market in Wuhan China (Wang, X.R., et al 2020) where till date its route of transmission still needs to be clarified. Recent studies indicate that on the first 425 cases reported in Huabei province of China; the

median age of infected patients was 59 years with higher mortality among the elderly and those with comorbidities, 56% were male and there were no cases of children less than 15 years (Faunci, L.H., et al 2020) meaning there are less likely to be infected or they show milder symptoms of infection (Velavan, M.C., et al 2020).

SARS-CoV-2 infects lung alveolar epithelial cells using receptor mediated endocytosis via Angiotensin Converting Enzymes II as an entry receptor. Observations so far suggest an incubation period of five days, with high titres in the oropharynx, where symptoms of upper respiratory infections including cough, fever, fatigue and nasal congestion manifest after less than a week progressing to severity with dyspnoea and pneumonia like symptoms in approximately 75% of patients (Na, T.J., et al 2021). Countries around the world placed different temporary measures to slow the spread of the virus such as restrictions of travel, social distancing, isolating ill patients, lockdown and curfews (Faunci, L.H., et al 2020).

Impact of covid-19 on adults with pre- existing psychiatric conditions.

The Coronavirus disease 2019 has negatively affected the mental health of the general population, changing people's lives dramatically with imposed strict measures put in place to minimise the spread of the

virus leading to an increased prevalence of psychiatric symptoms (Na,T.J., et al 2021). Studies have shown that people with pre-existing mental disorders are a special subpopulation particularly at high risk of contacting the covid-19 disease and have worse infection outcomes (Wang, X.R., et al 2021).This population is prone to relapsing during the pandemic, exacerbating their underlying psychiatric symptoms. Lockdown has disrupted the normal daily routine and rhythm of anxiety and depression patients leading in exacerbations of low mood, decreased energy and anhedonia (Chatterjee, M.C., et al 2020). Disruptions on prescripted medication availability and difficulty in compliance for Schizophrenia and Bipolar disorder patients may lead to difficulties of coping due to paranoia and nihilistic delusions while those with obsessive compulsive disorders (OCD) may experience increased frequency and intensity of obsessive thoughts such as washing compulsions and contamination obsession due to advise on the need to improve personal hygiene as advised by medical personnel (Torales, O.M., et al 2020). Lastly it could be a fatal period for those with substance use disorders due to no availability of substance and medications leading to serious medical consequences such as delirium and seizures (Tsamakis, T.D., et al 2021).

The pandemic has furthermore impacted the lives of adults with pre-existing psychiatric disorders by putting them at risk to contacting the infection as it poses challenges in grasping and understanding health information and complying with preventative measures like social distancing and frequent hand wash (Torales, O.M., et al 2020). Additionally limitations in access to healthcare makes them reluctant in seeking medical attention and has disrupted services such as psychotherapy, counselling, psychosocial interventions and management programmes including immature discharge from psychiatric wards to prevent overcrowding (Tsamakis, T.D., et al 2021).

Mental health conditions have been overlooked and deemed unimportant as compared to the chronic co-morbid diseases, however the afore mentioned difficulties clearly point out that this population is severely acutely affected than the rest (Na, T.J., et al 2021). To date research on the effects of covid-19 pandemic on mental health are limited and are only focused on the general population even if it challenges the patients, policy maker and health organizations (Chatterjee, M.C., et al 2020).

RESEARCH AIM

To find out the effect of covid-19 on mental health of adults with psychotic, mood and alcohol and substance use disorders.

OBJECTIVES

1. To understand if having a psychiatry condition poses a risk factor to contacting the SARS-Cov-2 virus.

2. To explore the role of pre-existing psychiatry condition in spreading the covid-19 virus.

METHODOLOGY

In order to answer the aims and objectives of the research topic, secondary data was systematically reviewed. The databases used for attaining the information included PubMed, Google scholar. The utilization of the multiple databases presented the opportunity to gain accurate and reliable information that signified the primary aspects of the study. Also, the research study used the PRISMA tool for screening the research resources.

RESULTS

Identified studies were uploaded into endnote (Thomas Reuters) and duplicates were removed. I vetted through the study based on the topic and abstracts that met the inclusion criteria. Studies selected after the first screening were further screened through a detailed full text browsing, to further exclude studies that had some of the exclusion criteria. Out of 50 studies identified, 20 were excluded due being limited to abstracts. Out of the 30 selected, 10 were further excluded due to year of publication while the 15 were removed due to unsatisfactory results and conclusion. Only 5 were finally used.

Fig 1.0 Prisma flow chart

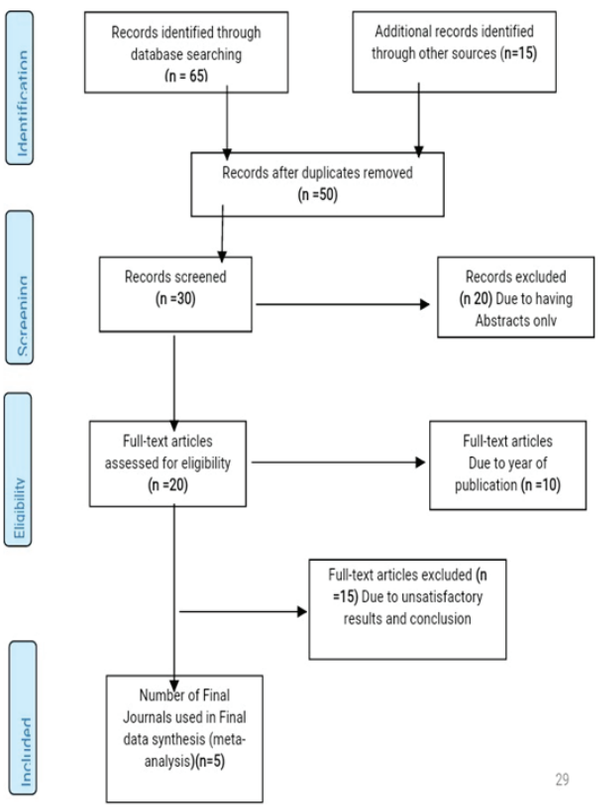
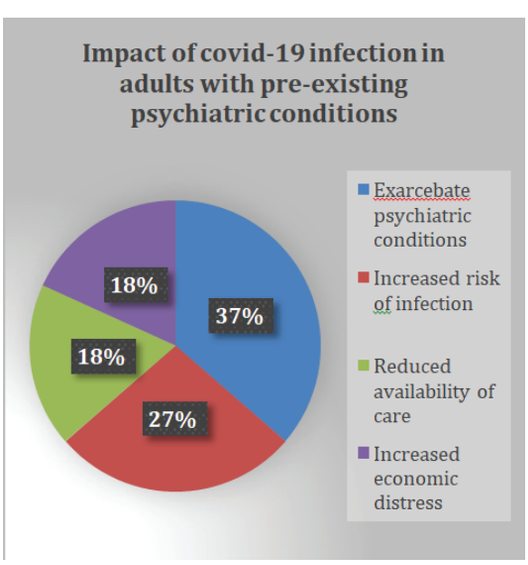


Fig 1.2 | KEY RESULTS AND DISCUSSION



DATA ANALYSIS AND INTERPRETATION

Exacerbate psychiatric symptoms

It is well accepted that covid-19 pandemic has a detrimental effect on mental wellbeing of the general population by either causing new onset of disease in previously fit individuals or exacerbating symptoms causing relapses in people with underlying psychiatric conditions such as anxiety, depression, panic, delirium, psychosis and suicide. Psychiatric individuals are highly sensitive to distress which makes it harder for them to cope with the uncertainties, forced isolations and economic challenges linked to the to the covid-19 pandemic increasing their risk of relapse and disease exacerbation. Measures placed aimed at combating the spread of the disease such as quarantines and lockdowns has jeopardized normal daily routines and taken away support systems from patients suffering from recurrent depressive disorder, worsening their depressive symptoms. The anxiety associated with all this can be so overwhelming, precipitating paranoia and nihilistic delusions moreover patients with known obsessive compulsive disorder may frequently check their temperature, swallow a lot of saliva to check if they have sore throat and wash their hands aggravating symptoms of patients with known washer's OCD. Additionally

medication proposed to treat covid-19 such as antivirals, steroids and interferon have be reported to cause or worsen psychiatric symptoms.

Increased risk of covid-19 infection and mortality

In comparison with the general population, individuals with psychiatric disorders are at risk of infection and its adverse outcome such as mortality. There are emerging studies suggesting a strong genetic link between at least one psychiatric diagnosis and increased risk of infection. Factors such as cognitive impairment, lack of risk awareness, reduction in personal protective measures (hand washing social distancing and isolation) and restrictions in populated psychiatric wards where infections can disseminate rapidly increases their risk of infection. Inattention in Attention Deficit Hyperactivity Disorder (ADHD) poses risk of forgetting use of face masks or maintain social distancing whereas lack of motivation in Depression patients may lead to neglect protecting themselves or seeking medical attention where indicated.

Additionally, delusions in Schizophrenia patient's poses risk of rejecting face masks. Co-existence of psychiatric disorders and covid-19 makes the treatment more challenging and maybe less effective. Patients with severe psychiatric disorders are more likely to suffer from co-existing diseases such as cancer, cardiovascular disease, obesity and type 2 diabetes mellitus, which all contribute to higher SARS-Cov-2 risk in patients with psychosis. This period could be lethal for patients with substance abuse disorders as no-availability of substances or medicine can precipitate withdrawal symptoms and medical emergencies like delirium or seizures, which can be life threatening due to inadequate accessibility to emergency services.

Schizophrenia, depression and bipolar patients are prone to drug use particularly tobacco and tend to smoke more heavily than people without mental disorders which accelerates risk of pulmonary pathology, making them more vulnerable to the covid-19 disease. A study by Nemani., et al (2021) stated that adults with schizophrenia spectrum disorder diagnosis were associated with increased risk mortality.

Reduced availability of care

In response to the pandemic, countries globally incorporated lockdowns and quarantines as their response plans. This meant closure of schools, workplaces and most importantly significant reductions in availability of care .This include disruptions of MNS service such as school and work related mental health programmes, psychotherapy, counselling, psychosocial interventions, home or community outreach programmes, critical harm reduction services, mental health

intervention during antenatal and postnatal period, suicide and overdose prevention as well as management of emergency MNS manifestations. Individuals with pre- existing psychiatric disorders may face more barriers accessing medical services after being infected with covid-19 or are reluctant to seek help due to fear of discrimination and stigma associated with psychoses and may face more barriers using telemedicine.

Worsen economic distress

Stay at home orders and closure of workplaces has resulted in limited employment opportunities globally. Patients with serious psychiatric disorders such as Schizophrenia who are commonly socioeconomically disadvantaged are further compromised hence worsening their economic distress. Inability to work, dwindling finances and long term impact of covid-19 pandemic in the economy might force them to work and live in unsafe environments further increasing their risk of infection and exacerbation of psychiatric symptoms since homelessness may affect their ability to quarantine.

CONCLUSION

The purpose of this study was to assess the impact of covid-19 infection on adults with pre-existing psychiatric conditions, with specific objectives to; find out the effect of covid-19 on mental health of psychotic, mood and alcohol and substance abuse disorders, to understand if having a psychiatric condition poses a risk to contracting the covid-19 disease as well as to explore if having a psychiatric condition contributes to spreading the covid-19 disease.

Covid-19 pandemic is still an ongoing bio threat that affects all worldwide regardless of colour, ethnicity or wealth. It has drastically spread from China to the rest of the world and has dramatically changed our lives. Its unforeseen magnitude of spread has in addition to relatively high mortality rates, economic strain and cardio-pulmonary consequences had a tremendous effect on mental health of the general population but most importantly on the psychological wellbeing of vulnerable groups such as the mentally ill.

Mental health is defined as a state of wellbeing in which the individual realises his or her abilities, can cope with normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her family. This state was disrupted by the outbreak and a series of events that followed in response to the pandemic. Measures put in place to mitigate the spread of the disease for instance lockdowns, closure of borders, curfews and quarantine of returning travellers and those infected has helped to minimize the spread but in turn led to an increase of the prevalence of new onset diagnosis of psychiatric conditions, exacerbation of psychiatric symptoms as

well as relapsing in most individuals worldwide.

Stress, fear, anger, depression and anxiety brought upon these individuals by the pandemic has led to difficulties coping as they were separated from their support structures (families, friends, psychologists, support groups) and resorted to unhealthy habits of binge eating and tobacco smoking further compromising their mental health and economic distress. These consequences were mostly a result of diminished access to health care services which led to increased risk of infection and mortality among these individuals, more especially those diagnosed of Schizophrenia spectrum disorders. This research further addressed that indeed having psychiatric condition poses a risk to infection due to lack of apprehension of information, lack of risk awareness and reduced personal protective preventative measures such as hand washing , wearing of masks and social distancing which in turn somewhat also has an effect on spreading of the covid-19 disease.

LIMITATIONS

There was insufficient time to carry out the research hence resorting to a systemic review which is subjective and less information on the impact of covid-19 infection on patients with pre-existing psychiatric disorders is available worldwide. Which could suggest this information to be biased towards a few articles used for this research

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CONFLICT OF INTEREST

No conflict of interest declared.

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EMOTIONAL, BEHAVIORALAND PSYCHOLOGICAL IMPACT OF COVID19 PANDEMIC: A SYSTEMATIC REVIEW

Author : : Sebetso Thabo

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Corresponding Author *Dr Derrick D.Tlhoiwe, Dr Tumelo Tlhoiwe, Larry.L. Mweetwa*
Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



ABSTRACT

Towards the end of 2019, a sudden acute atypical respiratory disease was identified in the Wuhan province of China, with most initial cases identified to have been exposed at the Huanan seafood market at which the sale of dead seafood and live animals occurred (Lary M. et., al 2020). The lockdown restricted citizens' physical mobility, advocated social distancing norms, and

limited a majority of public services while allowing the essential ones(Sharma, A.J. & Subramanyam, M.A., 2020), therefore peoples' normal way of living and interactions has drastically been affected. Despite high morbidity and mortality rate, the novel pandemic has also impacted people's emotions, behavior and psychology, which subsequently may lead to high burden of mental illnesses if not attended (Holmes et al., 2020 & Wood,L. J. et al., 2020), and interestingly; this impact has equally been noted across all population groups.

Keywords:
lockdown,restrictions,pandemic,emotions,Behavior ,psychology, mental illness, population,morbidity, Mortality

BACKGROUND

Since the outbreak of the novel corona virus pandemic, schools has been closed, children has been forced to stay home, subsequently behavioral problems associated with failure to follow lockdown protocols (Liu, Q. et al., 2021), has been noted among school going adolescents. Among the adult population, COVID-19 outbreak severely restricted people's movement, outdoor physical activities and exercises has been limited ((Jiménez-Pavón et al., 2020; Lyons et al., 2020), thus leading to a gross decline in mental health, behavior and their psychological wellbeing. Among other group studied; health care workers, the outbreak required the significantly increased working time and intensity for health professionals, which may cause stress signs (Dong, Z.Q et al., 2020). It is vital to know that when coping with a large- scale emergency like this, people often report a wide range of psychological needs, including out-of-control emotional reactions, (Lima, C. K. T. et al., 2020), and therefore healthcare workers' mental health has to be safeguard as well.

It is therefore vital to note that developing a detailed data on epidemiology,public health interventions and their outcomes are needed to develop a country-specific conceptual framework amongst each specific population group ((Kumar, A., Nayar, K.R. & Bhat, L.D., 2020).

Emotional, Behavioral and Psychological Impact of Covid 19 on Adults

Covid 19 has posed a threat to public health, due to prolonged activity restrictions, financial pressure, and other attendant adverse impacts; COVID-19 has triggered kinds of psychological problems (Brooks et al., 2020 & Wang et al., 2020). These disruptions could contribute towards adverse psychological outcomes such as post-traumatic stress symptoms (Hawry luck L. et al., 2004) and aggressive behaviors (Marjanovic Z, Greenglass E. R. & Coffey S 2007), in the elderly. Adults also face uncertainty, insecurity, instability for the present and future, reduced autonomy and self- directedness (Torales, J. et al., 2020). To help curb this devastating experiences; important to better promote the wish of having common goals with others, interdependence, and sociability (Germani, A. et al., 2020).

Emotional, Behavioral and Psychological Impact of Covid 19 on Health Care Workers

The current worldwide outbreaks of COVID-19 have demonstrated a dramatic gap in the current scientific literature regarding the mental health needs of health care workers to be addressed by occupational teams (Holmes, E.A. et al., 2020), therefore implementation of all the necessary measures to protect their occupational safety should be necessitated (Rajkumar, R.P. 2020). The COVID-19 outbreak has brought feelings of loss of control, uncertainty, and vulnerability, high levels of psychological issues, including anxiety and depressive emotion, sometimes severe among healthcare workers across the globe (Yang Y. et al., 2020 & Lai J et al., 2019). It is therefore a need to improve hospital staff psych educational strategies (seminars, videos and similar tools) in order to encourage health care workers to empower their emotional and cognitive skills (Duan, L, Zhu, G 2020).

RESEARCH AIM

To conduct systematic review on the emotional, behavioural and psychological impact of Covid 19 pandemic globally.

OBJECTIVES

1. To evaluate the prevalence of behavioural, emotional and psychological effect of Covid 19 pandemic in the general populations globally.
2. To conduct how the long term effects of Covid pandemic impact on behaviour, emotions and psychology.

METHODOLOGY

In order to answer the aims and objectives of the research topic, secondary data was systematically reviewed. The databases used for attaining the information included PubMed, Google scholar. The utilization of the multiple databases presented the opportunity to gain accurate and reliable information that signified the primary aspects of the study. Also, the research study used the PRISMA tool for screening the research resources.

RESULTS

Identified studies were uploaded into endnote (Thomas Reuters) and duplicates were removed. 5 reviewers vetted through the study based on the topic and abstracts that met the inclusion criteria. Studies selected after the first screening were further screened through a detailed full text browsing, to further exclude studies that had some of the exclusion criteria. Out of 20 studies identified, were excluded due to having abstracts only. Out of 9 selected, 11 were further excluded due to year of publication. Only 5 were finally used.

Fig. 1.0 Prisma flow chart

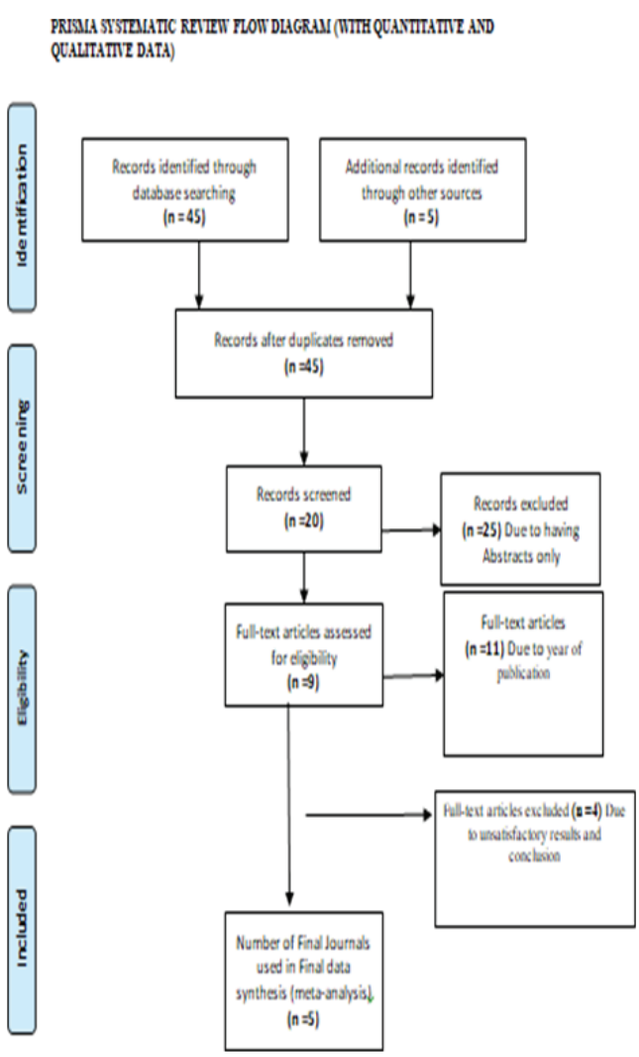
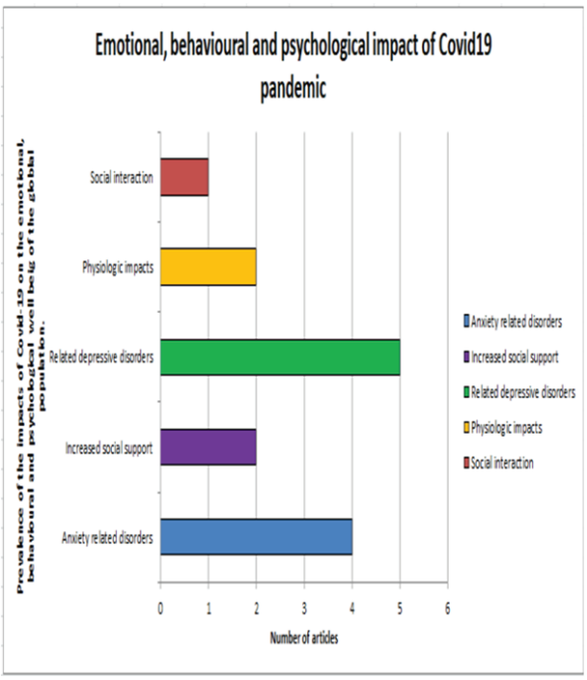


Figure 1.2 Key Results



DISCUSION

Data Analysis Social Interaction

Children were noted to experience high rates of reduced interaction, and according to European Pediatric Association–Union of National European Pediatric Societies and Associations (EPA-UNEPSA), it is vital for medical centers and academic institutions to form a collaborative working groups with the aim to exchange information and scientific evidence and strengthen efforts to raise psychological awareness on children's needs during the Covid19 pandemic. This is because children are forced to stay home for long periods due to enforced isolation and school closure, resulting in limited connection with classmates and reduced physical activity, thus impairing their social space (Jiao W.Y et al 2020).

Physiologic Impact

Companionship is essential for children's normal psychological development and wellbeing (Liu JJ. et al., 2020); separation from caregivers pushes children into a state of crisis and might increase the risk of psychiatric disorders (Norredam M. et al 2018). The parent–child separation initiated in the first few years after birth might also disrupt the ongoing attachment processes, which might be associated with poorer mental health outcomes (Humphreys KL. 2019). Children have mild clinical manifestations without fever or symptoms of pneumonia, compared to adults' population (Cai J. et al., 2020).

Related Depressive Disorders

In battling the sudden emergence of severe acute respiratory syndrome (SARS), psychological distress among medical staff and the general public across the globe; depression, psychophysiological symptoms and post-traumatic stress symptoms appeared later and lasted for a long time, leading to profound impact (Chong et al., 2004), with previous pandemics. Increase in financial and family stress in a disaster could be associated with some avoidance behaviors, which would have worsened their mental health and lead to a more passive lifestyle and increased re-occurrence of depressive episodes (Lau J.T. et al., 2005).

Anxiety Related Disorders

Separation from caregivers pushes children into a state of crisis and might increase the risk of developing related anxiety disorders especially in children who their parents tend to leave them during mandatory quarantines and isolations (Liu JJ. et al., 2020). Similar to other population groups, children are not indifferent to the dramatic impact of the COVID-19 epidemic as they also experience fears, uncertainties, and physical and social isolation and may miss school for a prolonged period (Jiao WY. et al., 2020). Medical staffs were also noted to have sub threshold mental health disturbance and increased prevalence of anxiety related disorders (Zhang, Y. & Ma, and Z.F. 2020).

Increased Social Support

COVID-19 pandemic was associated with increased / shared emotional support among relatives and friends of the people (Zhang, Y. & Ma, Z.F. 2020), and increased shared feelings. Furthermore healthcare workers when they see their colleagues rush to the center of the epidemic, infected employees feel guilty for not working, as their professional responsibility and energy drive them to do and help those in need (Pan X. et al., 2020).

CONCLUSION

As the world is battling with the pandemic, it is important to also aggressively come with majors that will also overcome the impact of Covid 19 on psychological and mental related illnesses during the pandemic, and post the pandemic among health care workers and all different age groups, to prevent high surge of mental related illnesses cases worldwide. This is because the impact of Covid 19 is not only attributed to morbidity and mortality, but also to the increase emotional instability, behavioral change and psychological impairment, which all predispose to mental related illnesses.

Botswana will have to join hands with other member states to ensure that the fight against the pandemic also in cooperate mental health wellbeing of its people, and establish mental health support services in order for people to cope with this devastating and trying times.

RECCOMENDATIONS

This study recommends that Botswana should join hands with other countries and come up with strategic policy making aimed at improving mental health services to the general population including health care workers during the this times of the pandemic, this will curb the prevalence or increased incidences of mental health and psychological related illnesses locally and across the globe. I also recommend the health authorities and the government of Botswana to prioritize is and support health care workers emotional being through scheduled sessions with professional councilors/psychologists in order to cope with the devastating impact of Covid 19. It is also of great benefit for health authorities/providers to tighten public health education policies on how to help those in need of mental support during this pandemic.

LIMITATIONS OF THE STUDY

The author worked under very limited resources including financial shortages and time constraints, this denied the opportunity to access many data sites/resources. Lack of enough information or data reviews in my setting (Botswana) related to the topic of study may impair current situation figures/ crises in the country with regard to the topic of study. Also the secondary study did not help the author to fully explore the current situation in Botswana.

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enquiries@ddtcollegeofmedicine.com

A Systematic Review of the Role of Physiotherapy Interventions in Palliative Care

Author: Dr Derrick D.Tlhoiwe,Dr Phokontsi, L.; Mweetwa, L.L.; Mweetwa, L.; Tlhoiwe, T.; Muya, C.K.; Mudawarima, T.; Silumesii, L.; Chisenge

1. Department for Medical Laboratory Science, DDT College of Medicine.

2. Department of Medicine, DDT College of Medicine.

Email: *journals@ddtcollegeofmedicine.com*

DDT College of Medicine,
P.O. Box 70587, Gaborone Botswana
Tel: +267(0)3904924/5
Cell: +267(0) 7710000
Fax: +267(0)3904935



Abstract

The aim of this research is to conduct a systematic review analysing the role of the physiotherapy interventions in palliative care. PRISMA as a critical appraisal tool was utilised for the selection of the research articles. The inclusion criteria were based on the year of publication, ease of availability, language, geographical location, and study type. To ensure the credibility, databases such as Elsevier, Proquest, and EBSCO Host were used to filter the grey content. Data published in the past ten years (2009-onwards) was only included to ensure the selection of the most recent interventions used by the physiotherapists. A total of 11 articles were selected which determined that physiotherapy interventions involving breathing exercises, aerobic exercises, manual therapies, and educational awareness were critical to promoting the functional capability and empower the patients.

Keywords: Physiotherapist, Palliative Care, Physical Therapy, End-of-Life Care, Non-pharmacological Intervention

Background

World Health Organisation (WHO) defined palliative care as the approach which enhances the quality of life of the patients who are encountered with life-threatening diseases through the management and relief from the suffering through early intervention, impeccable evaluation, and treatment of pain and other associated issues [1]. Patients in palliative care experience a greater level of functional incapability and disability as a result of disease progression, direct local and systematic impacts, and deconditioning pain. Impairment in physical functioning is a predominant contributor to a significant decline in the quality of life of such patients. Palliative care patients expressed a high desire to stay physically active during the course of the disease while sustaining and retaining physical independence [2]. Thus, the notion of rehabilitation in palliative care Spatients is to promote adequate treatment provided with the objective to eradicate disability through optimising the functional status, independence, autonomy, and standard of living.

The World Confederation for the Physical Therapy has defined physical therapy or physiotherapy as the provision of services to the people for the development, maintaining, and restoring the maximum mobility as well as functional capability throughout the entire life-span [3]. Physiotherapy, in particular, encompasses the services in situations where the function and the movement are threatened by the ageing process or due to any injury/disease [4]. Physiotherapists form an integral component of the multidisciplinary team (MDT) in the palliative care by focusing on the processes and procedures for enhancing the function and quality of life through multivariate care dimensions [5]. Of these care dimensions, the physical dimension in the palliative care treatment and management is linked to symptom control, improving the flexibility, mobility, endurance, deformity, gait, balance, co-ordination, deformity, energy expenditure, and exercise tolerance along with maintaining adequate breathing. The functional dimensions, on the other hand, are related to improving the daily activities and functions that include the sensorimotor performance [6]. Physiotherapists aim to improve the successful performance of the complicated physical functional activities such as housekeeping and maintaining personal hygiene which requires the involvement of the affective and cognitive abilities.

The integration of physiotherapists into the palliative care plan is a relatively new concept despite the fact that the physiotherapy interventions in palliative management were identified during the early 1960s [1]. The primary objective of including a rehabilitation approach while treating the palliative care patients is through goal setting to enhance the functional ability while subsequently reducing the disease consequences as long as possible [7]. The ultimate goal of the physiotherapist is to promote independence as much as possible to ensure the accomplishment of important activities to ease the end-stage life of the people. However, in cases where improving the functional ability is not possible, physiotherapy intervention is to promote the patient as well as the ability of the carer to cope with the deteriorating condition of the patient through awareness and education to improve the quality of life [8]. Therefore, the overall aim of the physiotherapist is to facilitate the patient to reach the best possible quality of living for the remaining patient's life.

Methodology

Research Design

The research design for this study has been based on the systematic review of the literature to determine the interventions of physiotherapists in palliative care. Through a systematic review, the selection of the appropriate data sources enabled the researcher in collecting pertinent, credible, and reliable information through the use of databases for the selection of peer-reviewed journal articles [9]. Provided the nature and phenomenon of the research topic, systematic qualitative review of literature is optimal as it enables in determining the interventions of physiotherapists from previous authenticated researches without the involvement of any statistical testing as no variables are involved in this research.

Search Strategy

The search strategy for the attainment of the most desirable information comprised on the use of the keywords "Physiotherapy", "Physiotherapist" "Physiotherapy interventions", and "Palliative care" alone as well as in combination with the utilisation of the Boolean Operators "AND" and "OR". The Boolean Operators were incorporated into the search strategy of the most reliable, authenticated, and prominent databases in the field of health sciences which included Elsevier, ProQuest and EBSCO Host. Here, it is important to signify that the entire research was constituted using the widely used and openly accessed databases to ensure the reproducibility and credibility of the literature.

Data Extraction

The criterion for the extraction of data was based on the inclusion versus the exclusion criteria. The inclusion criteria facilitate in setting the boundaries and restrictions for collecting the most viable, authenticated, and reliable information [10]. Different approaches for the inclusion criteria which had been specified for this research included the language, publication year, study type, geographical aspects, design of the research, and the interest exposure. In the regard, through the use of the inclusion criteria, the researches which had been published in the English language only were opted while literature in a language other than English was excluded. In a similar manner, the research studies which had been published in the last ten years were selected for this study to ensure the inclusion of the most updated and relevant context. Thus, literature published before 2009 was excluded from the selection.

Selection of the Study

The selection of the study in the systematic approach is regarded as the critical appraisal which ensures the value and trustworthiness of the study. Critical appraisal is commonly regarded as the implications of the values and rules that predominantly assist in the evaluation of the resulting viability, method, and procedures while adhering to the ethics. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) are used for the assessment of the critical appraisal tool for determining the validity and reliability of the data collection [11]. PRISMA promotes in easy filtration of the research articles to comply with the standards of the quality. Thestep-by-step assessment of the PRISMA to determine the physiotherapy intervention in palliative care is illustrated in the following figure below [5]

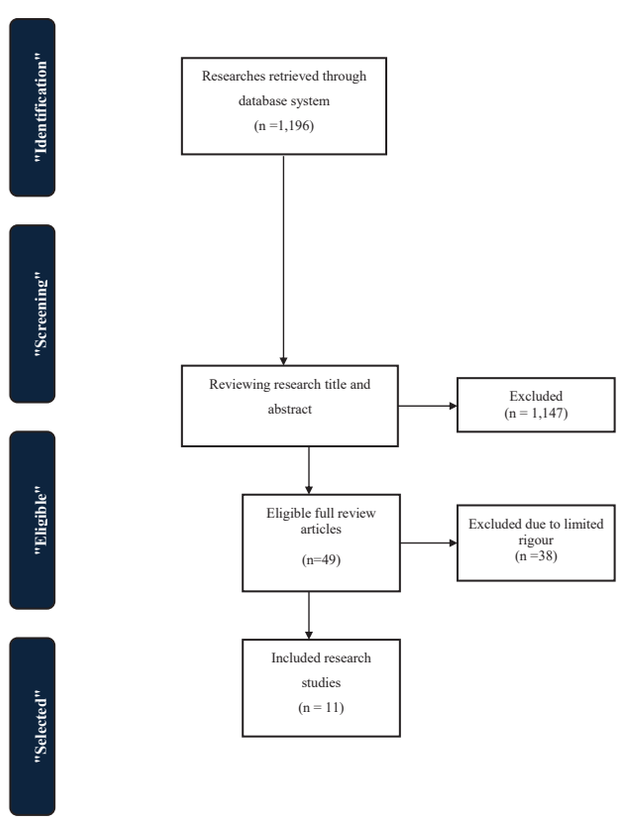
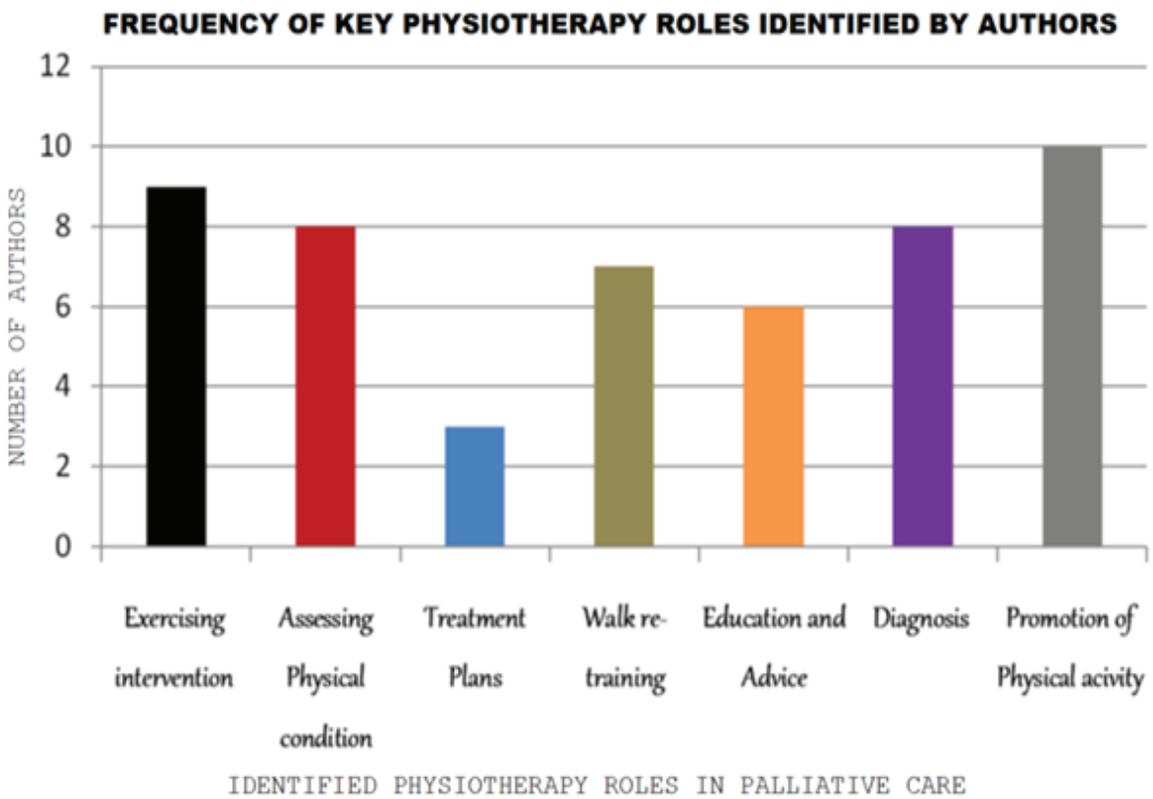


Fig 1I PRISMA Flow Diagram

Author	Year	Country	Methodology	Key Findings
Hegarty et al.	2016	Ireland	Cross-sectional Study	The key findings indicated that physiotherapy induced palliative exercising interventions in patients suffering from Parkinson's disease improved the strength of the lower limbs. The physiotherapist intervention specifically deduced that palliative exercising could serve as a potential modification for the accomplishment of clinically relevant results in the walking ability of the patients.
Lim and Ng	2015	Singapore	Mixed methodology	It was determined that improving the knowledge and skills of the physiotherapists through perception and knowledge in the palliative care domain could predominantly assist in analysing the challenges in acute hospital settings. Good palliative care is dependent on effective communication, education and advice, so physiotherapist intervention is based on developing communication skills to improve technical competencies.
Möller et al.	2016	Sweden	Pilot Study	Physiotherapist interventions in palliative care settings were determined through multiple therapeutic mechanisms focused on patient-centric needs, good diagnosis, promotion of physical activity, treatment plans. The pilot study determined that a better-nuanced investigation of the clinical complications could facilitate in the optimisation, clarification, and development of physiotherapy interventions.
Jensen et al.	2014	Germany	Retrospective, Descriptive Study	The key analysis indicated that physical exercise in advanced cancer patients had a beneficial impact on the mobility and functional ability with respect to the disease-related and socio-demographic aspects. Physiotherapeutic intervention including the relaxation and the breathing therapies improved the quality of living of terminally ill patients.
Przedborska et al.	2015	Poland	Quantitative Method	The findings indicated that though physiotherapy interventions did not exhibit a statistically significant relationship in enhancing the self-care and mobility of the

				patients in palliative care, however, prominent results were recorded in the management of the depression, anxiety, and intensity of dyspnea after the physiotherapy program. Walk retraining, education and advice on health as well promotion of physical activity.
Morrow et al.	2017	South Africa	Cross-sectional Descriptive Survey	Despite inadequate training, knowledge, and required skillsets, a large number of physiotherapists were able to manage the critical requirements of the patients during palliative care and thus proper inclusion of the palliative care knowledge in the graduate program could yield better and positive outcomes for optimising the individual functional capability.
Saher et al.	2018	India	Randomised Clinical Trial Retrospective Study	The final outcomes indicated that physiotherapists led interventions improved the functional capability while offering relief from the symptoms to the patients in palliative care. This signified the notion that physiotherapists in caring of patients could enhance the independence and quality of living during end-stage of life.
Cullum	2019	United Kingdom	Qualitative Semi-structured Interviews	Within the inpatient settings, rehabilitative palliative care has become a challenge for the inpatient hospice unit and physiotherapist could play an integral role in eradicating the barriers through effective communication and rehabilitative palliative care practices while improving the confidence and autonomy of the patients.
Wilson and Briggs	2017	United States of America	Review Article	Lack of the consistent integration of the physiotherapist within the hospital settings is constituted as a barrier in the provision of non-opioid alternatives for the management during the palliative care. Physical therapy supports pain management by improving the quality of life and reducing the dependency on opioid medication.
Pullen et al.	**2014**	**Nigeria**	**Case Study Analysis**	**The key analysis interpreted a complete eradication of the shortness of breath (SOB) upon exertion and relief from pain due to the physiotherapy sessions. In addition, a prominent reduction was also observed in muscle endurance, strength, and resting heart rate. Hence, the physiotherapy interventions comprising of**

				manual therapy and exercise were beneficial as an adjunct therapy.
Pyszora et al.	2017	Poland	Randomised Clinical Trial	Exercising program design led to a prominent decrease in the fatigue scores within the palliative care which positively influenced the day-to-day functioning. These findings led to the belief that physiotherapy is regarded as an effective and safe method in cancer-related fatigue to improve the quality of living.



Discussion

The data analysis has offered a comprehensive evaluation highlighting the contemporary role of the physiotherapist interventions in the treatment and management of palliative care, among key roles frequently identified was promotion of physical activity, exercise intervention, diagnosis and assessing physical condition, walk-retraining, education and advice and developing treatment plans in line with client need as well as involvement. Palliative care is regarded as a holistic practice which involves caring of the people living with life-threatening illnesses or individuals during the end stage of the lives. Though pharmacological interventions are the primary source to manage and treat the palliative care measures, exercise and the physical activity acts as a secondary mechanism to improve the quality of living thereby acting as a cornerstone to the non-pharmacological management [12]. In this context, a physiotherapist led palliative exercise programme (PEP-PD) was designed which was executed for a total of six weeks duration constituting of portable ankle weights. The outcomes of the study clearly signified that a progressive six-week physical therapy improved the muscle strength and intensity of the lower limbs in patients living with Parkinson's disease (PD).

Nonetheless, the improvement in the flexibility and strength did not incur any difference in the severity of the patient condition. Similarly, physiotherapy leads to the maximisation of mobility, independence, and mobility provided adequate treatment and monitoring [13]. In this regard, improving the attitude, knowledge, experience, and beliefs of the physiotherapists to improve the standard and quality of life for the patients in palliative care is important [14]. Hence, physiotherapy-led interventions are integral in promoting individual autonomy, independence, mobility, and body functioning during the end of life care.

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Other physiotherapy interventions included the strengthening exercises offered to patients determined that physiotherapy has a positive and direct relationship in improving the patient outcomes and perceived well-being in populations demanding palliative care [15, 21].

Despite the fact that the profession has been under-valued and underestimated across the globe, there is a growing impetus for the improved physiotherapist's interventions and involvements in the in-patient as well as outpatient settings to offer relief from symptom and pain through non-pharmacological interventions. Specific physiotherapy interventions included breathing/aerobic exercises which are beneficial and recommended during the advanced disease progression to offer timely relief to the patients. Physiotherapy leads to a significant reduction in the rate of fatigue in patients receiving palliative care [16, 24].

Physiotherapy interventions are beneficial in the symptom management and alleviation of troublesome pain and discomfort through increased mobility and focusing on physical activity. Additionally, physiotherapy interventions in advanced diseases play a crucial role in improving the overall state of well-being of the patient while subsequently limiting the severity of the comorbid symptoms [17]. Hence, aerobic exercising, awareness, education, and alteration in the breathing mechanisms through physiotherapy interventions could play a positive role in improving the general state of the patients receiving palliative care.

Another physiotherapy intervention is based on generating awareness and improving the educational needs of the patients and the carers. Lim and Ng focused on the effectiveness and importance of the educational needs of the physiotherapists in the domain of palliative care [18, 23]. A lack of confidence and knowledge could lead to a negative influence on the quality of care services thereby affecting the patient well-being receiving palliative care. As opposed, good palliative care is highly dependent on effective communication skills as well as the technical competencies of the physiotherapists. In addition, multivariate role of the physiotherapists is involved in the specialised palliative care through prioritising the patient needs and addressing the emergent issues which directly hamper in the sudden alterations in the health status of the patients [19]. Therefore, educating the patient and creating awareness among the caregivers is also identified as a critical intervention through which the quality of life and well-being of the patients receiving palliative care could be addressed.

Along with educating the patients, education and development of the skillset of the physiotherapists are equally important in developing effective communication and interpersonal therapeutic relationships to provide ease and independence during the last stages of life.

Kumar and Jim (2010) discussed different physical therapy techniques and interventions comprising of therapeutic exercise, electrical modalities, thermal modalities, additional physical agents, and miscellaneous modalities (manual therapies) which offer an inherent role in improving the functional ability and care dimensions during the palliative care. The therapeutic exercises constituted of assisted active movement for offering relaxation, stabilisation, and mobilisation.

Electrical modalities, on the other hand, included the neuromuscular electrical stimulation which has been regarded as useful specifically in pain relief and management. Thermal modalities included the utilisation of heating and cold packs to promote flexibility. Physiotherapists play integral part in the multidisciplinary team involved with patients receiving palliative care [20]. This is done through physical therapy interventions which improve flexibility, muscle strength, durability, and functional mobility, as well as through optimising the respiratory, circulatory, cardiac, and muscular functioning to control pain and improve the functional independence [22]. Thus, physical therapy in palliative care patients is significant in promoting physical strength and independence.

Conclusion

The aim of this research study was to evaluate the role of the physiotherapist intervention in palliative care through critical analysis of the past literature. This systematic review of literature facilitated in analysing different intervention techniques which are globally utilised by physiotherapists for improving the quality of life during the end-stage of the patients. The analysis of the 11 research articles published in a period of ten years (2009 onwards) has identified multivariate intervention techniques which are adopted by the physiotherapists to enhance the general well-being through functional mobility, independence, and educational awareness. The findings also emphasised on the active role of the physiotherapists in pain relief and improvement in the symptoms through non-pharmacological techniques which lead to better outcomes for the patients. Hence, it is subjugated that involvement of the physiotherapists in the multidisciplinary team designed for patients receiving palliative care is essential in improving the physical strength, independence, and autonomy of the patients through optimised control mechanisms.



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January

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DDT COM ACADEMIC DATES

12th-13th	January	Supplementary Exams
13th-14th	May	Registration
26th-27th	August	Registration
14th-15th	January	Registration
17th	May	Classes begin
30th	August	Classes begin
18th	January	Classes Begin
31st	May-3rd June	QUIZ 1
13th-17th	September	QUIZ 1
1st-4th	february	QUIZ 1
21st-25th	June	Midterm Exam
11th-15th	November	Midterm Exam
1st-4th	March	Mid term Exam
12th-16th	July	QUIZ 2
18th	November	Graduation
22nd -26th	March	Quiz 2
09th-13th	August	Final Exam
1st-5th	November	QUIZ 2
26th-30th	April	Final Exam
16th-20th	August	Orientation
29th	Nov-3rd Dec	Final Exam
20th	Decembe	College closes

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Jan 01st	New Year's Day
Jan 2nd	New year Holiday Day
Feb 14th	Valentine's Day
Apr 10th	Good Friday
Apr 13nd	Easter Monday
May 1st	Labor Day
May 21st	Ascension Day
Jul 1	Sir Seretse Khama Day Holiday
Jul 20th	President Day
Jul 21st	President Day
Sep 30th	Independence Day
Oct 1st	Holiday
Dec 25th	Christmas
Dec 26th	Boxing day

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