COVID 19 OMICRON: THE ORIGIN, PRESENTATION, DIAGNOSIS, PREVENTION AND CONTROL

ABSTRACT

Coronavirus has emerged as a global health threat due to its accelerated geographic spread over the last two decades. Coronavirus disease 2019 also known as COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first known case was identified in Wuhan, China, in December 2019 historically, it has caused two pandemics: severe acute respiratory syndrome and Middle East respiratory syndrome followed by the current COVID-19 that emerged from China. The virus is acquired from zoonotic source and spreads through direct and contact transmission. It manifests with different symptoms ranging from fever to cough and myalgia to severe respiratory failure. The diagnosis is confirmed using reverse transcriptase PCR. Management of COVID-19 is mainly by supportive therapy along with mechanical ventilation in severe cases. Preventive strategies form the major role in reducing the public spread of virus along with successful disease isolation and community containment. A vaccine has been developed to eliminate the virus from the host although it is not yet certain if the vaccines will work against the most recent variant of the virus, the Omicron Variant. In this review, we summarized the latest research progress of the structure, epidemiology and pathogenesis. We also looked at the mutation pattern which is an important feature in virology of the virus. We also looked at the existing variants especially Omicron Variant. The clinical characteristics of COVID-19, and the current treatment and scientific advancements to combat the epidemic novel coronavirus was discussed.

1.0 INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory illness caused by a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; formerly called 2019-nCoV). It was first identified amid an outbreak of respiratory illness cases in Wuhan City, Hubei Province, China. It was initially reported to the WHO on December 31, 2019. On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency. On March 11, 2020, the WHO declared COVID-19 a global pandemic, with its first such

designation since declaring H1N1 influenza a pandemic in 2009. The Illness caused by SARS-CoV-2 was termed COVID-19 by the WHO, the acronym derived from "coronavirus disease 2019. The name was chosen to avoid stigmatizing the virus's origins in terms of populations, geography, or animal associations.

Coronavirus comprises of a large family of viruses, seven of which are known to cause disease in humans. Some coronaviruses that typically infect animals have evolved to infect humans. SARS-CoV-2 is likely one such virus, assumed to have originated in a large animal and seafood market.

Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) are also caused by coronaviruses that evolved from infecting animals to humans. More than 8000 individuals developed SARS, nearly 800 of whom died of the illness (mortality rate, approximately 10%), before it was controlled in 2003. MERS continues to resurface in sporadic cases. A total of 2465 laboratory-confirmed cases of MERS have been reported since 2012, resulting in 850 deaths (mortality rate, 34.5%).

The mode by which people are infected with SARS-CoV-2 is through exposure to respiratory droplets carrying infectious virus (always within a space of 6 feet). Additional methods include contact transmission like shaking hands and airborne transmission of droplets that linger in the air over long distances (usually more than 6 feet). Virus released in respiratory secretions like coughing, sneezing, talking can infect other individuals via contact with mucous membranes.

On July 9, 2020, the WHO issued an update stating that airborne transmission can play a role in the spread of COVID-19, particularly involving “super spreader” events in confined spaces such as bars, although they stressed a lack of such evidence in medical settings. Thus, they emphasized the importance of social distancing and masks in prevention.

The virus can also persist on surfaces to varying durations and degrees of infectivity, although this is not believed to be the main route of transmission. One study found that SARS-CoV-2 remained detectable for up to 72 hours on some surfaces despite decreasing infectivity over time. Notably, the study reported that no viable SARS-CoV-2 was measured after 4 hours on copper or after 24 hours on cardboard. (Cennimo, Coronavirus Disease 2019 (COVID-19), 2021)

2.1 COVID 19 AND ITS ORIGIN

The name "coronavirus" is derived from Latin corona, meaning "crown" or "wreath", itself a borrowing from Greek κορώνη *korōnē*, "garland, wreath".The name was coined by June Almeida and David Tyrrell who first observed and studied human coronaviruses.

Coronavirus disease 2019 also known as COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 is a β-coronavirus, which is an enveloped non-segmented positive-sense RNA virus (subgenus *sarbecovirus*, *Orthocoronavirinae* subfamily). They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses. They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona, from which their name derives (Anthony R. Fehr, Stanley Perlman, 2020).

The coronaviruses (CoV) are divided into four genera, which are α−/β−/γ−/δ-CoV. The α- and β-CoV infects mammals, while γ- and δ-CoV infects birds. In recent times, six CoVs have been discovered to also infect humans, and they are α-CoVs HCoV-229E and HCoV-NL63, and β-CoVs HCoV-HKU1 and HCoV-OC43 which all have low pathogenicity and cause mild respiratory symptoms similar to a common cold. The other two known as β-CoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections. It was discovered that the genome sequence of SARS-CoV-2 is 96.2% identical to a bat's CoV RaTG13, although it shares 79.5% identity to SARS-CoV. Based on virus genome sequencing results and evolutionary analysis, bat has been suspected as natural host of virus origin, and SARS-CoV-2 might be transmitted from bats via unknown intermediate hosts to infect humans. SARS-CoV-2 could use angiotensin-converting enzyme 2 (ACE2), the same receptor as SARS-CoV, to infect humans (Yan-Rong Guo *et al.*, 2020).

2.1.1 EPIDEMIOLOGY OF COVID 19

The epidemic of unknown acute respiratory tract infection broke out first in Wuhan, China, since 12 December 2019, perhaps related to a seafood market. Several studies proposed that bat may be the potential reservoir of SARS-CoV-2. However, there is no evidence so far that the origin of SARS-CoV-2 was from the seafood market. Conversely, bats are the natural reservoir of a wide variety of CoVs, like SARS-CoV-like and MERS-CoV-like viruses. Upon virus genome sequencing, the COVID-19 was analyzed throughout the genome to Bat CoV

RaTG13 and it showed 96.2% overall genome sequence identity, suggesting that bat CoV and human SARS-CoV-2 might share the same ancestor, even though bats are not available for sale in this seafood market. Protein sequences alignment and phylogenetic analysis also showed that similar residues of receptor were observed in many species, which provided more probability of alternative intermediate hosts, such as turtles, pangolin and snacks (Liu *et al.,* 2020).

SARS-CoV-2 transmission between humans occurs frequently between family members, including relatives and friends who intimately contacted with patients or incubation carriers. It is has been reported that 31.3% of patients recent travelled to Wuhan and 72.3% of patients contacting with people from Wuhan among the patients of non-residents of Wuhan. Transmission between healthcare workers occurred in 3.8% of COVID-19 patients, issued by the National Health Commission of China on 14 February 2020. By contrast, the transmission of SARS-CoV and MERS-CoV is reported to have occurred mainly through nosocomial transmission. Infections of healthcare workers in 33–42% of SARS cases and transmission between patients (62–79%) was the most common route of infection in MERS-CoV cases. Direct contact with intermediate host animals or consumption of wild animals was also suspected to be the main route of SARS-CoV-2 transmission. Nevertheless, the source(s) and transmission routine(s) of SARS-CoV-2 remain elusive.

2.1.2 GENOME STRUCTURE OF COVID 19

Isolated from a COVID-19 pneumonia patient, a worker in the Wuhan seafood market, the complete genome of Wuhan-Hu-1 coronavirus (WHCV), one strain of SARS-CoV-2, is 29.9 kb. While SARS-CoV and MERS-CoV have positive-sense RNA genomes of 27.9 kb and 30.1 kb, respectively. It has been shown that the genome of CoVs contains a variable number (6–11) of open reading frames (ORFs). Two-thirds of viral RNA, mainly located in the first ORF (ORF1a/b) translates two polyproteins, pp1a and pp1ab, and encodes 16 non-structural proteins (NSP), while the remaining ORFs encode accessory and structural proteins. The rest part of virus genome encodes four essential structural proteins, like spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and other accessory proteins, that interfere with the host innate immune response. Deep meta-transcriptomic sequencing recently performed on WHCV, which contained 16 predicted NSP. WHCV exhibits some genomic and phylogenetic similarity to SARS-CoV, particularly in the S-glycoprotein gene and receptor-binding domain (RBD), indicating the

capability of direct human transmission. In comparison with the known SARS-CoV and MERS-CoV genome, SARS-CoV-2 is closer to the SARS-like bat CoVs in terms of the whole genome sequence. Most genomic encoded proteins of SARS-CoV-2 are similar to SARS-CoVs, as well as exist certain differences. At the protein level, there are no amino acid substitutions that occurred in NSP7, NSP13, envelope, matrix, or accessory proteins p6 and 8b, except in NSP2, NSP3, spike protein, underpinning subdomain, i.e., RBD. Another recent research suggested that the mutation in NSP2 and NSP3 play a role in infectious capability and differentiation mechanism of SARS-CoV-2. This provokes people to explore the difference of the host tropism and transmission between SARS-CoV-2 and SARS-CoV or conduct further investigations on the potential therapeutic targets (Wu *et al* 2020).

Analysis of genotypes of COVID-19 in different patients from several provinces and was discovered that SARS-CoV-2 had been mutated in different patients in China. Although the degree of diversification of SARS-CoV-2 is smaller than the mutation of H7N9 avian influenza. Tang *et al*. conducted a population genetic analyses of 103 SARS-CoV-2 genomes and classified out two prevalent evolvement types of SARS-CoV-2, L type (~ 70%) and S type (~ 30%). The strains in L type, derived from S type, are evolutionarily more aggressive and contagious. Thus, virologists and epidemiologists need to closely monitor the novel coronavirus, in order to inspect the virulence and epidemic (Zhang *et al.*, 2020).

2.1.3 COVID 19 REPLICATION AND PATHOGENESIS

ACE2, found in the lower respiratory tract of humans, is known as cell receptor for SARS-CoV and regulates both the cross-species and transmission between humans. Isolated from the bronchoalveolar lavage fluid (BALF) of a COVID-19 patient. It has been confirmed that the SARS-CoV-2 uses the same cellular entry receptor, ACE2, as SARS-CoV. The virion S-glycoprotein on the surface of coronavirus can attach to the receptor, ACE2 on the surface of human cells. S glycoprotein includes two subunits, S1 and S2. S1 determines the virus-host range and cellular tropism with the key function domain − RBD, while S2 mediates virus-cell membrane fusion by two tandem domains, heptad repeats 1 (HR1) and HR2. After the membrane fusion, the viral genome RNA is released into the cytoplasm, and the uncoated RNA then translates two polyproteins, pp1a and pp1ab, which encode non-structural proteins, and form replication-transcription complex (RTC) in double-membrane vesicle. Continuously RTC replicate and synthesize a nested set of subgenomic RNAs, which encode accessory proteins and structural proteins. Mediating endoplasmic reticulum (ER) and Golgi, newly

formed genomic RNA, nucleocapsid proteins and envelope glycoproteins assemble and form viral particle buds. Lastly, the virion-containing vesicles fuse with the plasma membrane to release the virus (Zhou *et al* 2020).

Because the binding of SARS-CoV-2 Spike (S) glycoprotein and ACE2 receptor is a critical step for virus entry, virus-receptor binding affinity is under a close study through different approaches. Systematic detection of β-CoV receptors showed that human cells expressing ACE2, but not human Dipeptidyl peptidase-4 (DPP4) or APN (Aminopeptidase N), occured as a result of enhanced entry of SARS-CoV-2 (Letko *et al.*, 2020).

Another study by Song and Gui showed that S-protein and ACE2 binding efficiency is 10- to 20- fold higher than that of SARS-CoV, evidenced by Cryo-EM Structure of the SARS-CoV-2 Spike in the prefusion conformation(Song and Gui, 2018).

For SARS-CoV, the cleavage of trimer S protein is triggered by the cell surface-associated transmembrane protease serine 2 (TMPRSS2) (Millet, *et al*, 2015) and cathepsin, while the possible molecules facilitated membrane invagination for SARS-CoV-2 endocytosis are still unclear. Up to the date this review paper was prepared, reports showed that the SARS-CoV-2 may readily transmit, while cause less serious human infection rather than human SARS-CoV. Based on the latest WHO report, the number of infected people (over 80,000 globally, updated on 1 March 2020). The global outbreak may due to the following factors: firstly, the unknown pneumonia outbroke at the time of China Spring Festival, when the mass population flowing. Secondly, more coincise molecular mechanisms of viral binding and entry manners await to be elucidated, which may hamper the development of targeted therapy. Thirdly, available data suggested that the SARS-CoV-2 may be less virulent than the SARS-CoV and MERS-CoV, with the currently analyzed mortality of COVID-19 is 3.4%, lower than death rate of SARS (9.6%) and MERS (around 35%), respectively(de Wit *et al.*, 2016).

Therefore, the potential mechanisms for transmission between humans and pathogenic mechanisms of the SARS-CoV-2 are under intensive studies.

2.2 MUTATION PATTERN OF COVID 19

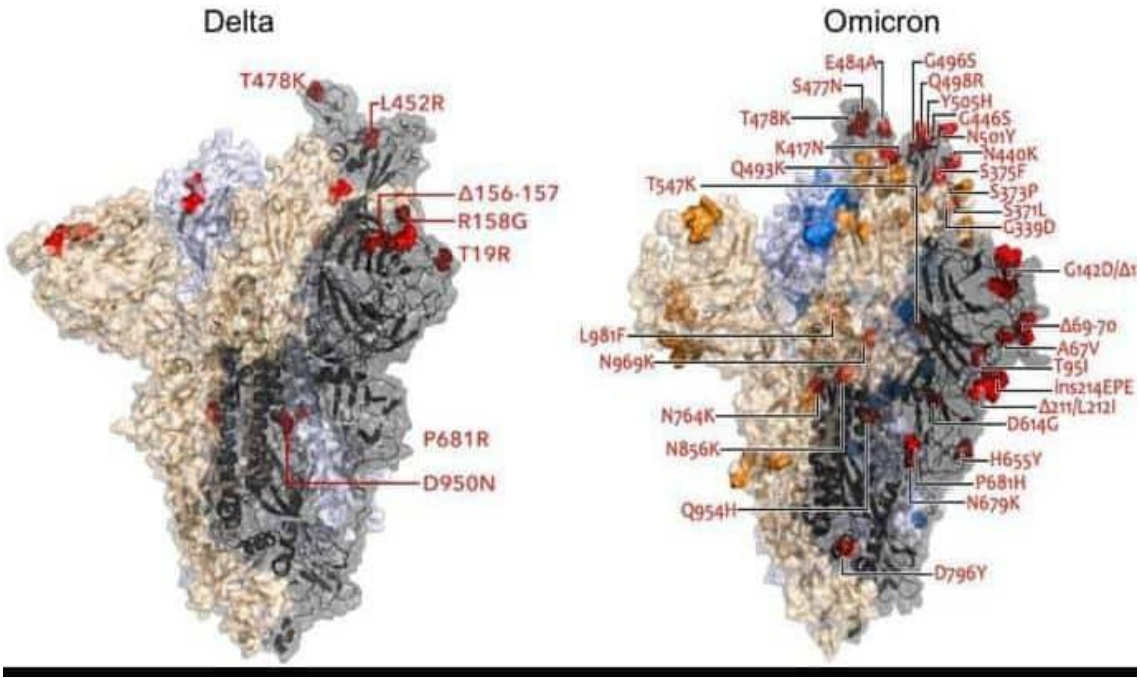

Figure 1: A comparison of Delta and Omicron variant spike mutation (Image source: Modified rom covid- 19 Genomics UK consortium)

All viruses naturally mutate over time, and Sars-CoV-2 is no exception. Since the virus was first identified a year ago, other mutations have arisen with majority of mutations been "passengers" and will have little impact But every once in a while, a virus mutates in a way that helps it survive and reproduce. That doesn’t change the behaviour of the virus, it just carries the virus along with the change in the environment. Viruses carrying these mutations can then increase in frequency due to natural selection, given the right epidemiological settings (Dorp, 2021). This is seems to be the case with the variant that has been spreading across the UK, known as 202012/01, and also a similar, but different variant, recently identified in South Africa (501.V2).

Infections with these strains are more severe, due to increased transmissibility, the impact of Covid-19 disease in terms of hospitalisations and deaths is assessed as high, most especially for people of older age groups or with co-morbidities. The variants have different origins but they all share a mutation in a gene which encodes the spike protein that the virus uses to latch on to and enter human cells. This is why they appear more infectious.

2.2.1 VARIANTS OF COVID 19

Viruses constantly change through mutation. When a virus has one or more new mutations it’s called a variant of the original virus.

A new strain occurs when a virus goes through one or more mutations that change its behavior in some way, but a variant develops when a virus goes through a mutation

The different variants of COVID 19 include

- **Delta Variant From India**

  This variant is believed to have first emerged in India in October 2020. It's since spread to the U.S. and currently has more than 6% of sequenced cases in the U.S., Dr. Anthony Fauci said at a recent news briefing. It also has increased transmissibility compared to other variants, according to the World Health Organization.
- **Alpha Variant: Uk Variant**

  The U.K. strain, called B.1.1.7, was first reported in the U.S. in late December, and it spreads faster and easily than other variants, according to the CDC. It is now in all 52 states and territories and is the dominant variant in the U.S. The CDC has also said it has "potential increased severity based on hospitalizations and case fatality rates
- **Beta Variant: South African Variant**

  This variant, known as B.1.351 or Beta, emerged independently from the U.K. strain but shares some of its mutations, according to the CDC. Data indicates that it first emerged in South Africa in October 2020 and has since spread to other countries, including the U.S. In late January. This variant could also make re-infection more likely; a vaccine study in South Africa found 2% of people who'd already had a version of the coronavirus had been reinfected with a variant. It also has an estimated 50% increase transmission.
- **Gamma Variant**

  The Brazilian variant, P.1, was first detected in mid-January 2020 in travelers to Japan from the Amazonas state of Brazil. It appears to contain mutations that raise concerns about its transmissibility and potential for reinfection, according to the CDC. Manaus, the largest city in the Amazon region, saw a surge in cases in December 2020, despite 75% of the population already having been infected by October.
- **Omicron Variant**

> This variant might spread more easily than other variants, including delta. But it’s not yet clear if omicron causes more severe disease. It’s expected that people who are fully vaccinated likely can get breakthrough infections and spread the virus to others

A new strain occurs when a virus goes through one or more mutations that change its behavior in some way, but a variant develops when a virus goes through a mutation of any kind

2.3 COVID 19 OMICRON

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Spike amino acid changes in OMICRON- B.1.1.529 [GR]

Deletions	Δ69-70	Δ143-145	Δ211
Insertion	214EPE		

Receptor Binding Domain (RBD) (residues 319-541)

G339D	S371L	S373P	S375F
K417N	N440K	G446S	S477N
T478K	E484A	Q493K	G496S
Q498R	N501Y	Y505H	

Other amino acid changes in the spike

A67V	T95I	G142D	L212I
T547K	D614G	H655Y	N679K
P681H	N764K	D796Y	N856K
Q954H	N969K	L981F	

Effects on transmissibility

Possibility: High to Very High

Vaccine escape potentiality

Possibility: Possible

The cross-neutralising capacity of Omicron variant needs to be evaluated.

Figue 2: Spike Amino acid changes in Omicron (Source: World Society For Virology)

The new COVID- 19 variant called the Omicron variant also know as B.1.1.529 variant has been named a variant of high importance by WHO based on the evidence that it has several mutations that may have an impact on how it behaves. There is still significant uncertainty regarding Omicron and a lot of research has been going on to evaluate its transmissibility, severity and reinfection risk this is because When a virus is circulating widely and causing

numerous infections, the likelihood of the virus mutating increases. The more opportunities a virus has to spread, the more opportunities it has to undergo changes (Unicef, 2021).

Vaccines so has so far been observed to reduce the rate but it has not been recorded to stop the virus but is very important that people get vaccinated when the vaccine is made available to them and continue to follow existing protocols on preventing the spread of the virus, including social distancing, wearing masks, regular handwashing and keeping indoor areas well ventilated.

The Omicron variant has now been detected in many countries around the world and Nigeria is no exception. The WHO reported that the Omicron Variant might be in some other countries even though it hasn't been discovered yet.

The B.1.1.529 variant was first reported to WHO from South Africa on 24 November 2021. The epidemiological situation in South Africa has been distinguished by three well defined peaks in reported cases, the latest of which was primarily the Delta variant which has had an increasingly steep infection rate in recent weeks, corresponding with the detection of B.1.1.529 variant. The first known confirmed B.1.1.529 infection was from a specimen collected on 9 November 2021.

This variant has a large number of mutations, some of which are concerning. Preliminary evidence suggests an increased risk of reinfection with this variant, compared to other Variants of Concern. The number of cases of this variant appears to be increasing in almost all provinces in South Africa. Current SARS-CoV-2 PCR diagnostics continue to detect this variant. Several labs have indicated that for one widely used PCR test, one of the three target genes is not detected (called S gene dropout or S gene target failure) and this test can therefore be used as marker for this variant, pending sequencing confirmation. Using this approach, this variant has been detected at faster rates than previous surges in infection, suggesting that this variant may have a growth advantage (UNICEF, 2021).

WHO reports that early evidence suggests that previous infection could offer less protection against Omicron in comparison to other variants of concern, such as Delta although, people who recover from COVID-19 may develop some natural immunity to the virus, but it is not yet known how long it will last or how well the person is protected (WHO, 2021).

Luka Lawal of the Nigeria Centre for Disease Control (NCDC) said Nigeria has recorded a total of 45 Omicron cases as of December 20, 2021 he said this, during a virtual media briefing on Friday.

Nigeria currently ranks third in the list of African countries with the highest cases of Omicron after South Africa and Botswana with 1,296 and 291 cases respectively.

Nigeria on December 1, 2021, joined the growing number of countries in Africa that have recorded cases of the omicron variant also known as B.1.1.529 lineage.

Iluyemi 2021 stated that the first cases of the Omicron variant were detected among travellers from South Africa to Nigeria, the NCDC explained that the subsequent cases detected are not from travellers but within Nigeria (Ileyemi, 2021).

Delta variant remains the most dominant since the outbreak of COVID-19, with 2,237 cases detected in Nigeria as of December 20, 2021.

2.4 DIAGNOSIS OF COVID 19 OMICRON VARIANT

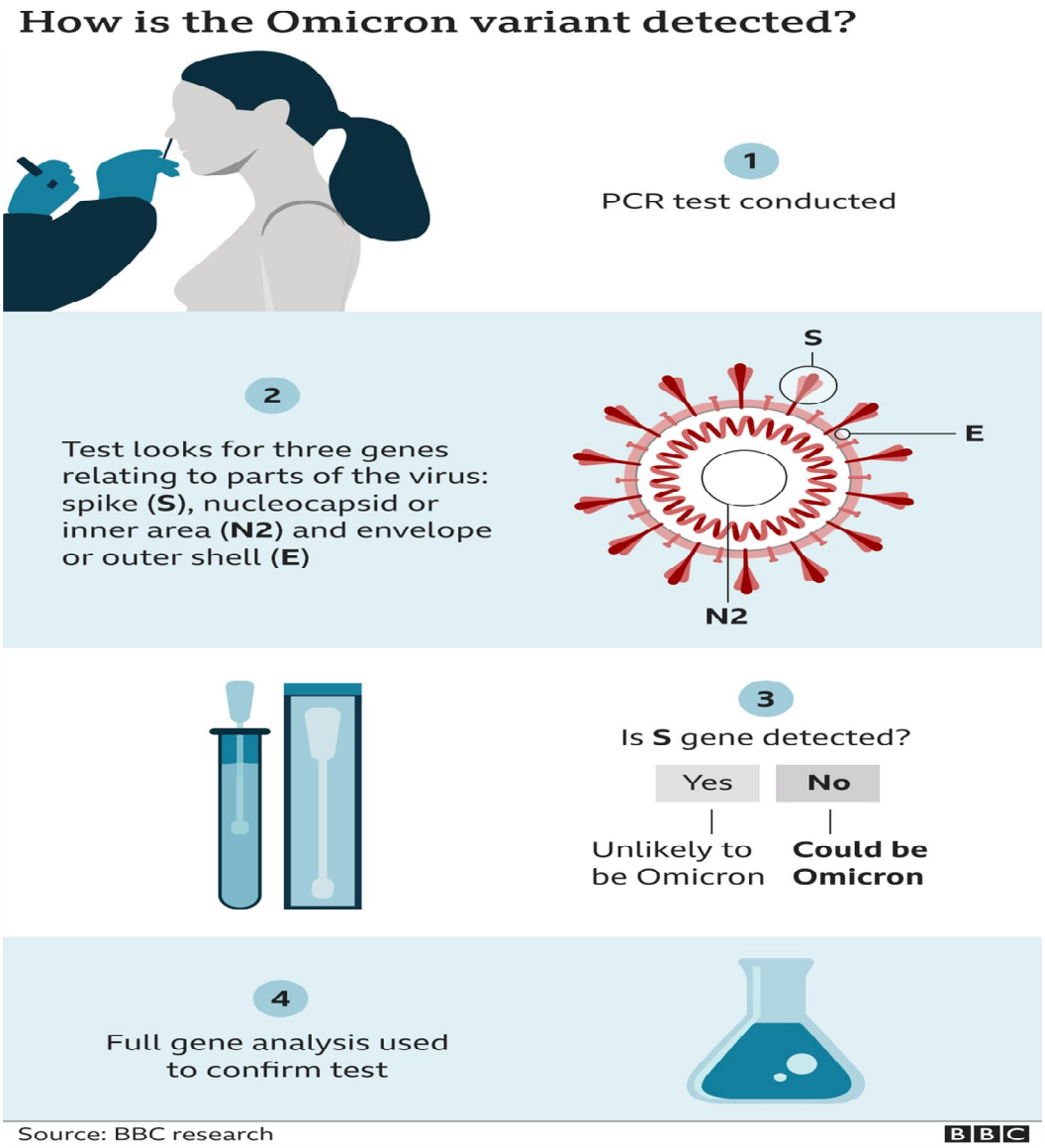

Figure 3 : Detection of omicron variant

Swabs from polymerase chain reaction (PCR) tests which are sent to the labs for analysis are used to detect the variant causing the infection wether it is Omicron or Delta or other variants.

In the UK, a technique known as genome sequencing is used to to detect the Omicron variant.

Another method of detecting the Omicron Variant is through the Rapid or Lateral flow tests (LFTs), which can also can used at home although it won't tell you which variant but if it conforms that the patient is positive, he or she has to go the hospital for further testing after

which PCR will be conducted to detect the variant. During the test the scientist will have to take note if the virus as three genes relating to the virus; Spike (S), Nucleocapsid or inner area (N2) and Envelope or outershell (E). If the S gene is not detected, that means the variant is likely to be Omicron then a full gene analysis is used to confirm the test (Roxby, 2021).

2.5 PREVENTION AND CONTROL OF COVID 19

The most important thing you can do is reduce your risk of exposure to the virus. To protect yourself and your loved ones, make sure to:

1. Wear a mask that covers your nose and mouth. Make sure that your hands are clean when you put on and remove your mask.
2. Keep a physical distance of at least 1 metre from others.
3. Avoid poorly ventilated or crowded spaces.
4. Open windows to improve ventilation indoors.
5. Wash your hands regularly.
6. When it's your turn, get vaccinated. WHO-approved COVID-19 vaccines are safe and effective.

3.1 CONCLUSION

It has been postulated that Corona Virus has been in exsistence in animals before it's first and recent infection in humans caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and so far the cases has been increasing daily. Currently it is not fully known if the vaccine can totally reduce the chance of getting an infection because other cases of reinfection has been occurring even after vaccination. Literature reviewed for this purpose indicated that Vaccination still remains an effective means of reducing the spread but obeying preventive measures too will help to reduce the spread of the virus.

REFFERENCE

Anthony R. Fehr, Stanley Perlman. (2020). Coronaviruses: An Overview of Their Replication and Pathogenesis.

Cennimo, D. J. (2021). Coronavirus Disease 2019 (COVID-19).

Cui J, Li F, Shi ZL. (2019). Origin and evolution of pathogenic coronaviruses.

de Wilde AH, Snijder EJ, Kikkert M, van Hemert MJ. (2018). Host factors in coronavirus replication. *Curr Top Microbiol Immunology*.

de Wit E, van Doremalen N, Falzarano D, Munster VJ. (2016). SARS and MERS: recent insights into emerging coronaviruses.

Dorp, D. L. (2021, january). Coronavirus variants. (H. Briggs, Interviewer)

Giovanetti M, B. D. (2020). The first two cases of 2019-nCoV in Italy: where they come from.

Hohman, M. (2021, june 10). Should I be concerned about COVID-19 variants? Experts break it down.

Ileyemi, M. (2021). *COVID-19: Nigeria third on list of African countries with Omicron cases.* Premium Times Nigeria.

Letko M, Marzi A, Munster V. (2020). Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses.

Liu Y, Gayle AA, Wilder-Smith A, Rocklov J. (2020). The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med*.

Liu Z, Xiao X, Wei X, Li J, Yang J, Tan H, et al. (2020). Composition and divergence of coronavirus spike proteins and host ACE2 receptors predict potential intermediate hosts of SARS-CoV-2. . *J Medical Virology*.

Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus. *implications for virus origins and receptor binding*.

Millet JK, Whittaker GR. (2015). Host cell proteases: critical determinants of coronavirus tropism and pathogenesis.

Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Sourvinos G, Tsiodras S. (2020). Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infective Genetic Evolution*.

Perrier A, Bonnin A, Desmarets L, Danneels A, Goffard A, Rouille Y, et al. (n.d.). The C-terminal domain of the MERS coronavirus M protein contains a trans-Golgi network localization signal.

Riou J, A. C. (2020). Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus .

Roxby, P. (2021). *Omicron: How do you detect it?* BBC NEWS.

Song W, Gui M, Wang X, Xiang Y. Cryo-EM. (2018). structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2.

Song Z, Xu Y, Bao L, Zhang L, Yu P, Qu Y, et al. (2019). From SARS to MERS, thrusting coronaviruses into the spotlight.

Srikanth Umakanthan , Pradeep Sahu , Anu V Ranade, Maryann M Bukelo, Joseph Sushil Rao , Lucas Faria Abrahao-Machado, Samarika Dahal, Hari Kumar Dhananjaya Kv . (2019). *origin, transmission,diagnosis and management of coronavirus disease.*

Tortorici MA, Veesler D. (2019). Structural insights into coronavirus entry.

UNICEF. (2021, December 17). What we know about the Omicron variant. *What is Omicron and what precautions should you take to protect your family?* .

WHO. (2021). *Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern.*

WHO. Coronavirus disease (COVID-2019) situation reports. (2020, March 5). Retrieved from World Health Organization: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.

Xia S, Zhu Y, Liu M, Lan Q, Xu W, Wu Y, et al. (2020). Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein. *Cell Molecular Immunology.*

Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin, Kai-Sen Tan, De-Yun Wang and Yan Yan. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Military Medical Research* .

Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin, Kai-Sen Tan, De-Yun Wang, Yan Yan. (2020). *the origin, transmission and clinical therapies on coronavirus disease 2019 (COVID- 19).*

Yin Y, Wunderink RG. (2018). MERS, SARS and other coronaviruses as causes of pneumonia. .

Yu F, Du L, Ojcius DM, Pan C, Jiang S. (2020). Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan, China. *Microbes Infection.*

Zhang L, Shen FM, Chen F, Lin Z. (2020). Origin and evolution of the 2019 novel coronavirus.

Zhang N, Jiang S, Du L. (2014). Current advancements and potential strategies in the development of MERS-CoV vaccines. *Expert Rev Vaccines.*

Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. . (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature.

Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. (2019). A novel coronavirus from patients with pneumonia in China.