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Management of Patients who Tested Positive for COVID-19 Infection through the Effect of Ivermectin Addition: Delta State in Focus

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ABSTRACT: The study examined a two-year pilot experiment undertaken in Delta State to determine the impact of incorporating ivermectin into the routine treatment regimen of patients with COVID-19 infection. The rationale is to explore the impact of adding 12 mg ivermectin on the recovery process of COVID-19 positive patients, as well as the combination of ivermectin with other COVID-19 medications. The research is an experimental evaluation to determine the efficacy of ivermectin in conjunction with other COVID-19 therapy methods. The study was conducted between 2020 and 2022 at three hospitals that gained official approval, especially the Federal Medical Centre Asaba, which is located in one of Delta State's three senatorial districts. Before beginning the investigation, the Board of Ethics gained ethical permission. Using a single-blind randomized approach, the patients were divided into two groups, namely the 'Study Group' and the 'Control Group.' Subjects with even numerical values were assigned to the study group, while those with odd numerical values were assigned to the control group. All participants were given informed consent before to participation in the trial, and eligible patients were subjected to a standardized symptom questionnaire and physical assessment utilizing the informed consent supplied. A complete blood count, thoracic tomography scan, biochemical blood analysis, and the initial SARSCOV-2 polymerase chain reaction (PCR) result were also recorded. The trial includes 72 patients, with 40 assigned to the study group and 32 assigned to the control group. Due to a mutation that affects ivermectin metabolism, 12 subjects were excluded from the study. In the study, 60% of the participants were men and 40% were women. Both patients in the trial and control groups who were COVID-19 positive received the reference therapies suggested by the National Disease Control Centre (NDCC). Patients in the study group were given ivermectin medication in the form of a 12 mg tablet orally for 5 days. Patients' respiratory observations and laboratory measurements were reported on the first, third, and fifth days of therapy, as well as the first, third, and fifth days following treatment and during the follow-up period. They demonstrated an early therapeutic response, lending credence to the idea that ivermectin at a dose of 12mg daily for 5 days, alone or in combination with the current standard regimen, could be evaluated as a possible treatment option for COVID-19 infection and in patients with co-morbidities. In the study, no significant adverse reactions were seen in the cohort of patients given ivermectin 12 mg versus those who got normal convectional treatment. Pharmacokinetic studies also revealed that ivermectin 12 mg was safe and well tolerated in the study group's participants. The study concluded that Invertmetic, when gradually administered to patients, improves COVID-19 recovery, and the study recommended that medical practitioners incorporate and adopt up to 3mg inclusive addiction patients because it has positive health benefits and a positive influence on recovery.

Keywords: Ivermectin, Covid -19, patients, Management, Delta State

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INTRODUCTION

Corona virus disease 2019 (COVID-19) is an illness caused by a novel corona virus called severe acute respiratory syndrome corona virus 2 (SARS-CoV-2; formerly called 2019-nCoV)(Oxford English Dictionary, 2020).The outbreak was initially reported to the World Health Organization (WHO) on December 31, 2019 by January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency(CDC, 2020). I**v**ermectin is a broad- spectrum antiparasitic endectocide active against a wide range of internal and external parasites. It was originally introduced as a veterinary drug, predominantly in domestic livestock, but since 1987 has been widely used in human medicine. Ivermectin at a dose of 150 or 200 mcg/kg is the first-line treatment for

Onchocerca volvulus (the cause of river blindness), *wuchereria bancrofti* (the cause of lymphatic filariasis), and *Strongyloides Stercoralis* (roundworm, an intestinal helminth). Ivermectin at these doses is used as MDA in annual campaigns for the control of river blindness and lymphatic filariasis in endemic areas. To date more than 1.8 billion treatments have been distributed (Aristovnik et al., 2020). The ivermectin MDA campaigns have been reported to have a secondary effect of reducing intestinal helminths in humans(Emmanuel et al., 2020).), and on ectoparasites such as nuisance insects including head lice, mites, bedbugs and scabies(Salajegheh et al. 2020). Ivermectin is currently commercially available and economically affordable in various regions worldwide Shadka and Forsman (2019). According to Vardavas and Nikitara, 2020), a study conducted in 2018 examined the cost of Ivermectin, a medication used to treat scabies. The study found that the price of one hundred 12-mg pills of Ivermectin was 2.90 USD. Therefore, the exploration of Ivermectin's therapeutic potential against SARS-CoV-2 could hold significant importance in settings with limited resources (Agyeman et al., 2020). If demonstrated to be efficacious as a therapy for COVID-19, its economic viability should be evaluated by considering the cost of existing therapeutics and preventive measures. This paper aims on the effect of Ivermectin addition in the management of patients who tested positive for COVID 19 Infection in Delta State.

The problem

International research on vaccines and medicines in COVID-19 is underway by government organizations, academic groups, and industry researchers (Reardon, 2020). The CDC has classified it to require a BSL3 grade laboratory (Kucharki *et al.,* 2020).There has been a great deal of COVID-19 research, involving accelerated research processes and publishing shortcuts to meet the global demand.As of December 2020, hundreds of clinical trials have been undertaken, with research happening on every continent except Antarctica. As of November 2020, more than 200 possible treatments had been studied in humans so far (Vabret, et al., 2020). However specific positions need to be held on patients in certain parts of the world, especially Delta State. Ivermectin is available as a generic prescription drug in Nigeria and most African countries in a 3 mg tablet formulation(National Center for Immunization and Respiratory Diseases (NCIRD) (9 July 2020).It is also sold under the brand names Heartgard, Sklice and Stromectol in the United States, Ivomec worldwide by Merial Animal Health, Mectizan in Canada by Merck, Iver-DT (Adams et al. 2020) in Nepal by Alive Pharmaceutical and Ivexterm in Mexico by Valeant Pharmaceuticals International, proper empirical evidence to support patients reaction to this drugs needs to be addressed. Ivermectin is commercially accessible as a non-branded pharmaceutical product in Nigeria and the majority of African nations, specifically in a 12 mg tablet configuration, as stated by the National Agency for Food and Drug Administration and Control (NAFDAC) in 2018. The compound in question is marketed under various trade names in different regions. In the United States, it is known as Heartgard, Sklice, and Stromectol. Worldwide, it is sold as Ivomec by Merial Animal Health, while in Canada it is marketed as Mectizan by Merck. In Nepal, the compound is known as Iver-DT, produced by Alive Pharmaceutical, and in Mexico, it is sold as Ivexterm by Valeant Pharmaceuticals International (Adhikhari, 2014). In response to the heightened global focus on ivermectin as a potential therapeutic option for COVID-19, a committee for guideline development was assembled. This collective constitutes an autonomous, global consortium of proficient individuals, encompassing specialists in various fields of clinical care, alongside an ethicist and patient-partners. Additionally, it is employed for the treatment of scabies. While COVID-19 vaccines remain central to protection, antiviral medications may be important for people whose bodies do not mount a strong response to the vaccine, who experience breakthrough infections, and for those who are unvaccinated. This study was needed to bring sound scientific evidence on the effect of the introduction of ivermectin in the treatment of COVID-19 infection in the study area.

Research objective

To determine the effect of ivermectin 12mg addition on patients recovery who tested positive for COVID19.

Research hypothesis

Ho_1: There is no significant effect of ivermectin 12mg addition on patients and their regimen to the recovery of patients tested positive for COVID-19.

Literature review

COVID-19

Corona virus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). The first known case was identified in Wuhan, China in December 2019. The disease has since spread worldwide, leading to an ongoing pandemic. Symptoms of COVID-19 are variable, but often include fever, cough, headache, fatigue, breathing difficulties, and loss of smell and taste. Symptoms may begin one to fourteen days after exposure to the virus. At least a third of people who are infected do not develop noticeable symptoms. Of those people who develop noticeable symptoms enough to be classed as patients, most (81%) develop mild to moderate symptoms (up to mild pneumonia), while 14%

develop severe symptoms (dyspnea, hypoxia, or more than 50% lung involvement on imaging), and 5% suffer critical symptoms (respiratory failure, shock, or multiorgan dysfunction). Older people are at a higher risk of developing severe symptoms. Some people continue to experience a range of effects (long COVID) for months after recovery, and damage to organs has been observed. Multi-year studies are underway to further investigate the long-term effects of the disease, Oran, and Topol, (2021).

Several testing methods have been developed to diagnose the disease. The standard diagnostic method is by detection of the virus' nucleic acid by real-time reverse transcription polymerase chain reaction (rRT-PCR), transcription-mediated amplification (TMA), or by reverse transcription loop-mediated isothermal amplification (RT-LAMP) from a nasopharyngeal swab. Preventive measures include physical or social distancing, quarantining, ventilation of indoor spaces, covering coughs and sneezes, hand washing, and keeping unwashed hands away from the face.

The use of face masks or coverings has been recommended in public settings to minimize the risk of transmissions. While work is underway to develop drugs that inhibit the virus (and several vaccines for it have been approved and distributed in various countries, which have since initiated mass vaccination campaigns), the primary treatment is symptomatic, (Xu, Han, Li, T, Sun, Wang, and Fu, 2020) Management involves the treatment of symptoms, supportive care, isolation, and experimental measures.

Signs and symptoms

Symptoms of COVID-19 are variable, ranging from mild symptoms to severe illness. Common symptoms include headache, loss of smell and taste, nasal congestion and runny nose, cough, muscle pain, sore throat, fever, diarrhea, and breathing difficulties. People with the same infection may have different symptoms, and their symptoms may change over time. Three common clusters of symptoms have been identified: one respiratory symptom cluster with cough, sputum, shortness of breath, and fever; a musculoskeletal symptom cluster with muscle and joint pain, headache, and fatigue; a cluster of digestive symptoms with abdominal pain, vomiting, and diarrhea. In people without prior ear, nose, and throat disorders, loss of taste combined with loss of smell is associated with COVID-19.(Coronavirus (COVID-19, 2020).

Cause

COVID-19 is caused by infection with the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) virus strain.

Transmission

The disease is mainly transmitted via the respiratory route when people inhale droplets and particles that infected people release as they breathe, talk, cough, sneeze, or sing. Infected people are more likely to transmit COVID-19 the when they are physically close. However, infection can occur over longer distances, particularly indoors. Infectivity begins as early as three days before symptoms appear, and people are most infectious just prior to and during the onset of symptoms. It declines after the first week, but infected people remain contagious for up to 20 days. People can spread the disease even if they are asymptomatic.

Virus protein

The association between SARS-CoV-2 and the Renin-Angiotensin-Aldosterone System (RAAS)**.** Multiple viral and host factors affect the pathogenesis of the virus. The S-protein, otherwise known as the spike protein, is the viral component that attaches to the host receptor via the ACE2 receptors. It includes two subunits: S1 and S2. S1 determines the virus-host range and cellular tropism via the receptor-binding domain. S2 mediates the membrane fusion of the virus to its potential cell host via the H1 and HR2, which are heptad repeat regions. Studies have shown that S1 domain induced IgG and IgA antibody levels at a much higher capacity. It is the focus spike proteins expression that is involved in many effective COVID-19 vaccines. The M protein is the viral protein responsible for the transmembrane transport of nutrients. It is the cause of the bud release and the formation of the viral envelope. The N and E protein are accessory proteins that interfere with the host's immune response.

Host factors

Human angiotensin converting enzyme 2 (hACE2) is the host factor that SARS-COV2 virus targets causing COVID-19. Theoretically the usage of angiotensin receptor blockers (ARB) and ACE inhibitors upon regulating ACE2 expression might increase morbidity with COVID-19, though animal data suggest some potential protective effect of ARB. However no clinical studies have proven susceptibility or outcomes. Until further data is available, guidelines and recommendations for hypertensive patients remain.

Host cytokine response

The severity of the inflammation can be attributed to the severity of what is known as the cytokine storm. Levels of interleukin 1B, interferon-gamma, interferon-inducible protein 10, and monocyte chemoattractant protein 1 were all associated with COVID-19 disease severity. Treatment has been proposed to combat the cytokine

storm as it remains to be one of the leading causes of morbidity and mortality in COVID-19 disease. A cytokine storm is due to an acute hyper inflammatory response that is responsible for clinical illness in an array of diseases but in COVID-19, it is related to worse prognosis and increased fatality. The storm causes acute respiratory distress syndrome, blood clotting events such as strokes, myocardial infarction, encephalitis, acute kidney injury, and vasculitis. The production of IL-1, IL-2, IL-6, TNF-alpha, and interferon-gamma, all crucial components of normal immune responses, inadvertently become the causes of a cytokine storm. The cells of the central nervous system, the microglia, neurons, and astrocytes, are also involved in the release of pro-inflammatory cytokines affecting the nervous system, and effects of cytokine storms toward the CNS are not uncommon.

Diagnosis

COVID-19 can provisionally be diagnosed on the basis of symptoms and confirmed using reverse transcription polymerase chain reaction (RT-PCR) or other nucleic acid testing of infected secretions. Along with laboratory testing, chest CT scans may be helpful to diagnose COVID-19 in individuals with a high clinical suspicion of infection. Detection of a past infection is possible with serological tests, which detect antibodies produced by the body in response to the infection.

Viral testing

The standard methods of testing for presence of SARS-CoV-2 are nucleic acid tests, which detects the presence of viral RNA fragments. As these tests detect RNA but not infectious virus, its "ability to determine duration of infectivity of patients is limited." The test is typically done on respiratory samples obtained by a nasopharyngeal swab; however, a nasal swab or sputum sample may also be used. Results are generally available within hours. The WHO has published several testing protocols for the disease. Several laboratories and companies have developed serological tests, which detect antibodies produced by the body in response to infection. Several have been evaluated by Public Health England and approved for use in the UK.

Pathology

Macroscopy: pericarditis, lung consolidation and pulmonary oedema, Lung findings, Blood vessles and Heart: cardiac muscle cell necrosis

Prevention

Preventive measures to reduce the chances of infection include getting vaccinated, staying at home, wearing a mask in public, avoiding crowded places, keeping distance from others, ventilating indoor spaces, managing potential exposure durations, washing hands with soap and water often and for at least twenty seconds, practising good respiratory hygiene, and avoiding touching the eyes, nose, or mouth with unwashed hands and avoiding crowded indoor spaces and ventilation

Vaccine

A COVID-19 vaccine is a vaccine intended to provide acquired immunity against severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), the virus that causes corona virus disease 2019 (COVID-19). The COVID-19 vaccines are widely celebrated for their role in reducing the spread, severity, and death caused by COVID-19. Prior to the COVID-19 pandemic, an established body of knowledge existed about the structure and function of corona viruses causing diseases like severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). This knowledge accelerated the development of various vaccine technologies during early 2020. On 10 January 2020, the SARS-CoV-2 genetic sequence data was shared through GISAID, and by 19 March, the global pharmaceutical industry announced a major commitment to address COVID-19.

Treatment

There is no specific, effective treatment or cure for corona virus disease 2019 (COVID-19), the disease caused by the SARS-CoV-2 virus. Thus, the cornerstone of management of COVID-19 is supportive care, which includes treatment to relieve symptoms, fluid therapy, oxygen support and prone positioning as needed, and medications or devices to support other affected vital organs. Most cases of COVID-19 are mild. In these, supportive care includes medication such as paracetamol or NSAIDs to relieve symptoms (fever, body aches, cough), proper intake of fluids, rest, and nasal breathing. Good personal hygiene and a healthy diet are also recommended. The U.S. Centers for Disease Control and Prevention (CDC) recommend that those who suspect they are carrying the virus isolate themselves at home and wear a face mask. People with more severe cases may need treatment in hospital. In those with low oxygen levels, use of the glucocorticoid dexamethasone is strongly recommended, as it can reduce the risk of death. Non invasive ventilation and, ultimately, admission to an intensive care unit for mechanical ventilation may be required to support breathing. Extracorporeal membrane oxygenation (ECMO) has been used to address the issue of respiratory failure, but its benefits are still under consideration.

Prognosis

The severity of COVID-19 varies. The disease may take a mild course with few or no symptoms, resembling other common upper respiratory diseases such as the common cold. In 3–4% of cases (7.4% for those over age 65) symptoms are severe enough to cause hospitalization. Mild cases typically recover within two weeks, while those with severe or critical diseases may take three to six weeks to recover. Among those who have died, the time from symptom onset to death has ranged from two to eight weeks.

The Italian Istituto Superiore di Sanità reported that the median time between the onset of symptoms and death was twelve days, with seven being hospitalized. However, people transferred to an ICU had a median time of ten days between hospitalization and death. Prolonged prothrombin time and elevated C-reactive protein levels on admission to the hospital are associated with severe course of COVID-19 and with a transfer to ICU. Some early studies suggest 10% to 20% of people with COVID-19 will experience symptoms lasting longer than a month.

A majority of those who were admitted to hospital with severe disease report long-term problems including fatigue and shortness of breath. On 30 October 2020 WHO chief Tedros Adhanom warned that "to a significant number of people, the COVID virus poses a range of serious long-term effects." He has described the vast spectrum of COVID-19 symptoms that fluctuate over time as "really concerning". They range from fatigue, a cough and shortness of breath, to inflammation and injury of major organs – including the lungs and heart, and also neurological and psychologic effects. Symptoms often overlap and can affect any system in the body. Infected people have reported cyclical bouts of fatigue, headaches, and months of complete exhaustion, mood swings, and other symptoms. Tedros Adhanom has concluded that therefore herd immunity is "morally unconscionable and unfeasible

Children

While very young children have experienced lower rates of infection, older children have a rate of infection that is similar to the population as a whole. Children are likely to have milder symptoms and are at lower risk of severe disease than adults. The CDC reports that in the US roughly a third of hospitalized children were admitted to the ICU, while a European multinational study of hospitalized children from June 2020 found that about 8% of children admitted to a hospital needed intensive care. Four of the 582 children (0.7%) in the European study died, but the actual mortality rate could be "substantially lower" since milder cases that did not seek medical help were not included in the study.

Complications

Complications may include pneumonia, acute respiratory distress syndrome (ARDS), multi-organ failure, septic shock, and death. Cardiovascular complications may include heart failure, arrhythmias (including atrial fibrillation), heart inflammation, and thrombosis, particularly venous thromboembolism. Approximately 20–30% of people who present with COVID-19 have elevated liver enzymes, reflecting liver injury. Neurologic manifestations include seizure, stroke, encephalitis, and Guillain–Barré syndrome (which includes loss of motor functions). Following the infection, children may develop paediatric multisystem inflammatory syndrome, which has symptoms similar to Kawasaki disease, which can be fatal. In very rare cases, acute encephalopathy can occur, and it can be considered in those who have been diagnosed with COVID-19 and have an altered mental status. In the case of pregnant women, it is important to note that, according to the Centers for Disease Control and Prevention, pregnant women are at increased risk of becoming seriously ill from COVID-19. This is because pregnant women with COVID-19 appear to be more likely to develop respiratory and obstetric complications that can lead to miscarriage, premature delivery and intrauterine growth restriction.

Longer-term effects

Some early studies suggest that ten to twenty percent of people with COVID-19 will experience symptoms lasting longer than a month. A majority of those who were admitted to hospital with severe disease report long-term problems, including fatigue and shortness of breath. About 5-10% of patients admitted to hospital progress to severe or critical disease, including pneumonia and acute respiratory failure.

Immunity

The immune response by humans to CoV-2 virus occurs as a combination of the cell-mediated immunity and antibody production, just as with most other infections. Since SARS-CoV-2 has been in the human population only since December 2019, it remains unknown if the immunity is long-lasting in people who recover from the disease. The presence of neutralizing antibodies in blood strongly correlates with protection from infection, but the level of neutralizing antibody declines with time. Those with asymptomatic or mild disease had undetectable levels of neutralizing antibody two months after infection. In another study, the level of neutralizing antibodies fell four-fold one to four months after the onset of symptoms. However, the lack of antibodies in the blood does not mean antibodies will not be rapidly produced upon re-exposure to SARS-CoV-2. Memory B cells specific for the

spike and nucleocapsid proteins of SARS-CoV-2 last for at least six months after the appearance of symptoms.

Mortality

Several measures are commonly used to quantify mortality. These numbers vary by region and over time and are influenced by the volume of testing, healthcare system quality, treatment options, time since the initial outbreak, and population characteristics such as age, sex, and overall health. The mortality rate reflects the number of deaths within a specific demographic group divided by the population of that demographic group. Consequently, the mortality rate reflects the prevalence as well as the severity of the disease within a given population. Mortality rates are highly correlated to age, with relatively low rates for young people and relatively high rates among the elderly. In fact, one relevant factor of mortality rates is the age structure of the countries' populations. For example, the case fatality rate for COVID-19 is lower in India than in the US since India's younger population represents a larger percentage than in the US, Zhao, et al. (August 2020)

Ethnic differences

In the US, a greater proportion of deaths due to COVID-19 have occurred among African Americans and other minority groups. Structural factors that prevent them from practicing social distancing include their concentration in crowded substandard housing and in "essential" occupations such as retail grocery workers, public transit employees, health-care workers and custodial staff. Greater prevalence of lacking health insurance and care of underlying conditions such as diabetes, hypertension, and heart disease also increase their risk of death.[316] Similar issues affect Native American and Latino communities. On the one hand, in the Dominican Republic there is a clear example of both gender and ethnic inequality. In this Latin American territory, there is great inequality and precariousness that especially affects Dominican women, with greater emphasis on those of Haitian descent. According to a US health policy non-profit, 34% of American Indian and Alaska Native People (AIAN) non-elderly adults are at risk of serious illness compared to 21% of white non-elderly adults.[318] The source attributes it to disproportionately high rates of many health conditions that may put them at higher risk as well as living conditions like lack of access to clean water. Leaders have called for efforts to research and address the disparities. In the U.K., a greater proportion of deaths due to COVID-19 have occurred in those of a Black, Asian, and other ethnic minority background. More severe impacts upon victims including the relative incidence of the necessity of hospitalization requirements, and vulnerability to the disease has been associated via DNA analysis to be expressed in genetic variants at chromosomal region 3, features that are associated with European Neanderthal heritage. That structure imposes greater risks that those affected will develop a more severe form of the disease. The findings are from Professor Svante Pääbo and researchers he leads at the Max Planck Institute for Evolutionary Anthropology and the Karolinska Institutet, (Henry, 2020).

Theoretical foundation

Modelling research has been conducted with several objectives, including predictions of the dynamics of transmission, diagnosis and prognosis of infection, estimation of the impact of interventions, or allocation of resources. Modelling studies are mostly based on epidemiological models, estimating the number of infected people over time under given conditions. Several other types of models have been developed and used during the COVID-19 including computational fluid dynamics models to study the flow physics of COVID-19,[401] retrofits of crowd movement models to study occupant exposure, mobility-data based models to investigate transmission, or the use of macroeconomic models to assess the economic impact of the pandemic. Further, conceptual frameworks from crisis management research have been applied to better understand the effects of COVID-19 on organizations worldwide, (EMA, 2020). In September 2020, the WHO released updated guidance on using corticosteroids for COVID-19. The WHO recommends systemic corticosteroids rather than no systemic corticosteroids for the treatment of people with severe and critical COVID-19 (strong recommendation, based on moderate certainty evidence) (EMA, 2020). The WHO suggests not to use corticosteroids in the treatment of people with non-severe COVID-19 (conditional recommendation, based on low certainty evidence). The updated guidance was based on a meta-analysis of clinical trials of critically ill COVID-19 patients (Public Health Agency of Canada (3 November 2020).

METHODOLOGY

The study adopted adopt a longitudinal design with a population of4, 112,445 (males: 2,069,309; females: 2,043,136) drawn from Delta State, Nigeria. The geographical area occupied by the state measures approximately 18,050 square kilometres (6,970 square miles), with over 60% of this area being comprised of land. The geographic coordinates of the state are situated approximately between 5 degrees 00 minutes and 6 degrees 45 minutes east longitude, and 5 degrees 00 minutes and 6 degrees 30 minutes north latitude. The region under consideration is situated in the Midwestern part of Nigeria. It is surrounded by Edo State to the north and west, Anambra, Imo, and Rivers States to the east,

Bayelsa State to the southeast, and the Bight of Benin to the southernmost point, encompassing approximately 160 kilometres of the state's shoreline. Delta State exhibits a predominantly flat topography, lacking notable elevations or prominent hills. The region exhibits a vast expanse of coastal terrain intricately intertwined with small watercourses and flowing bodies of water, constituting an integral component of the Niger River Delta. Atotal of 72 patients, were included in the study by which 40 were included in the study group and 32 in the control group, 12 patients were excluded from the study due to mutation which affects ivermectin metabolism. They were only given reference treatment. The demographic data and pre-treatment clinical and laboratory findings of the patients were subjected to comparative analysis.

There was no statistically significant difference observed between the study group and the control group in any of the measured parameters. The study by its nature used an all-inclusive sample of subjects who have T2DM-POAG co-morbidity in the 3 geopolitical zones of Delta State. This is similar to method adopted by Frank, et al, 2017 in their sample size selection, All patients received normal hospital treatment as well as one of the following treatments, chosen by chance: • Group 1 will receive ivermectin, given as one or two tablets. There is a 2 in 3 chance of being in this group • Group 2 will receive placebo, given as one or two tablets. There is a 1 in 3 chance of being in this group. Patient information, including blood pressure, pulse rate, temperature, blood oxygen levels, level of consciousness (awareness) and breathing status will be collected daily for 28 days. Weekly Laboratory tests, and swabs from the upper throat, behind the nose (nasopharyngeal) will be collected daily for the first week and then weekly for 28 days.

Heart and lungs was assessed by ECG (electrocardiogram) at screening, Chest X-ray and CT (computerized tomography) scan weekly for 28 days. Further assessments on Day 35, Day 45 and when the study finishes on Day 60 were made. Patient data was collected using standardized case reporting forms on tablet computers. A trial profile will be developed and presented as a flow chart following CONSORT guidelines, consisting of the number of participants screened, eligible, enrolled, randomized, and followed to 1 month, number contributing to primary efficacy outcomes. It included the number of participants who withdrew or were lost to follow-up. Descriptive statistics of baseline characteristics, overall and by treatment group was provided in a table consisting of parameters collected prior to randomization. No statistical comparisons were be made between the groups, but any differences between groups at baseline which are also associated with the outcome variable was taken into account in subsequent analysis, (World Health Organization, 2020).

RESULTS

This study was a prospective, controlled, randomized, single-blind clinical trial conducted from 2020 to 2023. Its objective was to evaluate the efficacy and safety of ivermectin administration in the treatment of patients lacking genetic mutations. The study included patients who were admitted to the hospital with a preliminary diagnosis of severe co-morbidity and subsequently diagnosed with Covid-19. Baseline demographics and characteristics of patients were well balanced between groups (Table 1). All the major senatorial district of Delta State were well represented in the study population, this gives a very comprehensive data for the study. For Delta North, Females were 265(66.3%) which is the highest through various senatorial districts that were studied and the highest for male was found in Delta Central with a mean values of 190(56%) of patients tested as carriers of Covid 19. Majorly in the all the senatorial district major ages of patients with COVID 19 was highest indexed between 40 years and below with values ranging from 298(74.5%), 246(72%) and 209 (70%) for the various senatorial districts respectively while those ages 40 years above the highest was found in Delta North with a value of 102(25.5%). For Body mass of patients with COVID 19 it was found from the table Delta North has a total number of patients with < 30 with a value 289(72%) patients within the and the lies was found in Delta South wuth 110(37%). Also those have body mass index 30 was highest in Delta South with a value of 190(63%) which indicates that patients in Delta South were well taken care off during the period of infection. The marital status of patients which indicates that total of 711(203.%%) of the patients were married and these can probably leave their households expose to the virus even when the Ivermectin were being administered to them across the various senatorial district. While 329 (96.5%) of the whole senatorial district were single (Verdecchia et al., 2020).

Mean effect of side effects of invermectin addition in drugs parameter of patients across various senatorial district are presented in (Table 2). The result shows that Delta South had significant increase in various sides which ranges from loss of appetite, closely followed by weakness of the body and least value was running nose. On the other hand patients in Delta North has the highest to sore throat closely followed by loss of appetite this indicates that the application and addiction of ivermectin has its effects at different levels of application to patients.
The result of patient's recovery and previous vaccinations of affected as affected by COVID-19 is presented in (Table 3) above. Significant ($P<0.05$) difference existed in all the haematological parameters of the patient($P>0.05$). The mean PCV (Packed Cell Volume) (38.63±0.69) and Haemoglobin concentration was significantly ($P<0.05$) different from other (14.12 ± 0.42^{a}). Patient recovery treatment (38.63 ± 0.69^{a} Delta State) had the least mean

Table 1: Baseline demographic and clinical characteristics of patients.

Characteristics		Delta North	Delta Central	Delta South
Gender	Male	135 (33.8%)	190(56%)	134(45%)
	Female	265(66.3%)	150(44%)	166(455%)
	Total	400 (100)	340(100)	300(100)
Age	≤ 40 Years	298(74.5%)	246(72%)	209 (70%)
	≥ 41 Years	102 (25.5%)	94 (28%)	91(30%)
	Total	400(100)	340(100)	300(100)
Body-Mass Index	<30	289 (72%)	190 (56%)	110(37%)
	≥30	111(28%)	150(44)	190(63%)
	Total	400(100)	340(100)	300(100)
Marital Status	Single	98 (24.5%)	120 (35%)	111 (37%)
	Married	302 (75.5)	220 (65%)	189 63%)
	Divorce	-	-	-
	Total	400(100)	340(100)	300(100)

Source: Covid Report 2020

Table 2: Side effects of ivermectin as a result of its addition to standard Covid 19 drugs.

Side Effects	Delta North	Delta Central	Delta South
Running Nose	56.3 ± 0.35^{a}	54.76 ± 0.34^{b}	$44.10\ \pm0.56^{NS}$
Lethargy	54.41 ± 0.55^{a}	34.27 ± 0.53^{b}	54.73 ± 0.33^{b}
Diarrhea	$45.10\ \pm0.53$	$33.10\ \pm0.56^{NS}$	56.44 ± 0.47^{a}
Sore throat	65.31 ± 0.35^{a}	49.73 ± 0.33^{b}	$67.10\ \pm0.53$
Constipation	56.15 ± 0.05^{b}	55.44 ± 0.47^{a}	78.31 ± 0.35^{a}
Weakness	51.31 ± 0.35^{a}	4.27 ± 0.53^{b}	89.15 ± 0.05^{b}
Loss of Appetite	65.15 ± 0.05^{b}	$453.10\ \pm0.56^{NS}$	98 ± 0.47^{a}

Table 3: Relationship between patients' recovery and previous vaccination status.

Parameters	Delta North	Delta Central	Delta South
PCV(%)	36.00 ± 1.47^{b}	37.88 ± 1.39^{a}	$38.63\ \pm0.69^{a}$
HB(g/dl)	13.25 ± 0.60^{cd}	14.12 ± 0.42^{a}	$13.50\pm0.46b^{c}$
WBC x 10^3/ml^3	55.00 ± 15.30^{a}	45.50 ± 16.99^{b}	56.00 ± 17.77^{b}
RBC x 10^6/mm^3	3.63 ± 0.24^{a}	4.48 ± 0.17^{ab}	3.38 ± 0.63^{b}
Plasma Protein (g/dl)	6.25 ± 0.59^{ab}	6.10 ± 0.23^{b}	6.50 ± 0.29^{a}
Neutrophils (%)	50.50 ± 0.50^{c}	$50.75\ \pm0.48^{c}$	53.25 ± 0.75^{b}
Monocytes (%)	2.00 ± 0.00^{a}	2.00 ± 0.00^{a}	0.50 ± 0.29^{c}
MCV (fl)	110.00 ± 12.08^{bc}	106.20 ± 13.15^{c}	121.37 ± 8.20^{a}
MCH (pg)	30.15 ± 3.32^{bc}	35.77 ± 4.36^{c}	26.16 ± 2.52^{a}
MCHC(g/dl)	33.33 ± 0.00^{a}	33.33 ± 0.01^{a}	33.33 ± 0.00^{a}

PCV (36.00 ± 1.47^{b}). White Blood Cell Count (56.00 ± 17.77^{b}) and Red Blood Cell Count ($4.48\ \pm0.17^{ab}$) of patients (0.00%) was observed to be higher ($P<0.05$).

DISCUSSION

It was found that patients who included ivermectin to the HFA combination treatment (study group) had a better rate of clinical enhancement compared to patients who gotten as it were HFA combination treatment (control group). Additionally, at the conclusion of the follow-up period, mortality rates were found to be lower within the study group, compared to the control group accepting as it were HFA combination treatment. Also, by the end of the follow-up period, the SpO2 levels in the study group reached the specified levels (95.4%) and were found to be significantly higher than those in the control group. Similarly, it can be asserted that the addition of ivermectin to the treatment regimen has a more favourable effect on the management of Covid-19 pneumonia compared to the current standard treatment protocol, (Ai et al., 2020).

Conclusion

This study has revealed that ivermectin could potentially serve as an alternative pharmaceutical agent for the management of COVID-19 infection, offering an additional

option alongside existing treatment protocols. Similarly, when administered to individuals with severe cases of COVID-19, this treatment has been shown to result in improvements in clinical recovery, alterations in prognostic laboratory indicators, and reductions in mortality rates. Finally, it is hypothesized that the administration of ivermectin can be conducted with minimal risk of adverse effects in patients lacking mutations in the MDR-1/ABCB1 and/or CYP3A4 genes.

Recommendations

i. That medical practitioners should incorporate and adopt up to 3mg inclusive addiction patient since its has positive health benefits and positive influence on recovery.

ii. For maximum recovery response in the application of ivermectin should not exceed 3mg per dosage.

REFERENCES

ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection. American College of Radiology. 22 March 2020. Archived from the original on 28 March 2020.

Adams, M.L., Katz, D.L.and Grandpre, J. (2020). Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States. *Emerging Infectious Diseases*.26 (8): 1831–1833. doi:10.3201/eid2608.200679. PMC 7392427. PMID 32324118.

Adhikari, S. (2014). Alive Pharmaceutical (P) LTD.: Iver-DT. Alive Pharmaceutical (P) LTD. Archived from the original on March 4, 2016. Retrieved October 7, 2015.

Advice for the public on COVID-19 – World Health Organization. World Health Organization (WHO). Retrieved 18 August 2020.

Agyeman, A.A, Chin, K.L., Landersdorfer, C.B, Liew, D, and Ofori-Asenso, R. (2020). "Smell and Taste Dysfunction in Patients With COVID-19: A Systematic Review and Meta-analysis. *Mayo Clin Proc*. 95(8). 95 (8): 1621–1631. doi:10.1016/j.mayocp.2020.05.030. PMC 7275152. PMID 32753137.

Ai, T., Yang, Z., Hou, H., Zhan, C., Chen, C,andLv, W. et al. (2020). Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology*. 296 (2): E32–E40. doi:10.1148/radiol.2020200642. PMC 7233399. PMID 32101510.

Aristovnik, A., Ravšelj, D. and Umek, L. (2020). A Bibliometric Analysis of COVID-19 across Science and Social Science Research Landscape. *Sustainability*. 12 (21): 9132. doi:10.3390/su12219132.

CDC (2020). Scientific Brief: SARS-CoV-2 Transmission. Centers for Disease Control and Prevention. Retrieved 10 May 2021..

Coronavirus (COVID-19) Update: FDA Authorizes Monoclonal Antibody for Treatment of COVID-19". U.S. Food and Drug Administration (FDA) (Press release). 9 November 2020. Retrieved 9 November 2020. This article incorporates text from this source, which is in the public domain.

EMA endorses use of dexamethasone in COVID-19 patients on oxygen or mechanical ventilation". European Medicines Agency (EMA) (Press release). 18 September 2020. Retrieved 21 September 2020. Text was copied from this source which is European Medicines Agency. Reproduction is authorized provided the source is acknowledged.

https://www.ema.europa.eu/en/documents/other/dexamethasone-covid19-article-53-procedure-assessment-report_en.pdf

Emanuel, E.J., Persad, G., Upshur. R., Thome. B., Parker, M.and Glickman A, et al. (2020). "Fair Allocation of Scarce Medical Resources in the Time of Covid-19". The New England Journal of Medicine. 382 (21): 2049–2055. doi:10.1056/NEJMsb2005114. PMID 32202722.

Epidemiology Working Group ForNcip Epidemic Response, Chinese Center for Disease Control Prevention (February 2020). "[The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]". Zhonghua Liu Xing Bing XueZaZhi = ZhonghuaLiuxingbingxueZazhi (in Chinese). 41 (2): 145–151. doi:10.3760/cma.j.issn.0254-6450.2020.02.003. PMID 32064853. S2CID 211133882.

Fisher, D.andHeymann, D. (2020). Q&A: The novel coronavirus outbreak causing COVID-19. *BMC Medicine*. 18 (1): 57. doi:10.1186/s12916-020-01533-w. PMC 7047369. PMID 32106852.

Gorman, J. (2021). The Coronavirus Kills Mink, So They Too May Get a Vaccine. The New York Times. ISSN 0362-4331. Retrieved 24 February 2021.

Henry, B. M. (2020). COVID-19, ECMO, and lymphopenia: a word of caution. *The Lancet. Respiratory Medicine. Elsevier BV*. 8 (4): e24. doi:10.1016/s2213-2600(20)30119-3. PMC 7118650. PMID 32178774.

Immune responses and correlates of protective immunity against SARS-CoV-2. European Centre for Disease Prevention and Control. 18 May 2021. Retrieved 3 June 2021.

Kucharski, A.J., Russell, T.W., Diamond, C, Liu, Y., Edmunds, J., Funk S, and Eggo, R.M. (2020). Early dynamics of transmission and control of COVID-19: a mathematical modelling study. *The Lancet. Infectious Diseases*. 20 (5): 553–558. doi:10.1016/S1473-3099(20)30144-4. PMC 7158569. PMID 32171059.

National Center for Immunization and Respiratory Diseases (NCIRD) (9 July 2020). COVID-19 Employer Information for Office Buildings". U.S. Centers for Disease Control and Prevention (CDC). Retrieved 9 July 2020.

Oran, D.P. and Topol, E.J. (2021). The Proportion of SARS-CoV-2 Infections That Are Asymptomatic : A Systematic Review. *Annals of Internal Medicine*. doi:10.7326/M20-6976. PMC 7839426. PMID 33481642.

Public Health Agency of Canada (3 November 2020). COVID-19: Main modes of transmission". aem. Retrieved 18 May 2021.

Reardon, S. (2020). For COVID Drugs, Months of Frantic Development Lead to Few Outright Successes. *Scientific American.* Retrieved 10 December 2020.

Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) (PDF) (Report). World Health Organization (WHO). February 2020. Archived (PDF) from the original on 29 February 2020. Retrieved 21 March 2020. Lay summary.

SalajeghehTazerji S, Magalhães Duarte P, Rahimi P, Shahabinejad F, Dhakal S, and Singh Malik Y, et al. (2020). Transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to animals: an updated review. *Journal of Translational Medicine.*18 (1): 358. doi:10.1186/s12967-020-02534-2. PMC 7503431. PMID 32957995.

SARS-CoV-2 RNA testing: assurance of positive results during periods of low prevalence. GOV.UK. Retrieved 19 September 2020.

Shadka, R.H., and Forsman, C.L, (2019).GM-CSF inhibition reduces cytokine release syndrome and neuroinflammation but enhances CAR T cell function in xenografts. *Blood*. 133 (7): 697–709. doi:10.1182/blood-2018-10-881722. PMC 6376281. PMID 30463995.

Vabret, N, Britton, G.J., Gruber, C., Hegde S, Kim J, and Kuksin M, et al. (2020). Immunology of COVID-19: Current State of the Science. *Immunity*. 52 (6): 910–941. doi:10.1016/j.immuni.2020.05.002. PMC 7200337. PMID 32505227.

Vardavas, C.I. and Nikitara, K. (2020). COVID-19 and smoking: A systematic review of the evidence. *Tobacco Induced Diseases*. 18: 20. doi:10.18332/tid/119324. PMC 7083240. PMID 32206052.

Verdecchia, P, Cavallini C, Spanevello, A. and Angeli, F. (2020). The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *European Journal of Internal Medicine*. 76: 14–20. doi:10.1016/j.ejim. 2020.04.037. PMC 7167588. PMID 32336612.

World Health Organization (2020). Corticosteroids for COVID-19: living guidance, 2 September 2020 (Report). hdl:10665/334125. WHO/2019-nCoV/Corticosteroids/2020.1. Lay summary.

Zhao YM, Shang YM, Song WB, Li QQ, Xie H, Xu QF, et al. (August 2020). "Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. *EClinicalMedicine*.25: 100463. doi:10.1016/j.ijtb.2020.11.003. PMC 7654356. PMID 32838236.