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The Treatment Period for Pediatric COVID-19 Patients is Reviewed from the Use of Antibiotics

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Abstract
Antibiotics were used in Covid-19 infection. The study's objective was to examine the children patients' length of stay in Covid 19, those who received antibiotics and those who did not. Fifty-seven children ranging from 1 to 17 years old, consisted of twenty-eight females and 29 males. Fifty-one individuals took antibiotics, whereas six did not. Out of the 51 individuals, 12 received azithromycin, and 39 received ceftriaxone. Patients who get ceftriaxone undergo treatment for seven days, with a minimum of 3 days and a maximum of 29 days. Azithromycin treatment for patients lasts 6.5 days, with a minimum of 3 days and a maximum of 11 days. Patients who were not receiving antibiotics must undergo treatment for a minimum of 2 days and a maximum of 15 days. For pediatric Covid patients, there was no difference in length of stay between those receiving azithromycin, ceftriaxone, or no antibiotics (P=0.684).

Keywords: Antibiotics, Azithromycin, Ceftriaxone, COVID-19, The Treatment Period.

1. Introduction

The World-Health-Organization (WHO) was notified on December-31, 2019, that many cases of pneumonia of undetermined origin had been found in Wuhan City, Hubei Province, China. The virus's name was SARS-CoV-2, and the sickness it caused was COVID-19. As of January 5, 2020, China had 9692 cases recorded, 213 of which were fatal. When COVID-19 affects children, the clinical presentation is frequently mild. Several lower respiratory tract infections may occur[1].

Currently, according to the severity of the symptoms, COVID-19 is categorized into four levels: mild, moderate, severe, and critical. Patients who are mildly ill have minimal or no signs, as well as no prominent radiological findings. Patients who meet one of three criteria—shortness of breath with a respiratory rate (RR) greater than 30, oxygen saturation below 93% in ambient air, or partial pressure of oxygen/fractional inspired oxygen below 300 mmHg—are considered to have severe symptoms. Patients who are critically ill meet one of three criteria: (1) Failure of the respiratory system, (2) septic shock, and (3) failure of numerous organs[2].

Most countries' health systems are currently under urgent and severe threat from the Covid-19 outbreak. However, for two reasons, the latter should emphasize rather than overwhelm the problem of antimicrobial resistance. First, secondary bacterial infections frequently result in mortality during influenza pandemics, as was the case with the 1918 influenza outbreak and the 2009 H1N1 influenza pandemic. Similarly, a Wuhan-based study that examined the outcomes and medical care for 191 patients hospitalized with COVID-19 found that secondary bacterial infections were to blame for 50% of fatalities. Antibiotics are an essential preventative measure against mortality in Covid-19 patients. Second, mortality with Covid-19 is predicted to be significantly impacted by antimicrobial resistance, which is already thought to account for 700,000 deaths annually globally. The Infectious Diseases Society of America modified their recommendations for treating influenza in 2018, no data support the safety or efficacy of antibiotic chemoprophylaxis to prevent bacterial complications." According to the Covid-19 recommendations of the China National Health Commission

(CNHC), "double-blind or improper use of antimicrobial drugs must be avoided, especially broad-spectrum antibiotics[3].

The survey was done in COVID-19 wards at two centres in Singapore on April 22, 2020, at 8:00 a.m., adapting Global-PPS on antibiotic use. Patients receiving systemic antibiotics were included, and the appropriateness of the medication was assessed. Results: A total of 577 people underwent screening. Thirty-six patients (6.2%) who began taking antibiotics on average seven days after the onset of symptoms were on them. These patients received 51 antibiotic prescriptions. Co-amoxiclav was the most often given antibiotic overall (51.0%). Thirty-one out of fifty-one (60.8%) prescriptions for antibiotics were appropriate. 18 (90.0%) of the 20 improper prescriptions were started on individuals who had low chances of having bacterial illnesses. When reviewed by infectious diseases doctors (13/31 [41.9%] as opposed to 2/20 [10.0%], p = 0.015; justifications for use mentioned in notes (31/31 [100%] as opposed to 16/20 [80.0%], p = 0.019); antibiotic prescriptions were more suitable. Despite the low prevalence of antibiotic usage among confirmed and suspected COVID-19 patients at 2 Singaporean centres, a sizable share of antibiotics were used inappropriately in situations where bacterial infections were improbable[4].

The goal of this study was to analized the period of stay for children with COVID-19 who received antibiotics and those who did not.

2. Materials and Methods

This study used secondary data from hospital medical records. For the years 2021–2022, this study will conduct a survey at the Medan City Government Hospital in North Sumatra, Indonesia. The sample of 57 hospitalized children with mild Covid-19 disease. The Kruskal-Walli's test was used to do univariate and bivariate analyses of the data.

3. Results and Discussion

The sample were 57 children, 29 male and 28 female. Age 1-17 years. The treatment period for children with COVID-19 was based on the use of antibiotics.

Table 1: Treatment Period for Children With COVID-19 Based on The Use of Antibiotics.

Period of Treatment on Antibiotics	N	Mean	Std. Deviation	Minimum	Maximum	Std. Error of Mean	Median
Azithromycin	12	6.67	2.060	3	11	.595	6.50
Seftriakson	39	8.10	4.333	3	29	.694	7.00
Without Antibiotics	6	7.50	4.231	2	15	1.727	7.00
Total	57	7.74	3.939	2	29	.522	7.00

Source: Primary Data (2022).

Table 1 **s**hows the sample of 57 children, of which 39 received ceftriaxone, 12 received azithromycin, and 6 did not receive any medications. Ceftriaxone was administered to patients for a 7-day course of treatment, with a minimum of 3 days and a maximum of 29 days. Patients were receiving azithromycin must stay for 6.5 days, with a minimum of 3 days and a maximum of 11 days. Without antibiotics, patients must stay for a minimum of 2 days and a maximum of 15 days.

Table 2: Treatment Period for Children With COVID-19 Based On The Use of Antibiotics.

	Antibiotic Group	N	Mean Rank	P-Value
The Treatment Period	Azithromycin	12	25.42	0,684
	Seftriakson	39	30.13	
	Without Antibiotic	6	28.83	
	Total	57		

Source: Primary Data (2022).

Table 2 shows a sample of 57 children, azithromycin, ceftriaxone, and samples without antibiotics had different lengths of stay. A value of p = 0.000 (p 0.05) was achieved for the normality test using the Kolmogorov-Smirnov test. The information was not distributed normally. The Kruskal-Walli's test yielded p = 0.684 (p > 0.05) for the difference in length of stay between samples receiving azithromycin, ceftriaxone, and no antibiotics. The samples treated with azithromycin, ceftriaxone, and without antibiotics underwent the same amount of time.

Coronavirus is the common name for Coronaviridae and Orthocoronavirinae, also called Coronavirinae. Coronaviruses, which primarily infect birds with a few infecting mammals, - and -coronaviruses only infect mammals. The following human CoVs are also known as 2019-nCoV: -coronaviruses (229E and NL63), -coronaviruses (OC43 and HKU1), severe acute respiratory syndrome-related coronavirus (SARS-CoV), and Middle East respiratory syndrome-related coronavirus (MERS-CoV). The bat-SARS-like (SL)-CoVZC45, bat-SL-CoVZXC21, SARS-CoV, MERS-CoV, and 2019-nCoV are all members of the -coronavirus genus[5].

On April 30 and May 7, 2020, the search was carried out using the Ovid database and Google. The characteristics of the patients, the clinical outcomes, and a few aspects of antibiotic use (indication, class, rates and types of bacterial secondary and co-infection, and length of therapy) were examined. Results: 2834 participants were enrolled in 19 clinical studies that reported data. 74.0% of cases used antibiotics on average. Ten research, or 50% of the investigations, noted the presence of a bacterial co-infection or consequence. In the latter group, at least 17.6% of those who took antibiotics had secondary illnesses. According to data from four trials combined, half of the patients receiving antibiotics were neither critically ill nor in a serious condition[3].

The national prescribing activity in general practice is also reported on a monthly basis by NHS England. These statistics include information on antibiotic use, which the NHS has pledged to lower in order to prevent the development of antibiotic resistance brought on by improper prescription (for instance, for viral diseases like the flu or COVID-19). Between April 1 and August 31, 2020, general practitioners wrote 10 191 805 antibiotic prescriptions, which is 15•48% fewer than the 12 058 979 written over the same time period in 2019. However, this number of prescriptions is 6•71% greater than anticipated (9 551 238), a statistically significant increase (p0•0001) given the decline in the absolute number of appointments throughout this time. The reduction in the overall number of antibiotic prescriptions reflects both the goal of reducing overprescribing and the downward trend in antibiotic consumption in general practice since 2014. The unusually high percentage of prescriptions made during COVID-19 may, however, be related to more cases of inappropriate antibiotic use during telephone consultations[6].

On February 1 through April 30, 2019, the usage of antibiotics before COVID-19 and February 1 through April 30, 2020, during the pandemic's rise, were compared. During the designated COVID-19 period at SGH, the overall number of hospital admissions declined by 16.8% year over year, from 19 589 to 16 300. Additionally, from 130 597 bed days prior to COVID-19 to 113 449 bed days during COVID-19, the number of bed days fell. The usage of broad-spectrum antibiotics grew by 25.5%, with de-fined daily doses (DDD) going from 14.92 to 18.72 per 100-bed days. Examples of these antibiotics include cefepime, piperacillin/tazobactam, carbapenems, and vancomycin. The usage of antibiotics for community-onset pneumonia also increased, moving from 48.74 DDD per 100-bed days to 50.81 DDD per bed days. The COVID-19 pandemic began in February 2020, at which point the DDD of ceftriaxone, co-amoxiclav, levofloxacin, moxifloxacin, azithromycin, and clarithromycin rapidly increased month over month from 47.4 to 54.0 per 100 bed days (see Figure 1). This increase was especially apparent at that time. The average monthly proportion of patients getting antibiotics increased in accordance with the COVID-19 pandemic as compared to the same period the year prior (47.4% vs 49.9%), with the highest proportion being noted at the outbreak[7].

The primary clinical "evidence" for azithromycin's ability to effectively treat COVID-19 infection comes from a 14-day open-label, non-randomized trial with 42 hospitalized COVID-19 patients that were conducted in France. To avoid bacterial superinfection, six patients were given daily dosages of hydroxychloroquine of 600 mg together with 250 mg of azithromycin for the following four days. In contrast to 57.1% of patients getting hydroxychloroquine monotherapy (n = 14) and 12.5% in the control group (n = 16), the researchers found that 100% of patients receiving hydroxychloroquine plus azithromycin (n = 6) on day six after enrollment had no detectable viral load (p 0.001). The methodological issues with this paper have been widely examined elsewhere and include poor reporting, missing PCR data, and the arbitrary exclusion of patients with clinically meaningful outcomes[8].

These weaknesses severely reduce the study's quality and cast doubt on the reliability of its conclusions. Inconsistent outcomes were found in a recent small French study with eleven COVID-19 patients who underwent hydroxychloroquine and azithromycin treatment at the precise dosage recommended by Gautret et al. One of the 11 patients died, two were admitted to an intensive care unit, and one had a prolonged QT interval and had to discontinue receiving medication. Eight patients (73%) had SARS-CoV-2 tests done five to six days after the study's treatment began[9].

Azithromycin (AZM), a synthetic macrolide antibiotic, is effective against certain bacterial and mycobacterial diseases. Due to a wider range of antiviral and anti-inflammatory properties, it has been given to patients with the coronaviruses SARS-CoV or MERS-CoV. It is being investigated as a potential candidate treatment for SARS-CoV-2 now that it has been identified by both in vitro and in silico drug screens as a viable therapeutic for this virus. Even though numerous trials are in progress, there is no randomised trial data on its effectiveness in any novel coronavirus disease. This review summarises findings from in vitro, murine, and human clinical studies on macrolides' antiviral and anti-inflammatory properties, particularly AZM. Numerous virus families, including coronaviruses, influenza A, Zika, Ebola, and rhinoviruses, exhibit decreased in vitro proliferation when AZM is used. In addition to inducing antiviral type I and type III interferon responses, AZM also increases the expression of antiviral pattern recognition receptors. Additionally, AZM has anti-inflammatory properties relevant to severe COVID-19 disease, which is characterised by an overly innate inflammatory response. These properties include suppression of IL-1beta, IL-2, TNF, and GM-CSF. AZM suppresses T cell proliferation by inhibiting calcineurin signalling, mammalian target of rapamycin activity, and NF-B activation. As it concentrates most noticeably in lysosomes, AZM primarily impacts the accumulation, adhesion, degranulation, and death of neutrophils in granulocytes[10].

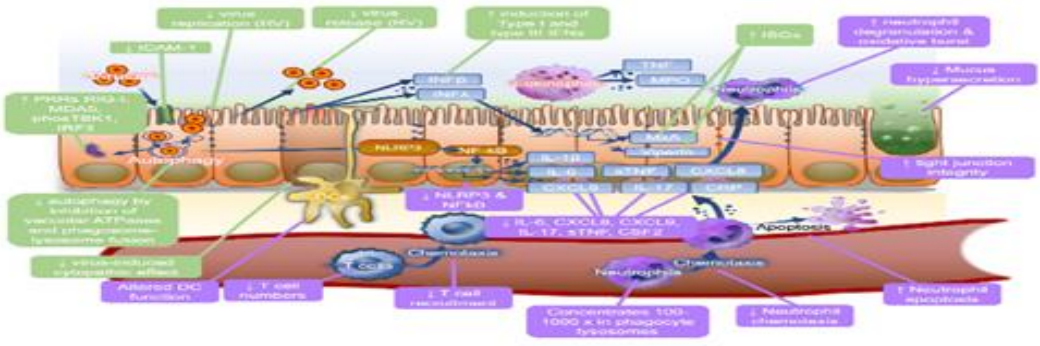

Fig 1: Macrolides' antiviral and anti-inflammatory properties.

An illustration of the critical concepts underlying azithromycin's antiviral (green), anti-inflammatory (purple), or immunomodulatory (purple) effects. Examples of medications include azithromycin, Colony-stimulating factor 2 (GM-CSF), CXCL, and AZM are examples of inflammatory markers. Interferons, interleukins, interferon regulatory factor 3, interferon-stimulated genes, dendritic cells, intracellular cell adhesion molecule 1, pattern recognition receptors, phosphorylated TANK binding kinase 1, melanoma differentiation-associated protein 5, myeloperoxidase, and myxoma resistance protein 1[10].

The antiviral and immunomodulatory effects of azithromycin are supported by scant evidence; this information is not based on outcomes from COVID-19 patients specifically. Because cytokine release syndrome (CRS), also known as cytokine storm, appears to be a primary driver of mortality in COVID-19, many drugs with immunomodulating activity have been proposed as potential treatments repurposed for treating COVID-19 patients in 2020[11] . /[12].

Furthermore, there is no evidence taking azithromycin during COVID-19 reduces the cytokine storm[13]. Additionally, there is some evidence that azithromycin works well against COVID-19-like viral infections. A retrospective cohort study conducted in 14 tertiary-care hospitals found that the use of macrolides (97 patients received azithromycin, 28 received clarithromycin, and 22 received erythromycin) did not reduce 90-day mortality (adjusted odds ratio) in 349 patients with laboratory-confirmed Middle-East Respiratory Syndrome (MERS), which is brought on by a coronavirus related to SARS-COV-2. To date, azithromycin (with hydroxychloroquine/chloroquine) is ineffective against COVID-19, not even for treating viral infections similar to SARS-CoV-2[14].

4. Conclusions

For pediatric Covid patients, there was no difference in length of stay between those receiving azithromycin, ceftriaxone, or no antibiotics (P=0.684). There was no difference in the size of treatment for pediatric Covid patients utilizing azithromycin, ceftriaxone, or no antibiotics.

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