

ORIGINAL ARTICLE

Febrile Neutropenia and Indications for Administration of Antibiotics: A Perspective from PakistanHASSAN MAHMOOD¹, ZIA ULLAH², BILAL HASSAN³, ASMA KAZI⁴, SHEHRBANO BATOOL⁵, FAIZA IRSHAD⁶¹Assistant Professor OF Medicine KEMU and Mayo Hospital Lahore²Assistant Professor Department of Biochemistry Dera Ghazi Khan Medical College DG Khan³Medical Officer Tehsil Headquarters Hospital, Sarai Alamgir, Gujrat⁴Associate Professor Department of Medicine Rashid Latif Medical College Lahore⁵House officer, Medical unit 1 Holy family hospital Rawalpindi⁶MBBS, Mphil Anatomy Associate professor Anatomy University medical & dental college. FaisalabadCorrespondence to: Zia Ullah, Email: ziaullahbirmani@gmail.com, Cell: +92 306 7751310**ABSTRACT****Background & Objectives:** The administration of antibiotics within one hour of the patient's presentation is a conventional treatment aim for febrile neutropenia (FN). The objective of this study was to identify what proportion of children diagnosed with FN had a time to antibiotic administration (TTA) of less than one hour and to understand the causes of the delay..**Place of Study:** Mayo Hospital Lahore**Study Duration:** January 2021 to June 2021**Methods:** The children who presented with FN were the subject of a prospective investigation. The most significant metric of success was the proportion of patients who were administered antibiotics within one hour after the conclusion of the triage process. The presentation's location, the time of day, and the day of the week are all significant predictive variables. An study was conducted on the causes of the delayed TTA.**Results:** Evaluations for TTA were performed on a total of 200 children (mean age: 7 years) diagnosed with FN. The primary impact as a result 60% of parents were able to complete the TTA within sixty minutes. The likelihood of a delayed TTA occurred less frequently when patients were examined when the night was still young. Patients who did not have a focus of care had a higher risk of having a delayed TTA. The infection, both during the evaluations that took place in the oncology daycare and those that took place over the weekend, was found in none. Patients who were seen during the daytime or on the weekends had a longer time to treatment than those who presented at the AM or night or weekdays.**Interpretation & Conclusions:** Antibiotics were administered more quickly to the children who were being monitored for fever. The most significant factors contributing to the delay were admission and the need to await blood levels**Keywords:** Febrile neutropenia, support care, and delay to antibiotics**INTRODUCTION**

The rapid treatment of febrile neutropenia (FN) is a crucial feature in the management of juvenile cancers. This is especially important in developing countries, which have a higher mortality rate in childhood cancer as a result of infections when compared to high-income nations. The morbidity and mortality rates of children who present with FN are quite variable. It only takes a few short hours for a child who appears to be in good health to go from that state to one of septic shock and multiple organ failure. Because of this, it is imperative that every child who is febrile and neutropenic receives immediate medical attention as soon as they check into the hospital. Even if the risk varies based on the phase of chemotherapy, the duration of fever, and the site of infection, the timely administration of the first dose of intravenous antibiotic treatment can prevent major morbidity and mortality. This has been established beyond a reasonable doubt by several investigations conducted in various regions of the world. It has been suggested that the time required to administer antibiotics, or TTA for short, could serve as a potential indicator of the quality of care delivered for infectious diseases. Because the illness in these patients has the potential to spread quickly, the typical time before antibiotics are given is sixty minutes, according to the consensus reached around the world. It appears that there will be more than one obstacle in the way of accomplishing this goal. The delay may be caused by a number of different circumstances, such as the attending physician, nurse, or other logistical considerations. The time it takes to receive the first dosage of antibiotics, also known as TTA, after triaging in the context of a referral hospital in a nation with low to moderate income, was the focus of this study. Additionally, the primary factors that contributed to the delay were investigated

THE MATERIALS AND THE METHODS

This was a prospective cross sectional study on children with malignancy who presented with FN at the Paediatric Haematology-Oncology Unit, Mayo Hospital Lahore . The study focused on

children who were receiving treatment for their illness at the aforementioned facilities. Participants in the study ranged in age from infants to adolescents who had just turned 16 years old. Patients who had fever at the time of their cancer diagnosis, patients who arrived with haemodynamic instability, and patients who had previously been treated with antibiotics for the episode of FN on an outpatient basis were not eligible for inclusion in the study. There was only ever one episode recorded for each patient. The enrollment of patients was carried out using a nonprobability sampling approach. This meant that patients were only included in the study if they fulfilled the requirement of being accessible during the testing period.

Criteria for the Evaluation of the Parameters of the Study: The primary outcome was determined to be the percentage of patients diagnosed with FN who were given antibiotics within one hour of the completion of the triage assessment. The length of the patient's stay in the hospital, transfer to a paediatric intensive care unit (PICU) within 24 hours of admission, and death throughout the course of that particular hospital admission were all considered secondary outcomes. The predictive variables that were investigated for TTA were the time of day, place of presentation, whether symptoms manifested over the weekend or throughout the week, and the presence of a focus of infection. Patients who did not reach the primary goal of receiving antibiotics within one hour of triage were subjected to a root cause analysis to help identify the source of the treatment delay. Antibiotics were administered to patients within one hour of triage as the primary outcome. The presence of a single oral or axillary temperature of less than 38.3 degrees Celsius (101 degrees Fahrenheit) or a temperature of less than 38.0 degrees Celsius (100.4 degrees Fahrenheit) for more than or equal to one hour; and an absolute neutrophil count are diagnostic criteria for febrile neutropenia (FN). The time that the physician spent charting antibiotics is the one that is entered into the patient's chart, whereas the time that the nurse spent administering the antibiotics is the one that gets entered. In most cases, a peripheral cannula is put instead of a central line, which is because central lines are only utilised sometimes. The patient's

family is responsible for purchasing the antibiotics from the pharmacy, and the nurse will be the one to prepare the medicines for administration to the patient. When a kid is in the intensive phase of treatment, antibiotics are frequently administered prior to the receipt of blood count results because it can take anywhere from two to four hours to acquire a complete blood count report. When we were carrying out the research, the laboratory reports that we used were not yet digitized.

Possible Indicators of Delayed Administration Include the Following: The time of presentation, the location of presentation (PODC, HO ward, or clinic), and the presence of a focus of infection were among these factors. The presentation was broken up into three parts: morning (9:00 AM to 5:00 PM), afternoon (5:00 PM to 10:00 PM), and evening (10:00 PM or later). Our hospital operates on a five and a half day work week, therefore weekdays began at 2:00 PM on Monday and ended on Saturday. Weekends lasted from Saturday afternoon until Monday morning at 9:00AM. Patients who received parenteral antibiotics but still had normal temperature readings were not included in the study because they did not meet the inclusion criteria. Patients were selected at random for participation in the study, and the physician conducting the research documented the patients' clinical histories on the study's case record form at the time of patient enrollment. Within the first twenty-four hours after admission, participants were enrolled in the study. (i) The physician level delays included (a) not being informed regarding the patient, (b) being occupied with other work, (c) waiting for blood results, (d) being uninformed of the need for antibiotics, (e) making the decision to defer parenteral antibiotics. (f) difficulty gaining access to the intravenous line; (ii) delays at the nursing level (a) they were not told about the patient, (b) they were late in preparing the antibiotics, (c) they were busy with other duties, (d) the patient did not have intravenous access.

Anexamination of the Statistics: Measures of central tendency (mean, median, and mode) and measures of dispersion (standard deviation, interquartile range (IQR)) were included in the descriptive analysis of continuous variables, while frequencies and proportions were included in the study of categorical variables. The effect size measure of odds ratio was used to conduct the analysis on the outcome variable of time to obtain antibiotics after hospitalization. This variable was studied as a dichotomous variable, with the categories "60 min" and ">60 min." The non-parametric Mann–Whitney U test and the Chi-square test, along with Fisher's adjustment where necessary, were utilized in order to conduct statistical research on univariate risk factors associated with delayed administration of antibiotics (beyond 60 minutes). All statistical tests were conducted with two branches, and an hour and a half was chosen as the lower limit of significance. There was a correlation found between delayed TTA and the possible predictor variables, which included the time and site of presentation, as well as the presence of a center of infection.

RESULT

In terms of the time of presentation, the odds of delayed TTA in participants who were evaluated during the day were (OR=1.29; CI; 0.69 -1.98; P=0.26) greater than those evaluated at other times, although this difference was not statistically significant. In a similar vein, the odds of delayed TTA in patients seen in the evening were greater(OR=1.14; CI; 0.60-2.17; P=0.67) in comparison to those evaluated during the day and night, although this difference was not statistically significant. It is interesting to note that the majority of patients who presented at night (78%) had a TTA of less than sixty minutes. The odds of having a delayed TTA (OR=0.39; CI; 0.12-1.10; P=0.051) at night were lower in comparison to other times, but this difference did not reach statistical significance. The odds of having a delayed TTA were higher over the weekend (OR = 1.11; 9 CI;0.4-1.99; P = 0.84). In terms of the place of presentation, it was discovered that the chances of a delayed TTA were higher in participants who were evaluated in the PODC as opposed to those who were evaluated in other areas (such as the Paediatric Oncology Clinic and the HO

ward), despite the fact that this finding was not statistically significant. (OR=1.40; CI; 0.72-2.61; P=0.56). 26 percent of the total number of participants who had a delayed TTA were seen in the PODC.

The odds of delayed TTA were higher (OR=1.68; CI; 0.69-3.99; P=0.39) in participants who had no focus of infection at the time of the study's presentation as compared to children who had a focus of infection at the time of the study's presentation. Table II presents the correlation that can be found between TTA and a number of other predictor factors. In children with a TTA of less than sixty minutes, the average length of hospital stay was 7.7 days, while it was 6.6 days for individuals whose TTA was greater than sixty minutes (P = 0.34). After only 24 hours in the hospital, however, three of the patients required admission to the paediatric intensive care unit. None of the people who participated in the study passed away while they were being admitted. An investigation of the factors that led to the delay at the physician or nursing level, as well as other logistical problems, was conducted through the use of root cause analysis. The reason for the obstruction, which resulted in a delayed TTA, is detailed in Table II below. It was discovered that there was a delay at more than one level in twenty of the incidents (28 percent). TTA was delayed for 61 out of 100 patients because of the waiting time at the physician level. The most common explanations given were that the physician was waiting for the results of a blood test (43%), was occupied with another patient (19%), and was delaying making a choice for antibiotics (13%).Twenty-three out of Hundred patients experienced a delay that could be attributed to the nursing level, and the preparation of antibiotics was the cause of a delay in sixty-five percent of the cases. A total of 27% of delays might be attributed to the fact that the nursing staffs were preoccupied with ot activities. It was shown that eight percent of delays occurred as a result of the nurse not having enough information of the patient. It was found that the distribution of pharmaceuticals had to be delayed because of logistical issues in 31 out of 100 patients (31 episodes), which accounts for 31 percent of all delays. The length of time it took to obtain an inpatient file and a bed in the ward was the most common cause, accounting for 62 percent of the observed delays. The remainder of the delays might be attributed to the length of time it took to acquire antibiotics.

Reason for delay	Number (%)
Physician level	61 (61)
Nursing level	23 (23)
Logistical issues	31 (31)
Other	5 (5)
Total	100 (100)

Focus of infection	Number (%)
No focus of infection	39 (39)
Focus of infection	61 (61)
Total	100 (100)

Figure 1:

DISCUSSION

The amazing rates of childhood cancer remission were one of the most important medical advances of the 20th century. However, death owing to sepsis remains an issue in the care of tumours with the potential for rapid escalation of infection in children with low white blood cell counts due to chemotherapy or cancer. This can be a problem since tumours can lead to the rapid spread of infection in youngsters. In the case of a child with FN symptoms,

the initial dose of antibiotics must be administered as quickly as feasible. In an oncology ward with competing demands, such as a low doctor-to-nurse ratio and a large number of patients, it may be challenging to do any work within the allotted time frame. This is especially true in countries with a low-to-middle income. Despite the obvious simplicity of the concept, achieving high levels of compliance with the early administration of antibiotics can be difficult. Despite the fact that the concept is straightforward, this is the case. It has been suggested that the prompt administration of antibiotics could serve as a quality indicator for oncology centres that treat neutropenic and febrile patients. However, only a small number of research have explored the prevalence of antibiotic delay in FN12 as well as its predictive factors. Sixty-seven percent (67%) of our patients received antibiotics within the sixty-minute time limit that was established for this purpose. In clinical trials involving adults, the time necessary to administer antibiotics correctly ranged between 106 and 210 minutes. Only one study found that 80 percent of children received antibiotics within the minimum time period of two hours. trials reported that none of the patients had been given antibiotics within the provided hour. It takes an average of 75 minutes from the time of admission to the emergency room till the patient is examined, 210 minutes to obtain antibiotics, and 5.5 hours for the patient to be admitted to the hospital. A initiative aimed at reducing treatment delays for patients with FN revealed three areas for improvement: 1 inpatient orders, the admission communication process, and multidisciplinary staff accountability. The cycle time on the inpatient unit dropped by roughly fifty percent once these modifications were made. Through research, it was revealed to what extent predictor variables such as time of presentation during the day and week, place of examination, and focus of infection all contributed to a delay in TTA. Patients who were checked in the middle of the night received antibiotics faster than patients who were evaluated at any other time of day. It was made extremely apparent to the resident staff who worked evenings and nights that they were required to respond as quickly as humanly possible to these patients. This, along with the apparent belief that a patient arriving at night is more likely to be ill and should not be kept waiting, could explain the shorter TTA at night compared to the daytime. Unexpectedly, the fact that the daycare had been running behind schedule was found. It is likely that the delay was caused by daycare employees juggling multiple conflicting obligations simultaneously. 66% of patients admitted on weekends experienced a longer time to admission (TTA) than 34% of patients admitted during the week; however, this difference was not statistically significant. Patients admitted on weekends had a lengthier time to admission (TTA) than those hospitalised during the week. Similar to a previous study, this one indicated that a greater proportion of patients who arrived on the weekend experienced adverse occurrences in their composite. Due to the fact that both studies were conducted throughout the same time frame, they were identical.

On the weekend, there may be a lesser number of medical professionals accessible to answer calls. This is a possible outcome. Patients tested in the clinic (on Tuesdays and Fridays) had a 20% lower probability of having a delayed TTA when compared to patients evaluated at any other site. This was true independent of the age of the patient. The TTA for patients who presented to the emergency room was 145 minutes longer than for patients who presented to the inpatient unit (60 minutes) or the clinic. These discoveries were made by Fletcher and colleagues. A survey of paediatric cancer centres found that a fraction of kids presenting to the emergency room had a mean TTA greater than sixty minutes. In contrast, a much smaller number of patients presented themselves to the outpatient department and inpatient facilities. According to the study, a delayed TTA is not only associated with a longer hospital stay and an unfavourable outcome, but it also has no link with death or hospitalisation duration. This is the conclusion that can be derived from the studies conducted. There appears to be no correlation between the late delivery of the antibiotics and the investigation's findings, at

least none that we could uncover. It cannot be stressed enough that youngsters with poor hemodynamics were not allowed to participate in this study. This limitation was rigorously enforced. The most significant factors that contributed to the delay were the time spent waiting for blood test results, the time spent preparing antibiotics, the time required to receive an inpatient file, and the procedure of assigning a bed. Several studies indicate that the availability of laboratory data, medical evaluation, and intravenous access are among the most significant factors that contribute to delay. The provision of antibiotics to individuals diagnosed with FN is also delayed since a complete blood count is required before a medical evaluation can be performed. By making an emergency antibiotic box available to First Nation children who are treated at the PODC and the HO ward, it is possible to save a large amount of time that would otherwise be spent preparing and acquiring medications. Even at the best-run clinics, administrative issues about the availability of beds might be challenging. Antibiotic therapy should be administered to patients as they wait for a bed, and every effort should be made to do this. In order to prevent a delay in treatment, it is feasible to consider initiating antibiotic therapy in a child who appears to be ill prior to the diagnosis of neutropenia. This is done to guarantee that the youngster receives prompt treatment. Due to the difficulty of coordinating the necessary logistics, participation in the trial was restricted and not randomised. Unfortunately, this is one of the issues with the research. The fact that residents and nurses knew they were participating in the study may have contributed to bias. To reconstruct the sequence of events that led to the delay, the investigators relied on the memories of the doctors and nurses who participated in the investigation. The instances of children who appeared with compromised hemodynamics were excluded from our study since they were treated according to the emergency protocol. In accordance with the emergency protocol, children with compromised hemodynamics were treated. According to the findings of this study, 67% of our patients in settings with limited access to resources met the surviving sepsis campaign's recommended target time to antibiotic administration (TTA) of 60 minutes. This objective was set by the sepsis survivor campaign. After performing a comprehensive examination into the causes of the TTA, it was determined which components of the TTA could be improved by the implementation of focused interventions. A speedy evaluation approach, the availability of an emergency antibiotic trolley or box, and an automatic token system that alerts the on-duty staff to the patient's presence are essential interventions to improve the quality measure. This should be the standard operating protocol for all child cancer units. As a direct outcome of this study, we have installed an antibiotic emergency box and instructed the ward staff to dispense antibiotics before assigning beds. In later investigations, we will be able to examine how the numerous steps done have affected the TTA.

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