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ORIGINAL ARTICLE

Frequency of Resistance to Third Generation Cephalosporin in Neonates with Septicemia at a Tertiary Care Hospital

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ABSTRACT

Background and Objective: Sepsis in newborns is a serious medical issue everywhere [1]. With an incidence of 1 to 10 per 1000 live births worldwide, newborns are more susceptible to developing bacterial sepsis [2]. With a sepsis-related mortality rate of up to 50% for untreated neonates, the problem of sepsis is significantly more prevalent in poor nations than in industrialised ones. Neonatal sepsis is a clinical illness that affects infants younger than 28 days of age and is characterised by a variety of generalised, non-specific systemic symptoms [3]. Therefore, this study was conducted to determine the frequency of resistance to 3rd generation cephalosporin in neonates with septicemia at a tertiary care hospital.

Materials and Methods: A cross-sectional study was conducted at the NICU of the Aga Khan University Hospital Karachi and nursery departments of the four affiliated secondary care Hospitals from December 2020 to December 2021. We included 477 neonates with sepsis aged 0 to 28 days of life using the non-probability consecutive sampling method. Data were analysed in SPSS version 23.0. All categorical variables were presented as frequencies with percentages, and continuous variables (were presented as mean ±SE. Poststratification applies in gchi-squaretest taken p-value less than equal to 0.05 taken as significant.

Results: A total of 377 patients were enrolled. Majority of the patients were preterm neonates, and 70% of the bacterial isolates were resistant to cefotaxime or ceftazidime. 36(9.5%) neonates had bradycardia, 301(79.8%) of neonates had tachycardia, 294 (78%) of neonates had tachypnea, 153 (40.6%) of neonatal sepsis suffered from hypothermia, and 121 (32.1%) of neonatal sepsis patients had a depressed TLC count.

Conclusions: We conclude that frequent use of cephalosporin antibiotics has evolved into a high resistance burden. We need local guidelines for the empiric use of antibiotics to cut down the use of cephalosporin, infection control policies to break the chain of infection transmission.

Keywords: Neonatal Sepsis, Early-Onset Sepsis, Blood Culture. Cephalosporin Resistance,

INTRODUCTION

Sepsis in newborns is a serious medical issue everywhere [1]. With an incidence of 1 to 10 per 1000 live births worldwide, newborns are more susceptible to developing bacterial sepsis [2]. With a sepsis-related mortality rate of up to 50% for untreated neonates, the problem of sepsis is significantly more prevalent in poor nations than in industrialised ones. Neonatal sepsis is a clinical illness that affects infants younger than 28 days of age and is characterised by a variety of generalised, non-specific systemic symptoms [3].

Early-onset sepsis (EOS) is defined as infections that appear during the first 72 hours of life and are typically transmitted during childbirth by mothers, while late-onset sepsis (LOS) is defined as infections that appear within the first three days of life and are acquired postnatally [4]. Neonatal sepsis is caused by a variety of pathogens; studies from underdeveloped nations tend to focus on Gram-negative organisms more frequently [5, 6], however Gram-positive species have also been noted [6,7, 8].

Early neonatal sepsis often has different susceptibility patterns than late neonatal sepsis; hospital acquired late sepsis is likely to have more resistant organisms than vertically transmitted, community-acquired early sepsis. But according to a paper from a developing nation, some resistant microbes can really cause early newborn sepsis [9]. Neonatal sepsis requires rapid empirical antibiotic therapy because it is a life-threatening condition. It's crucial to select an antibiotic cocktail that protects against the most prevalent pathogens [10]. Despite its limited sensitivity, which may be caused by the tiny blood sample size or the use of empirical antibiotics prior to collection, blood culture is still the gold standard for the diagnosis of newborn sepsis [11]. Therefore, in this study, we observed the frequency of resistance to 3rd generation cephalosporin in neonates with septicemia at a tertiary care hospital.

MATERIALS AND METHODS

A cross-sectional study was conducted at the NICU of the Aga Khan University Hospital Karachi and nursery departments of the four affiliated secondary care hospitals. Three hospitals are located in Karachi: The Aga Khan Hospital for Women, Karimabad, Karachi; The Aga Khan Hospital for Women, Garden, Karachi; The Aga Khan Hospital for Maternal and Child Care, Kharadar, Karachi; and one secondary care level is located in Hyderabad, The Aga Khan Hospital for Maternal and Child Health Care, Hyderabad.

We included 477 neonates with sepsis aged 0 to 28 days of life using the non-probability consecutive sampling method. All the term and preterm neonates with culture-proven sepsis admitted at the study settings were included in the study. However, neonates with no growth or growth of non-bacterial isolates such as fungus in the blood culture and neonates without willing mothers were excluded from the study.

This study was conducted with the approval of the Hospital Ethical Review Committee. Subjects who fulfilled the eligibility criteria were enrolled in the study. The sensitivity patterns were determined using the Kir-Bauerdisk diffusion method using standard guide lines recommended by CLS I. [12] Neonates with a diagnosis of culture-proven sepsis or neonatal sepsis made by the primary physician were enrolled in the study, and a blood culture sensitivity pattern for cefotaxime and Ceftazidime was recorded. Besides the socio-demographic data, the clinical history of the neonate, including history of fever, hypothermia, tachycardia, bradycardia, and tachypnea, was documented.

The final diagnosis and blood culture growth of the isolate, the name of the isolate, and the sensitivity patterns of the isolate to the 3rd generation cephalosporins (Cefotaxime and Ceftazidime) were documented. The data were analysed in SPSS (Statistical Package for Social Sciences) version 20.0. All categorical variables were presented as frequencies with percentages, and continuous variables (were presented as mean ±SE. Poststratification: applying the chi-squared test to a p-value less than or equal to 0.05 is taken as significant.

RESULTS

In the Present study, 377 patients who fulfilled the inclusion criteria were enrolled. All neonates admitted to the NICU and/or nursery

and/or neonatology ward through the emergency department, operating room, labor rooms, and consulting clinics of the department of paediatrics at the Aga Khan University Hospital had their blood culture samples sent routinely to the clinical laboratory of the Aga Khan University Hospital.

In this study, the mean age, gestational age, and birth weight 7.69±5.41, 36.80±5.80 and ,2.90±0.90 respectively. Table I

Table 1: Descriptive Statistics of the Numerical Variable in the Study

Variables	n	Mean	Standard Deviation
Age	377	7.69	5.41
Gestational Age	377	36.8	5.8
Birth Weight	377	2.9	0.9

In this study, there were 250(66.3%) study participants having gestational age less than 37 weeks and 127(33.7%)having more than37week of gestational period. There were 145 (38.5%) female study participants and 232(61.5%) were male. There were 155(41.1%) participants with early onsetand222(58.9%) with late on set. There were 188(66.3%) multipara mothers and 189(33.7%) primipara mothers. Table II

Table 2: Frequency Distribution of the of Sociodemographic Characteristics of the Participants

Variable	n	%
Gestational Age		
<37 WEEKS	250	66.3
>37 WEEKS	127	33.7
GENDER		
FEMALE	145	38.5
MALE	232	61.5
ONSET		
EARLY ONSET	155	41.1
LATE ONSET	222	58.9
PARITY		
MULTI	188	66.3
PRIMI	189	33.7

Table 3: Frequency of the Symptoms among study Participants

Variable	n	%
BRADYCARIA		
NO	341	91
YES	36	9.5
TACYCARDIA		
NO	76	20
YES	301	80
TACYPNEA		
NO	83	22
YES	294	78
H/O FEVER		
NO	160	42
YES	217	58
HYPOTHERMIA		
NO	224	59
YES	153	41
TLC		
DEPRESSED	121	32
ELEVATED	117	31
NORMAL	139	37
BAND CELL		
NO	350	93
YES	27	7.2
CEFOTAXIME		
SENSITIVE	164	44
RESISTANCE	213	57
CEFTAZIDIME		
SENSITIVE	325	86
RESISTANCE	52	14
ANTIBIOTIC RESISTANCE		
RESISTANCE	265	70
SENSITIVE	112	30

In this study, 36 (9.5%) neonates had bradycardia, 301 (79.8%) had tachycardia, 294 (78%) had tachypnea, 217 (57.6%) of neonatal sepsis patients had a history of fever, and 153 (40.6%) of neonatal sepsis patients suffered from hypothermia. Distribution of TLC showed that 121 (32.1%) of neonatal sepsis patients had a depressed TLC count, and 117 (31.3%) had an elevated TLC. Distribution of band cells showed that 350 (92.8%) of neonatal sepsis patients had no band cells. In this study, 164 (43.5%) neonates were sensitive to cefotaxime, 325 (86.2%) patients were sensitive to ceftazidime, and in general, 265 (70.3%) patients were sensitive to the 3rd-generation cephalosporin. Table III

Table IV shows the stratification of third-generation cephalosporin resistance with regards to age, gestational age, gender, onset of neonates, parity, TLC count, and band cells separately, where age showed significance with (p-value=0.001), gestational age showed significance with (p-value=0.027), and gender showed significance with(p-value=0.020) where onset showed insignificance with (p-value = 0.356), where parity showed in with (p-value = 0.356), where TLC showed significance with (p-value = 0.010), and where band cells showed significance with (p-value = 0.001).

Table 4: Chi Square Association of Various factors with Antibiotic Resistance

Variable	n	Resistance		P- Value
		Resistant	Sensitive	
AGE GROUP				
<10	235	195	40	0.001
>10	142	70	72	
GESTATIONAL AGE				
<37 WEEKS	250	185	65	0.027
>37 WEEKS	127	80	47	
GENDER				
FEMALE	145	112	33	0.02
MALE	232	153	79	
ONSET				
EARLY ONSET	155	105	50	0.356
LATE ONSET	222	160	62	
PARITY				
MULTI	188	127	61	0.256
PRIMI	189	138	51	
TLC				
DEPRESSED	121	94	27	0.01
ELEVATED	117	86	31	
NORMAL	139	85	54	
BAND CELLS				
NO	350	255	95	0.001
YES	27	10	17	

DISCUSSION

The primary cause of illness and mortality among newborns is neonatal sepsis. Regular epidemiological surveys of etiologic agents and their antibiotic sensitivity patterns can help identify the most frequently encountered bacteria in a given area, reducing the uncertainty around the clinical strategy for treating neonatal septicemia. Studying the bacteriological profile and antimicrobial sensitivity pattern is important for the efficient management of septicaemia sufferers [13].

In the present study, the mean age, gestational age, and birth weight 7.69±5.41, 36.80±5.80 and,2.90±0.90 respectively. There were 145 (38.5%) female study participants, and 232 (61.5%) were male. Like our findings, other studies have shown male predominance [14]. In the present study, the distribution of TLC showed that 121 (32.1%) of neonatal sepsis patients had a depressed TLC count and 117 (31.3%) had an elevated TLC. Gram-negative species predominated (54.6%) compared to gram-positive organisms (45.4%), according to a 2010 study by Muhammad et al. [15].

According to a study from Bangladesh, PROM causes 29.2% of septicemia. According to reports from India, VLBW are more vulnerable, and 50–60% of septic neonates are preterm infants [16]. In the present study, There were 155 (41.1%) participants with early onset and 222 (58.9%) with late on set.Concerning the timing of EOS and LOS, there is disagreement. Early onset may take two to seven days [17–19]. In addition to varying between EOS and LOS, developing and developed counties also have different bacteriological profiles. Gram-positive organisms predominate in both EOS and LOS in industrialised areas, but GBS is more common in EOS. Gram-negative

organisms are more common in EOS and LOS in underdeveloped nations, while E. coli is more common in EOS [20, 21]. Since the first 7 days were deemed to be the earliest onset, our series' EOS was fairly high (70.7%) [19–22].

In this study, 164 (43.5%) neonates were sensitive to cefotaxime, 325 (86.2%) patients were sensitive to ceftazidime, and in general, 265 (70.3%) were sensitive to the 3rd-generation cephalosporin.

Ipenem, ciprofloxacin, gentamicin, and cotrimoxazole are the most sensitive medicines. Costly imipenem and insufficient safety evidence for ciprofloxacin are both factors. Different generations of cephalosporin are no longer effective against some bacterial strains. In wealthy nations, 10–20% of all newborns are treated for suspected sepsis, yet only 1–10/1000 live births have significant sepsis [17]. Bacterial patterns are constantly shifting with respect to time and location. Due to the indiscriminate usage of commonly used antibiotics, previously susceptible organisms are quickly developing resistance, making treatment challenging and expensive.

In conclusion, third-generation cephalosporin is the most commonly used antibiotic in neonatal wards, and septicemia is the most common infection. By periodically examining the etiological agent and their pattern of antibiotic susceptibility, the ambiguity surrounding the selection of antibiotics can be reduced [23, 24]. Antibiotic resistance is spreading around the world and is now a severe public health issue in both hospitals and the general population. Treatment failure, higher morbidity and mortality, as well as higher costs, have all been linked to infections with resistant microbes. As a result, the development, implementation, and evaluation of policies for the use of antibiotics have become necessary [25–27].

CONCLUSION

The bulk of newborn sepsis cases are early-onset infections, which account for roughly one-third of the health issues in neonatal wards. The most common infection observed is septicemia, and the antibiotic of choice for treating it is a pricey third-generation cephalosporin.

We conclude that frequent use of cephalosporin antibiotics has emerged as a high resistance burden. We need local guidelines for the empiric use of antibiotics to cut down on the use of cephalosporin and infection control policies to break the chain of infection transmission.

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