Journal of Pharmaceutical Research International

32(25): 106-111, 2020; Article no.JPRI.62026
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Neonatal Bacterial Sepsis and Its Susceptibility Pattern in Neonatal Care Unit of Tertiary Care Hospital

Abdul Hameed Tunio[1*], Delijan Mugheri[1], Muhammad Khan[2], Wasim Sarwar Bhatti[2], Abdul Majeed Soomro[2], Pir Bux Ghumro[3], Sultan Othman Alolayan[4,5], Waseem Abbas Malhani[6], Nadeem Baloch[6], Altaf Ali Mangi[7], Zehra Ahraf[8], Saika Lashari[3], Kanwal Baloch[6] and Shumaila Parveen Arain[4,5]

[1]Shaheed Mohtarma Benazir Bhutto Medical University, Pakistan.
[2]Pir Abdul Qadir Shah Jillani Institute of Medical Science Gambat, Pakistan.
[3]Shah Abdul Latif University, Khairpur, Pakistan.
[4]Faculty of Pharmacy, University of Sindh Jamshoro, Pakistan.
[5]College of Pharmacy, Taibah University, Al-Madinah Al-Munawarah, Saudi Arabia.
[6]Institute of Pharmacy, Shaheed Mohtarma Benazir Bhutto Medical University, Pakistan.
[7]Faculty of Pharmacy, Gomal University, DI Khan, Pakistan.
[8]Faculty of Pharmacy, Jinnah University for Women Karachi, Pakistan.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AHT, PBG, SOA, DM and MK involved in conception or design of work. Authors AMS, AAM, WSB and SPA involved in data interpretation. Authors WAM, NB, ZA, SL and KB involved in data collection and drafting of the work. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2020/v32i2530828
Editor(s):
(1) Dr. Syed A. A. Rizvi, Nova Southeastern University, USA.
Reviewers:
(1) Uri Adrian Prync Flato, University of Marilia, Brazil.
(2) Pricilia Gunawan Halim, Lambung Mangkurat University, Indonesia.
Complete Peer review History: http://www.sdiarticle4.com/review-history/62026

Original Research Article

Received 05 August 2020
Accepted 11 October 2020
Published 28 October 2020

ABSTRACT

Background: The drug resistance and pathogens are different in various Hospitals of any country. Very high resistance pattern is observed nowadays to the frequently used antibiotics. The important observation has been noted that most of the doctors do not obtain blood cultures before start of the

**Corresponding author: E-mail: drahameedpk@yahoo.com;*

antibiotics, which becomes competent source of resistance. For the same purpose, this study has been done to find out the responsible microbes causing ailment and their susceptibility towards antibiotics to plan early and effective management.

Materials and Methods: A number of 100 new borns admitted in the NICU CMC Children Hospital Larkana with signs and symptoms of sepsis were included in this research work. The study will help in provision of a comprehensive record on microorganisms causing sepsis in the neonates and their antibiotic sensitivity. The epidemiology and presence of neonatal sepsis in particular area makes it more easy and convenient to implement the rationale of empirical antibiotic strategy.

Results: From100 neonatal blood samples taken for culture, only 21 proved to be positive which stands 21%. In majority gram positive bacteria were found in (85.71%=18 cases) and gram negative bacteria stood (14.28%=3 cases).Staphylococcus species were found on the large scale (52.38%=11 cases) secondly Streptococcus species (33.33%=7 cases) and the remaining were Escherichia species being least common (14.28%=3 cases).

Conclusion: Staphylococcus species provided major share as gram positive bacteria and Escherichia species were found to be major gram negative bacterial population responsible for neonatal sepsis. Profound resistance pattern is seen against widely used antibiotics. It is mandatory to have a routine check over the antibiotic resistance.

Keywords: Neonates; bacterial sepsis; antibiotics; susceptibility pattern.

1. BACKGROUND

Neonatal sepsis refers to the positivity of the septic focus in the blood of a newborn in the setting of fever, also referred as "sepsis neonatorum". Clinically presumed with the presence of symptoms and signs in initial 28 days of age of the newborn [1,2]. The significant source of illness and death in all the neonates, is the internal reaction of the toxins released by microbes and host factors specially cytokines and other mediators [1,3]. Prenatal death rate is 50-60/1000 and newborn death rate is 50/1000 [1,4]. According to WHO the frequency of newborn infections in developed world is 1-10/1000 live well born, whereas approximately 3 fold greater within under developed countries.

The causative agents or micro-organisms may vary from one era to another by the time but also from one destination to another. Accurate reason is not known but socioeconomic, geographic, irrational use of antibiotics and season may be the major role player. In developed countries coagulase negative *Staphylococci* and group B *Streptococci* are the most wide spread causes for late onset and early onset sepsis accordingly [5,6]. In under developed or third world countries these microbes are occasional with a totally variable microbial scenario. The microbial report of newborn septicaemia is continuously changing with application of new techniques in early diagnosis and treatment [5,6]. Diagnosis of neonatal sepsis is almost very critical. Modalities are available for neonatal sepsis including, CBC, C - reactive protein and ESR but blood culture and platelet count is the highest quality level [1,7].

The aim of this study was to isolate and identify the most possible bacterial etiological agents being responsible for neonatal infections and determine their antibiotic susceptibility pattern in neonatal sepsis as antibiotic resistant is one of the most common cause of infectious disease related death all over the world.

2. MATERIALS AND METHODS

This study was conducted after approval from the Board of Advanced Studies and Research Shah Abdul Latif University Khairpur. The objective of this research was, to find out bacterial aetiological agents and their antibiotic susceptibility pattern in Neonatal Intensive Care Unit (NICU) Chandka Medical College Children Hospital Larkana.

All the neonates of Age (1-28 days) of life, Clinically suspected cases of neonatal sepsis are included in this study and patients with age greater than 28 days and who were receiving antibiotic in last three days were excluded from the study.

2.1 Sample Collection Method

3 to 5 ml of blood were collected from each suspected neonatal sepsis case after ensuring proper aseptic measures on behalf of clinical signs and symptoms, admitted in NICU CMC Children Hospital Larkana. Collected blood samples were immediately inoculated under

aseptic measures into Tryptic soy broth containing bottles (Blood culture bottles) and incubated at 37°C for 2 to 5 days.

2.2 Antibiotic Sensitivity Test

2.2.1 Disc diffusion method

Antibiotic sensitivity test of the bacterial isolates were performed by disk diffusion method on Mueller Hinton Agar (MHA). Inoculums of each isolate was prepared in 3 ml of sterilized normal saline and compared with 0.5 McFarland turbidity standards ($0.5x10^8$ cfu/mL). Each bacterial culture was streaked on MHA plates with sterile cotton swab and antibiotic disks were dispensed aseptically on the surface of culture plates at equal distances with the help of disc dispenser. All the plates were incubated at 37°C for 24 hours. After completing 24 hours time period, take all the incubated plates from incubator and record/ measure the zones of inhibition with the help of measuring scale in milli meters (mm) and compare all of these with standardized international protocols.

The patients who matchedinclusion criteria were put in this study. The cause, procdure and resulting benefits of the study were well explained to the parents before taking signature on informed consent proforma. The demographics of the participant such as age, gender, adress were taken carefully and registered on prescribed proforma. The clinical/physical examination was done and also recorded. All the data were collected by predesignedstructured proforma by investigator himself.

3. RESULTS

A number of 100 patients of both sex ranging 1-28 days of age were included in the study to find out bacterial etiological agents and their antibiotic susceptibility pattern in Neonatal Intensive Care Unit (NICU) Chandka Medical College Children Hospital Larkana and 28 samples out of 100 were positive with microbes presence. Descriptive statistics were used by SPSS version 16. Stratification was done, and post stratification Chi Square test was applied to observe the effect of modifiers on outcome. P value ≤0.05 was considered as significant. The overall mean age of study subjects was 14.71±8.176 days. The mean weight of study subjects was 2.27±0.14 kg while gestational age was 36.04±1.05 weeks.

Table 1. Descriptive statistics of age, weight and gestational age

	Mean	SD	Range	Minimum	Maximum
Age (days)	14.71	8.176	27	1	28
Weight (kg)	2.27	0.14	0.50	2.0	2.50
Gestational age (weeks)	36.04	1.05	34	37	3

Table 1. Antibiotic susceptibility pattern results

Staphylococcus species	**Antibiotics**
(All-11/11=100%) were sensitive to	Chloromphenicol, Imipenem and Clindamicin.
(5/11 =45.45%) were sensitive to	Amikacin.
(4/11 =36.36%) were sensitive to	Ceftriaxone.
(3/11 =27.27%) were sensitive to	Amoxicillin,Ampicillin,Penicillin-G, Gentamycin, Ceftazidime and Ciprofloxacin
(1/11 =9.09%) was sensitive to	Vancomycin.
Streptococcus species	**Antibiotics**
(6/7 =85.71%) were sensitive to	Imipenem.
(5/7 =71.42%) were sensitive to	Chloromphenicol and Clindamicin.
(2/7 =28.57%) were sensitive to	Amikacin, Ampicillin, Ceftazidime, Ciprofloxacin and Gentamycin
(1/7 =14.28%) was sensitive to	Amoxicillin, Ceftriaxone and Penicillin-G.
Escherichia species	**Antibiotics**
3/3 =100%) were sensitive to	Chloromphenicol, Clindamicin and Gentamycin
(2/3 =66.66%) were sensitive to	Amikacin, Ampicillin, Amoxicillin, Ceftazidime, Imipenem and Penicillin-G.
(1/3 =33.33%) was sensitive to	Ceftriaxone, Ciprofloxacin and Vancomycin.

Table 2. Summary of antibiotic susceptibility pattern results against isolated all 3 species

S. no	Name of antibiotic	S/I/R	Obtained results	Percentages
01	Amoxicillin	S	08	38.09%
		I	02	09.52%
		R	11	52.38%
02	Ceftiaxone	S	07	33.33%
		I	00	00.00%
		R	14	66.66%
03	Chloromphenicol	S	19	90.47%
		I	00	00.00%
		R	02	09.52%
04	Amikacin	S	12	57.14%
		I	03	14.28%
		R	06	28.57%
05	Ampicillin	S	09	42.85%
		I	00	00.00%
		R	12	57.14%
06	Vancomycin	S	07	33.33%
		I	08	38.09%
		R	06	28.57%
07	Penicillin G	S	07	33.33%
		I	02	09.52%
		R	12	57.14%
08	Imipenem	S	19	90.47%
		I	00	00.00
		R	02	09.52%
09	Gentamycin	S	10	47.61%
		I	00	00.00%
		R	11	52.38%
10	Ceftazidime	S	08	38.09%
		I	01	04.76%
		R	12	57.14%
11	Clindamycin	S	19	90.47%
		I	00	00.00%
		R	02	09.52%
12	Ciprofloxacin	S	08	38.09%
		I	02	09.52%
		R	11	52.38%

(S= Sensitive. I=Intermediate. R= Resistant)

The detailed descriptive statistics of age, weight and gestational age are presented in Table 1, antibiotic sensitivity pattern results in Table 2, frequency distribution of antibiotic sensitivity and frequencies and Association of Isolated Organism with Antibiotic Sensitivity in Table 4 respectively.

4. DISCUSSION

This may be due to ecological division and geographical distribution of microorganisms that *Staphylococcus aureus* was the most pathogen in various studies [8]. It is also found *Staphylococcus aureus* as etiologic agent in both EOS and LOS but contrary were found in LOS compared to EOS which is in agreement with WHO reports (1999).

On the second number, the regular isolate among Gram negative was *E. coli* [9]. But in our studies *E. coli* found on number third as etiologic agent n neonatal sepsis. *Staphylococcus epidermidis* was found in 13.1% of cases in our examination adding to both early beginning sepsis (EOS) in 3.1% of cases and late beginning sepsis (LOS) in 10% of cases [10]. In 2005 explained *Staphylococcus epidermidis* in 10.51% contributing, 2.77% cases to LOS and 7.8% cases to EOS, whereas

Staphylococcus epidermidis was more predominant in LOS in our investigation. *Acinobacter* was in same rate as that of *Staphylococcus epidermidis*, i.e., 13.1%. One study have found *Acinobacter* in 7.67% of cases, with EOS in 2.15% of cases and LOS in 5.55% of cases [10]. *Acinobacter* was even more commonly isolated in LOS (9.3%) as appear differently in relation to EOS (5.8%).

"Klebsiella species were isolated in 10% of cases, which were all found in late onset sepsis (LOS) [8,10] as the second most routinely isolated Gram negative bacteria, i.e. in 18.32% and 30% of cases respectively. This may be due to change of environmental conditions. *Streptococcal species* were found in 5.4% of cases, and all cases were isolated in EOS and depicted those *streptococci species* that cause neonatal sepsis just in 5% of cases, principally found in EOS, which is exceedingly a solid support to our investigation. Another study have found *streptococcal species* in 10.72% of cases [8], which essentially have restricted in EOS (7.69%). These similarities are moreover delineated in a study" [11].

"Both Gram positive and Gram-negative microorganisms have been found sensitive against third generation cephalosporins. Cefotaxime and ceftriaxone highly resistant and ceftazidime found less resistant. Various different investigations including [8] have depicted the developing resistance against cefotaxime and ceftriaxone, and decently low impenetrability to ceftazidime" [10]. "Expected that this may be changing example of resistance because of unnecessary use of antibiotics. Imipenem is extensively used nowadays and has high efficacy against both Gram positive and Gram negative bacteria as shown in this study that 90% of isolated microbes are sensitive to imipenam whereas according to [8] have found 100% sensitivity of Imipenem against, *Acinobacter, Staphylococcus aureus, Streptococci, Enterobacter species* and *Klebsiella, E. coli* [10] also have found Imipenem 100% sensitive against afore mentioned microorganisms. In our focus high resistance rate may because of inappropriate and frequent use of antibotics against microorganisms. Vancomycin have remarkable effectiveness against *Staphylococci"* [8].

Table 3. Frequency distribution of antibiotic sensitivity

Antibiotic	Sensitive/ Resistant	Staphylococcus Species (n)	Streptococcus Species (n)	Escherichia species (n)
Amoxicillin	S	04	01	02
	R	07	06	01
Ceftriaxone	S	04	01	01
	R	07	06	02
Chloromphenicol	S	11	05	03
	R	00	02	00
Amikacin	S	05	02	02
	R	06	05	01
Ampicillin	S	03	02	03
	R	08	05	00
Vancomycin	S	01	00	03
	R	10	07	01
Penicillin G	S	03	01	02
	R	08	06	01
Imipenem	S	11	06	02
	R	00	00	01
Gentamycin	S	03	02	03
	R	08	05	00
Cetazidime	S	03	02	02
	R	08	05	01
Clindamycin	S	11	05	03
	R	00	02	00
Ciprofloxacin	S	03	02	02
	R	08	05	01

5. CONCLUSION

Among all, *Staphylococcus species* were most common isolates 18 (85.71%) and sensitive to Chloramphenicol, Clindamycin and Imipenen. In case of Gram-negative bacilli, the *Escherichia species* 3(14.28%) were found sensitive to Clindamycin, Chloramphenicol and Gentamicin. High incidence of resistance pattern was noted with vancomycin Ampicillin, Penicillin, Gentamycin, Ceftazidime and Ciprofloxacin in case of *Staphylococcus species*. The *Streptococcus* species were resistant to Amoxicillin, Ceftriaxone and Penicillin G while, *Escherichia species* were resistant to the Ceftriaxone. An increasing trend of antibiotic resistance to the previously used first line drugs has been noted. Continued surveillance for antibiotic sensitivity adds great potential to reduce neonatal mortality.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Khan MA, Khan A, Shah F, Munir A. Neonatal sepsis: A study of causative pathogens and their antimicrobial sensitivity pattern at tertiary hospital. Gomal J. Med. Sci. 2012;10:244-247.
2. Roy I, Jain A, Kumar M, Agarwal. Bacteriology of neonatal septicaemia in a tertiary care hospital of Northern India. S. J. I. J. O. M. M. 2002;20:156.
3. Hotchkiss RS, Karl. The pathophysiology and treatment of sepsis. I. E. J. N. E. J. O. M. 2003;348:138-150.
4. Khan A, Qazi A, Yousaf A, Hanif R, Agha M, Baseer. Differences in detection rates for serious neonatal diseases before and after institution of newborn rounds by paediatricians in a private sector hospital. M. J. J. O. A. M. C. A. 2010;22:143-146.
5. Shams R, Khan N, Hussain. Bacteriology & anti-microbial susceptibility of neonetal septicemia in NICU, PIMS, Islamabad-A Tertiary Care Hospital of Pakistan. S. J. A. P. I. M. S. 2010;6:191-195.
6. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, Lemons JA, Donovan EF, Stark AR, Tyson. Changes in pathogens causing early-onset sepsis in very-low-birth-weight infants. J. E. J. N. E. J. O. M. 2002;347:240-247.
7. Rahman S, Hameed A, Roghani M, Ullah. Multidrug resistant neonatal sepsis in Peshawar, Pakistan. Z. J. A. O. D. I. C.-F. & Edition, N. 2002;87:F52-F54.
8. Shaw C, Shaw P, Thapalial. Neonatal sepsis bacterial isolates and antibiotic susceptibility patterns at a NICU in a tertiary care hospital in Western Nepal: A retrospective analysis. A. J. K. U. M. J. 2007;5:153-160.
9. Vergnano S, Sharland M, Kazembe P, Mwansambo C, Heath. Neonatal sepsis: An international perspective. P. J. A. O. D. I. C.-F. & Edition, N. 2005;90:F220-FF224.
10. Waseem R, Khan M, Izhar T, Qureshi. Neonatal sepsis. A. J. P. M. J. 2005;12: 451-56.
11. Aftab R, Iqbal. Bacteriological agents of neonatal sepsis in NICU at Nishtar Hospital Multan. I. J. J. O. T. C. O. P. & JCPSP, S.P. 2006;16:216-219.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62026