Original Article

OPEN ACCESS

Frequency of Culture-Proven Sepsis in Neonates Born to Mothers with Premature Rupture of Membranes

Sana Ejaz Abbasi[1], Nighat Haider[2], Bushra Adeel[3], Faiza Qayyum[4], Sara Ambreen[5], Hifza Rehman[6]

[1]Resident Peads Medicine, PIMS/SZABMU, [2] Associate Professor Peads Medicine, [3]Fellow in FCPS Neonatology
[4,5,6]Resident in Pediatric medicine, PIMS/SZABMU , Islamabad

Author`s Contribution

[1]collection of data, conception of the study and participated in its design
[2]design of the study and performed the statistical analysis along with drafting of manuscript
[3]guided throughout the process of study and helped in literature search for the discussion
[4]questionnaire and helped in data collection and literature search
helped in data interpretation and [5.6]final drafting of the manuscript helped in data interpretation

Funding Source: None
Conflict of Interest: None

Received: Sept 23, 2023
Accepted: May 11, 2024

Address of Correspondent
Dr. Sana Ejaz Abbasi
Resident Peads medicine,
PIMS/SZABMU
Sanaaa756@gmail.com

ABSTRACT

Objectives: To determine frequency of culture proven sepsis in neonates born to mother with premature rupture of membranes (PROM).

Methodology: This observational cross-sectional study was carried out from June 2022 to December 2022 at department of neonatology PIMS Islamabad. A total of 305 neonates fulfilling the inclusion criteria were included in the study. At the time of inclusion baseline characteristics were documented. After that blood samples of all the children with signs and symptoms of neonatal sepsis were sent for blood culture and sensitivity for diagnosis confirmation, organism identification and antibiotic sensitivity. Data was analyzed using SPSS 22.0.

Results: In our study, mean gestational age of neonates was 38.33 ± 1.84 weeks. There were 177 (58.04%) male and 128 (41.96%) female. Mean duration of PROM was 20.98 ± 1.44 hours. Frequency of culture proven sepsis in neonates born to mother with PROM was 82 (26.88%). Most common organism which was isolated in blood cultures was Klebsiella spp. 40 (48.78%).

Conclusion: Premature rupture of membranes increases the chances of neonates to acquire sepsis. Special care should be taken for such neonates in NICU for improved outcomes.

Keywords: Neonate, Organism, PROM, Drug sensitivity, Sepsis.

Cite this article as: Abbasi SE, Haider N, Adeel B, Qayyum F, Ambreen S, Rehman H. Frequency of Culture-Proven Sepsis in Neonates Born to Mothers with Premature Rupture of Membranes. Ann Pak Inst Med Sci. 2024; 20(SUPPL-1):646-649. doi. 10.48036/apims.v20iSUPPL-1.855

Introduction

About four million babies die each year at birth, a staggering number that demands significant effort from health system and advocates working to decrease and control it. Ninety-eight percent of newborn deaths occur in low-income nations, and sixty to seventy percent of all neonatal fatalities happen in their initial week of lifetime.[1] In low-income regions like Pakistan, a significantly high number of cases of infant deaths, approximately 18%, occur in the first month of life due to neonatal sepsis.[2] A positive blood culture within the initial twenty-eight days following birth is diagnostic of neonatal sepsis. Its hallmarks are inflammation and collapse of the circulatory system manifest themselves clinically as fever, lethargy, resistance to feed and poor perfusion, and is divided into early (within the first 72 hours of a baby's life) and late (beyond 72 hours). [3, 4]

There is diversity of organism that are found as culprit, when neonates with neonatal sepsis are investigated including *Klebsiella* species, *Salmonella parathypi*, *Escherichia coli*, *Serratia* species, *Staphylococcus aureus*, Group A *Streptococcus* and *Pseudomonas* species.[5] In addition, there has also been a grave concern of growing resistance of various antibiotics that are used for the treatment of neonatal sepsis.[7] There are many maternal risk factors that have the tendency to increase the propensity of a new born baby to contact an infectious agent in their body that results in a life threatening neonatal sepsis. One such major risk factor is PROM.[8] Physiologically, placental membranes act as a natural barrier against transference of microbes to the fetus trans

placentally, however, in case of PROM, microbes from the mother's lower genital tract rise into the uterine cavity and result in neonatal sepsis.[9]

Since, sepsis is the major cause of early infant death in impoverished countries, and since PROM is a significant contributory factor of preterm labor, intra uterine infection, and neonatal sepsis, we conducted this study with the aim to determine the frequency of culture-proven cases of neonatal sepsis and to identify the organisms that are responsible for sepsis in neonates who were born to mothers who had PROM defined as premature rupture of membrane 28 hours prior to delivery of baby.[10,11] If we have this knowledge, we will be able to start empirical treatment more quickly with more effective antibiotics, which will result in earlier recovery and a better prognosis.

Methodology

We conducted this randomized controlled trial at neonatal unit of Children hospital PIMS after obtaining approval from the ethical review board of SZABMU PIMS Islamabad. ERB No.F1-1/2015/ERB/SZABMU/961. Sample size of 305 was calculated using WHO sample size calculator by assuming confidence level of 95%, absolute precision of 2.5% and anticipated frequency of culture proven sepsis in neonates born to mother with PROM of 5.2% according to WHO calculator.[12,13]

We included neonates who were born after 28 weeks of gestation, either male or female, whose mothers had PROM which is defined as premature rupture of membrane 28 hours prior to delivery of baby.

We excluded syndromic children, children born to mothers with systemic infection and PROM of less than 18 hours duration.

We selected our study population by using non-probability consecutive sampling method. A written consent which was signed by the parents of all the study participants was made an essential pre-requisite. Baseline characteristics of all the included study participants, including gestational age (in weeks), gender, birth weight (in kg) and duration of PROM (in hours) were documented. Once born, neonates were monitored closely for the presence of spectrum of signs and symptoms of neonatal sepsis including fever, lethargy, reluctance to take feed, jaundice, abdominal distension, vomiting, increased heart rate and respiratory distress.[14,15] In case of presence of any of above mentioned signs and symptoms, neonate was labeled as a case of suspected neonatal sepsis and blood culture sample of neonate was sent to internal hospital laboratory for diagnosis confirmation, identification of the culprit organism and antibiotic sensitivity pattern.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) 22.0. Quantitative data was represented using mean with standard deviation. Qualitative data was represented by using percentage and frequency. Chi square test and Student t-test was applied where appropriate and a p-value of ≤ 0.05 was considered as statistically significant.

Results

A total of 305 neonates who were born to mothers who had PROM were included. In our study, we found out that the mean gestational age of included neonates was 38.33 ± 1.84 weeks. There were 177 (58.04%) male neonates while remaining 128 (41.96%) neonates were female. Mean birth weight of neonates was 3.08 ± 0.28 kg. Mean duration of PROM was 20.98 ± 1.44 hours. These are summarized in tabulated form below in table I.

Table I: Baseline characteristics.(n = 305)

Characteristics	Value
Mean gestational age	38.33 ± 1.84 weeks
Gender	
Male	177 (58.04%)
Female	128 (41.96%)
Mean birth weight	3.08 ± 0.28 kg
Mean duration of "premature rupture of membranes (PROM)"	20.98 ± 1.44 hours

In our study, we found that the frequency of culture proven sepsis in neonates born to mother with PROM was 82 (26.88%). Amongst these, 59 (71.95%) had early onset neonatal sepsis while 23 (28.05%) had late onset neonatal sepsis.

We also found out that the most common organism which was isolated as a culprit of culture proven sepsis in neonates (n = 82) born to mother with PROM was *Klebsiella* spp. 40 (48.78%), *Escherichia coli* 14 (17.07%), Streptococci 12 (14.63%), *Salmonella* spp. 8 (9.76%) and *Pseudomonas* spp. 8 (9.76%) as depicted in table II.

Along with culture growth we also checked antibiotic susceptibility pattern of various antibiotics including amikacin, ampicillin, cefotaxime, ceftazidime, ceftriaxone, clindamycin, co-amoxiclav, gentamicin, linezolid, meropenem, penicillin, piperacillin – tazobactam and vancomycin. This pattern of susceptibility of antibiotics is given below in table III.

Table II: Organisms causing culture proven sepsis in neonates. (n = 82)

Organism Isolated	N (%)
Klebsiella spp.	40 (48.78%)
Escherichia coli	14 (17.07%)
Streptococci	12 (14.63%)
Salmonella spp.	8 (9.76%)
Pseudomonas spp.	8 (9.76%)

Table III: Antibiotic susceptibility pattern in neonates with sepsis. (n = 82)

Antibiotic	Sensitivity n (%)	Resistance n (%)
Amikacin	60 (73.17%)	22 (26.83%)
Ampicillin	13 (15.85%)	69 (84.15%)
Cefotaxime	41 (50.00%)	41 (50.00%)
Ceftazidime	21 (25.61%)	61 (74.39%)
Ceftriaxone	11 (13.41%)	71 (86.59%)
Clindamycin	53 (64.63%)	29 (35.37%)
Co-amoxiclav	21 (25.61)	61 (74.39%)
Gentamicin	48 (58.54%)	34 (41.46%)
Linezolid	75 (91.46%)	7 (8.54%)
Meropenem	58 (70.73%)	24 (29.27%)
Penicillin	3 (3.66%)	79 (96.34%)
Piperacillin – tazobactam	49 (59.76%)	33 (40.24%)
Vancomycin	70 (85.37%)	12 (14.63%)

Discussion

Premature rupture of membranes is a condition that affects roughly between eight and ten percent of pregnancies and is rupture of the membranes that lasts for over eighteen hours before the birth.[16] Neonatal sepsis has been identified as the major event and likely consequence of PROM and is also the most common cause of premature labor.[17] This study was focused primarily on the frequency of neonatal sepsis that occurred in the newly born infants to the mothers who had PROM.

In our study, we found that the frequency of culture positive neonatal sepsis was significantly high in neonates with mothers who had PROM. Most of these neonates had early onset sepsis (EONS). As compared to what we found in this study, much lower frequency was reported in a study conducted by Rathore *et al.* [18] The low frequency observed could be attributed to the fact that they exclusively enrolled neonates with early onset neonatal sepsis, as opposed to our study, which included both types. Similarly, Altaf *et al.* reported a relatively low frequency of neonatal sepsis in children born to mothers who had PROM.[19] In line with the results of our study, Ashraf *et al.* [20] and Sirivunnabood *et al.*[21] reported somewhat similar frequency of neonatal sepsis in children born to mothers who had PROM as compared to our study.

In our study, most common organism that was identified as a culprit organism in neonatal sepsis was *Klebsiella* spp. This was similar to what was found in various previous studies.[5, 6] In our study, we found that in terms of antibiotic susceptibility, antibiotics that are newer and possess broader antimicrobial spectrum had much less level of resistance as compared to older antibiotics like penicillin and ampicillin. Similar finding was observed in a study conducted by Waseem *et al.* [22] At one end, this finding that level of resistance in many antibiotics is still low, is encouraging but at the same time, very high level of resistance of some of the antibiotics is a major concern. Based on the findings of our study, it is safe to consider PROM as a major factor that can increase the neonatal likelihood to develop sepsis. Additionally, we recommend to start broad spectrum antibiotics as empirical therapy while waiting for culture results due to higher sensitivity to such antibiotics and avoid conventionally used, older antibiotics like penicillin, ampicillin and ceftriaxone, etc.

Conclusion

Premature rupture of membranes increases the chances of neonates to acquire sepsis. Special care should be taken for such neonates in NICU for improved outcomes. This will contribute, in future, to reduce the alarmingly high neonatal mortality rate in developing nations like Pakistan.

References

1. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet. 2003;361(9376):2226-2234. doi: 10.1016/S0140-6736(03)13779-8.
2. Mustufa MA, Korejo R, Shahid A, Nasim S. Infection remains a leading cause of neonatal mortality among infants delivered at a tertiary hospital in Karachi, Pakistan. J Infect Dev Ctries. 2014;8(11):1470-1475. doi: 10.3855/jidc.3569.
3. Ahmed M, Yasrab M, Khushdil A, Qamar K, Ahmed Z. Neonatal sepsis in a tertiary care hospital: bacteriological profile and its antibicrobial sensitivity and its antibicrobial sensitivity. Pak Armed Forces Med J. 2018;68(6):1654-1658.
4. Shobowale EO, Solarin AU, Elikwu CJ, Onyedibe KI, Akinola IJ, Faniran AA. Neonatal sepsis in a Nigerian private tertiary hospital: Bacterial isolates, risk factors, and antibiotic susceptibility patterns. Ann Afr Med. 2017;16(2):52-58. doi: 10.4103/aam.aam_34_16.
5. Bhutta ZA, Naqvi SH, Muzaffar T, Farooqui BJ. Neonatal sepsis in Pakistan. Presentation and pathogens. Acta Paediatr Scand. 1991;80(6-7):596-601. doi: 10.1111/j.1651-2227.1991.tb11916.x.

6. Zelellw DA, Dessie G, Worku Mengesha E, Balew Shiferaw M, Mela Merhaba M, Emishaw S. A systemic review and meta-analysis of the leading pathogens causing neonatal sepsis in developing countries. Biomed Res Int. 2021;2021:6626983. doi: 10.1155/2021/6626983.
7. Yadav SK, Agrawal SK, Singh SK, Giri A, Singh GK, Ghimire R, *et al*. Antimicrobial resistance in neonates with suspected sepsis. Public Health Action. 2021;11(Suppl 1):6-12. doi: 10.5588/pha.21.0038.
8. Zhuang L, Li ZK, Zhu YF, Ju R, Hua SD, Yu CZ, *et al*. The correlation between prelabour rupture of the membranes and neonatal infectious diseases, and the evaluation of guideline implementation in China: a multi-centre prospective cohort study. Lancet Reg Health West Pac. 2020;3:100029. doi: 10.1016/j.lanwpc.2020.100029.
9. Ibishi VA, Isjanovska R, Malin AE. Early-onset neonatal infection in pregnancies with prelabor rupture of membranes in Kosovo: A major challenge. Turk J Obstet Gynecol. 2018;15(3):171-176. doi: 10.4274/tjod.73600.
10. Olita'a D, Barnabas R, Vali Boma G, Pameh W, Vince J, Duke T. Simplified management protocol for term neonates after prolonged rupture of membranes in a setting with high rates of neonatal sepsis and mortality: a quality improvement study. Arch Dis Child. 2019;104(2):115-120. doi: 10.1136/archdischild-2018-315826.
11. Al-Lawama M, AlZaatreh A, Elrajabi R, Abdelhamid S, Badran E. Prolonged rupture of membranes, neonatal outcomes and management guidelines. J Clin Med Res. 2019;11(5):360-366. doi: 10.14740/jocmr3809.
12. Ocviyanti D, Wahono WT. Risk factors for neonatal sepsis in pregnant women with premature rupture of the membrane. J Pregnancy. 2018;2018:4823404. doi: 10.1155/2018/4823404.
13. Charan J, Biswas T. How to calculate sample size for different study designs research? Indian J Psychol Med. 2013;35(2):121-126. doi: 10.4103/0253-7176.116232.
14. Stefanovic IM. Neonatal sepsis. Biochem Med (Zagreb). 2011;21(3):276-281. doi: 10.11613/bm.2011.037.
15. Li X, Ding X, Shi P, Zhu Y, Huang Y, Li Q, *et al*. Clinical features and antimicrobial susceptibility profiles of culture-proven neonatal sepsis in a tertiary children's hospital, 2013 to 2017. Medicine (Baltimore). 2019;98(12):e14686. doi: 10.1097/MD.0000000000014686.
16. Alam MM, Saleem AF, Shaikh AS, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. J Infect Dev Ctries. 2014;8(1):67-73. doi: 10.3855/jidc.3136.
17. August Fuhr N, Becker C, van Baalen A, Bauer K, Hopp H. Antibiotic therapy for preterm premature rupture of membranes - results of a multicenter study. J Perinat Med. 2006;34(3):203-206. doi: 10.1515/JPM.2006.035.
18. Rathore H, Rahman AJ, Salman M, Nasir M, Sherali S. Frequency of early-onset neonatal sepsis following prolonged rupture of membranes. Cureus. 2020;12(2):e6864. doi: 10.7759/cureus.6864.
19. Altaf S, Tahir M, Javed M, Afroz N, Subhani AR, Liaqat AS. Frequency of neonatal sepsis in babies born to mothers with prom more than 18 hours. Pak J Med Health Sci. 2023;17(3):353-356. doi: 10.53350/pjmhs2023173353.
20. Ashraf MN, Ul Haq MZ, Ashraf MW, Sajjad R, Ahmed F. Frequency of early onset neonatal sepsis in preterm premature rupture of membranes. Pak Armed Forces Med J. 2015;65(2):226-230.
21. Sirivunnabood T, Wanitpongpan P, Yapan P. Incidence and risk factors of neonatal sepsis in preterm premature rupture of membranes before 34 weeks of gestation. Siriraj Med J. 2022;74(3):169-177. doi: 10.33192/Smj.2022.21.
22. Waseem H, Sadaf R, Khan AJ, Naeem A, Ali S, Usman J. Antimicrobial susceptibility pattern of neonatal sepsis in neonatal intensive care unit. Ann Allied Health Sci. 2022;8(2):9-13.