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Identification of Risk Factors for Late-Onset Neonatal Sepsis in Post-Operative Neonates

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ABSTRACT

Introduction:Defined As The Systemic Condition That Arises From Viral, Bacterial Or Fungal Etiology, Associated With Hemodynamic Changes And Clinical Findings, Sepsis Is One Of The Most Common Causes Of Neonatal Mortality And Morbidity. Various Preventable Risk Factors Are Associated With The Developed Of Late-Onset Sepsis In Neonates. The Problem Of Neonatal Sepsis, Especially In Post-Op Neonates In Low-Income Countries Is Plagued By A Scarcity Of Research. Conducted In The Hdu Of Pediatric Surgery Department Of Holy Family Hospital, This Longitudinal Study Is Part Of The Quality Improvement Project To Improve Neonatal Outcomes.

Objectives:This Study Aims To Identify The Risk Factors Associated With Late-Onset Sepsis In Post-Op Neonates In The Hdu Of Paeds Surgery Department Of Holy Family Hospital, A Tertiary Care Hospital In Punjab, Pakistan. In Addition To Risk Factors Already Elaborated By Previous Studies, This Study Also Aims To Delineate Additional Risk Factors Associated With Sepsis In The Context Of Post-Op Setups I.E. Fever Prior To Surgery, General Hygienic Measures Observed By The Attendants And Doctors And Severity Of Surgical Wounds.

Methods:In Compliance With The Guidelines Issued By The Ethical Board, A Prospective Observational Study Recruiting 91 Neonates Was Carried Out For 6 Months From June, 2022 To December,2022. Periodic Evaluation Was Carried Out Using Standardized Checklists Which Recorded The Possible Predictor Variables I.E. Birth Weight, Severity Of Surgical Wounds, General Hygienic Practices, Fever Prior To Surgery And Duration Of Iv Catheterization. Data Obtained Was Subject To Multivariate Logistic Regression Using Spss V23.

Results:Sepsis Was Prevalent In 34 (37.4%) Post-Op Neonates. Low Birth Weight [Or 3.08 95% Ci (1.12-8.47) And Fever Prior To Surgery [Or 2.79 95% Ci (1.03-7.55)] Were Found To Be Statistically Significant Factors Contributing To Neonatal Sepsis, Whereas The Study Of General Hygienic Practices, Severity Of Surgical Wounds And Duration Of Iv Catheterization Failed To Yield Statistically Significant Results, Possibly Owing To Small Sample Size.

Conclusion:Further Studies Employing A Larger Sample Size Are Mandated In Order To Establish The Association Of The Aforementioned Risk Factors For Neonatal Sepsis. Low Birth Weight Neonates And Those With Fever Prior To Invasive Procedures Require Rigorous Monitoring For The Prompt Diagnosis And Prevention Of The Complications Associated With Neonatal Sepsis..

Keywords: *Neonatal Sepsis,Postoperative Complications,Pediatric Surgery,Neonatal Mortality,Birth Weight,Sepsis Prevention.*

1. INTRODUCTION

Identified as one of the leading causes of neonatal mortality according to the 2015 Global Burden of Disease study (1), neonatal sepsis is defined as the systemic condition that arises from viral, bacterial or fungal origin, associated with hemodynamic changes and clinical findings, causing severe morbidity and mortality (2). In 2017, 20% of all neonatal deaths.

were due to sepsis globally (3).Weakened immune systems, low birth weight, pre-maturity, nosocomial infections and added stress after surgery are just some of the factors that predispose the neonatal population to disseminated infections. The neonatal case fatality rate increases from 2% to 20% when dealing with premature infants as compared to term infants (4). Depending on whether the causative organism was acquired through vertical transmission from the mother, or from an external source, neonatal sepsis is classified as either early or late onset, respectively (4)

Neonatal sepsis can lead to a range of complications, including septic shock, respiratory distress, neurological deficits, and multi-organ failure (5) (6) (7). These complications can have long-lasting effects on the affected newborn, such as developmental delays, chronic lung disease, and impaired cognitive function. In addition, neonatal sepsis can also have a significant emotional and financial impact on families, as it may require prolonged hospitalization and specialized medical care. Therefore, identifying and preventing neonatal sepsis is crucial in minimizing the risk of complications and improving the overall health outcomes of newborns.

The risk factors for neonatal sepsis are multifactorial and can be related to the mother, the baby, or the healthcare environment. Maternal risk factors include infections during pregnancy, maternal fever, prolonged rupture of membranes, and chorioamnionitis (8) (9). Infant-related risk factors include low birth weight, prematurity, birth asphyxia, and congenital anomalies (10) (11) (12). Healthcare-related risk factors include invasive procedures, inappropriate use of antibiotics, and poor infection control practices.

The public health care sector of low-income countries like Pakistan, (especially pertaining to pediatric care), is plagued by a multitude of issues that cause numerous hurdles in the early diagnosis, prevention and prompt treatment of neonatal sepsis. Our study was directed at identifying the risk factors that predispose a neonate to late onset sepsis after invasive surgery in the surgical department of a tertiary care hospital in Pakistan. In the existing set-up of, some of the most common procedures are for gut atresias (involving foregut, midgut and hindgut), genitourinary and anorectal malformations. These neonates are then subject to post-op care in the HDU.

As part of the Quality Improvement Project for improving neonatal outcome, the following parameters were studied in order to discern the risk factors significantly associated with late-onset neonatal sepsis in post-op neonates:

1-General hygienic measures (use of masks, sanitizers, headcovers and shoe covers by attendants and diaper status)

2-Low birth weight

3- Fever prior to surgery (greater than 100.4 F)

4- Duration of post-op IV catheterization in days

5- Severity of surgical wound as ascertained by the Wound-Southampton Classification (13) given below:

Grade	Appearance
0	Normal Healing
I	Presence of erythema
II	Erythema plus other signs of inflammation
III	Clear or serous Discharge
IV	Purulent Discharge
V	Deep or severe wound infection with or without tissue breakdown

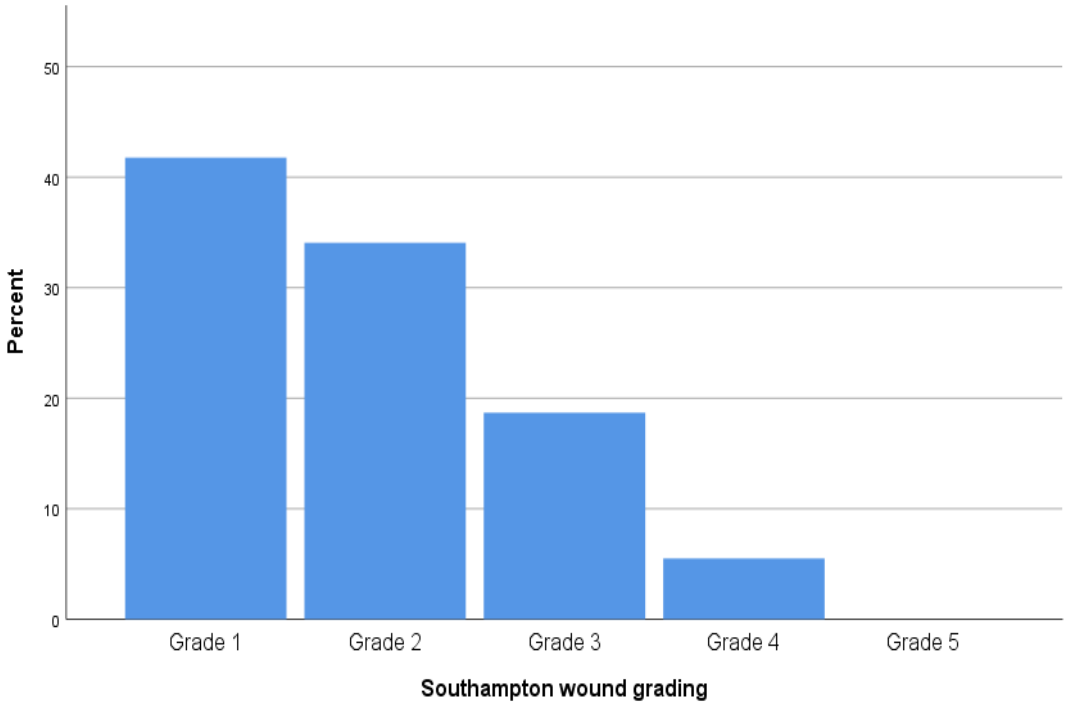
These potential risk factors were studied after a meticulous literature review. Out of these, general hygienic measures (6), fever prior to surgery and severity of surgical wound were added as novel parameters that haven't been studied as of yet in the context of late-onset neonatal sepsis.

2. METHODOLOGY:

In the span of 6 months (from June, 2022 to December, 2022), a prospective observational study was carried out in the HDU of the Pediatric Surgery Ward of Holy Family Hospital, Rawalpindi, Pakistan.Approval for this study was obtained from the Ethical Review Board (ERB) of the Resident Research Forum via letter number: ID-21-18-2022. Standardized checklists were used to obtain relevant data pertinent to the risk factors aforementioned. Inclusion criteria was limited to all post-op neonates with an IV cannula in place for at least 24 hours. All neonates, warranting ventilatory support in NICU, were excluded from the study. A total of 91 neonates were included in the study.Late onset neonatal sepsis is defined as sepsis occuring at or after 72 hours of life.Elevated CRP levels (>5mg/dl) (14) or markedly deranged TLC (<4000/µL or >12,000/µL) (15) along with clinical manifestations(Heart rate >180 bpm or <100 bpm, Respiratory rate >60 breaths per min, temperature >100.4F) (16) were ascertained as the diagnostic criteria for possible neonatal sepsis. These lab investigations were done on the 1st post-op day and on every third day subsequently. This criteria was extracted from an algorithm proposed by a 2014 study (17). Based on the use or lack thereof, of 1-masks, 2-sanitizers, 3- headcovers and 4-shoe covers by attendants, and the 5-status of diapers (clean/dry or dirty), 6- dignity sheet (clean/dry or dirty) and 7--clothes (clean/dry or dirty), hygienic measures were classified as either satisfactory (5-7 parameters fulfilled), poor (3-5 parameters fulfilled) and very poor (<3 parameters fulfilled). Low birth weight neonates are defined as newborns having birth weight less than 2.5 kg (5.5 lbs) at time of delivery. The presence or absence of fever (>100.4 F) prior to surgery was also noted. The duration of all peripheral IV cannulations was recorded in days and the cannula having the longest lifespan was chosen as the pertinent possible risk factor for sepsis. Surgical wound severity was ascertained by the Wound Southampton Grading System. The grade of wound was noted as the highest grade that was reached during the neonate's stay in the HDU. All the aforementioned risk factors were enumerated as possible predictor variables that contributed to sepsis. The presence or lack of sepsis was the primary outcome variable. Chi-Square test was applied to categorical variables and a p value of <0.05 was considered significant. Multivariate logistic regression was carried out using SPSS V23 in order to obtain the relevant odds ratios.

3. RESULTS:

Results revealed that out of 91 neonates, 41 (45.1%) underwent possible sepsis, out of which 26 neonates eventually expired. The case fatality rate of neonatal sepsis turned out to be 63.4%. Surgical wound severity was classified using the Southampton Grading System, according to which 38 (41.8%) neonates had a Grade 1 wound, while the number of Grade 2 and Grade 3 surgical wounds was 31 (34.0%) and 17 (18.6%). The number of neonates with Grade 4 wounds was 5 (5.5%).



Baseline characteristics are given below:

Characteristics	n=91
Sex	
Male (n, %)	57 (62.6%)
Female (n, %)	34 (37.4%)
General Hygienic Practices	
Satisfactory (n, %)	26 (28.6%)
Poor (n, %)	36 (39.5%)
Very Poor (n, %)	29 (31.8%)
Fever	
Present (n, %)	39 (42.8%)
Absent (n, %)	52 (57.1%)
Birth Weight	
Normal (n, %)	60 (65.9%)
Low birth weight (n, %)	31 (34.0%)
Southampton Wound Grade	
Grade 1 (n, %)	38 (41.8%)
Grade 2 (n, %)	31 (34.0%)
Grade 3 (n, %)	17 (18.6%)
Grade 4 (n, %)	5 (5.5%)
Duration of IV cannulation in days (mean, SD)	2.275 ± 0.857

The study recruited 57 (28.6%) males and 34 (37.4%) females. General hygienic practices were graded as satisfactory, poor and very poor in 26 (31.8%), 36 (39.5%) and 29 (31.8%) neonates respectively. 39 (42.8%) neonates had fever prior to surgery. 31 (34.0%) low-birth weight neonates were part of the study. The mean duration of an IV line during a neonate's stay in the HDU after surgery was 2.275 days with a standard deviation of 0.857.

Multivariate regression analysis was done to calculate relevant odd ratios and significant factors that contributed towards development of neonatal sepsis were identified. The results of regression analysis are given below:

Risk Factors	Adjusted Odds Ratio	95% confidence intervals	P value
Low birth weight	3.25*	1.15- 9.21	0.027*

Fever prior to surgery	3.16*	1.19 - 8.37	0.020*
Duration of IV cannulation	1.76	0.98 – 3.17	0.058
Hygienic Measures			
Satisfactory	1		
Poor	1.20	0.35 – 4.16	0.774
Very poor	1.83	0.53 – 6.36	0.341
Southampton Wound Grade			
Grade 1	1		
Grade 2	1.56	0.52 - 4.61	0.427
Grade 3	2.92	0.79 – 10.74	0.107
Grade 4	0.69	0.09 – 5.46	0.733

4. DISCUSSION:

Establishing a prompt and accurate diagnosis of neonatal sepsis is essential for timely initiation of appropriate treatment and minimizing the risk of complications. The diagnosis of neonatal sepsis is challenging, as the clinical features can be non-specific and overlap with other neonatal conditions.

The diagnosis of neonatal sepsis involves a combination of clinical and laboratory parameters. Clinical signs such as fever, respiratory distress, lethargy, poor feeding, and abnormal vital signs can raise suspicion for neonatal sepsis. Laboratory tests such as blood cultures, complete blood count, and inflammatory markers such as C-reactive protein (CRP) and procalcitonin (PCT) can help confirm the diagnosis and assess the severity of the infection [4].

However, the interpretation of laboratory tests can be challenging, particularly in premature and low-birth-weight infants who may have different reference ranges for these tests. In addition, false-positive and false-negative results can occur with laboratory tests, emphasizing the need for a high degree of clinical suspicion and careful interpretation of laboratory results.

Although positive blood cultures remain the diagnostic gold standard for neonatal sepsis, an elevated CRP has emerged as one of the most common and expeditious biomarker in identifying and gauging the severity of neonatal sepsis [5].

Advanced logistic regression revealed that low birth weight [OR 3.25 95% CI (1.15-9.21) and fever prior to surgery [OR 3.16 95% CI (1.19-8.37)] were found to be statistically significant factors contributing to neonatal sepsis. A previous study has also revealed that low birth weight is a statistically significant factor for neonatal sepsis [OR 5.17 ($p<0.001$)] (18). A meta-analysis conducted in 2019 (19) has also associated low birth weight with an increased risk of sepsis [OR 2.27 95% CI (0.4-12.9)]. Low birth weight is a well-known risk factor for neonatal sepsis, as low birth weight infants not only have an immature immune system but also have a decreased level of maternal immunoglobulins (6), making them more susceptible to infections.

Fever prior to surgery was a significant risk factor for neonatal sepsis identified in this study. Fever is often the first sign of infection in neonates and may indicate an ongoing infection that, if left untreated, can progress to sepsis. Possible reasons for the observed findings could be that the fever is indicative of an infection that was present before the surgery and the surgery may have contributed to the dissemination of the infection. It is to be noted that pre-op sepsis was ruled out beforehand in order to circumvent any confounding that could have occurred. It is crucial to evaluate the cause of the fever and initiate appropriate treatment promptly to prevent the development of sepsis. In addition, the surgical management plan in such neonates should be reviewed so as to minimize the possible cause of post-op sepsis and optimize neonatal outcomes.

Although clinically significant, poor [OR 1.20] and very poor hygiene measures [OR 2.58] and duration of peripheral IV cannulation in days [OR 1.83], were not found to be statistically significant risk factors for sepsis in post-op neonates. (20)

Increase in wound severity also contributed to increased risk of sepsis, albeit with an insignificant p value, possible owing to a smaller sample population. Odds ratios were 1.56, 2.92 and 0.69 for grade 2, 3 and 4 wounds respectively (when compared to grade 1). This indicates that these factors may play a paramount role in the development of sepsis in neonates undergoing surgery. Possible reasons for the insignificant findings could be that the hospital has already implemented effective infection control measures and that the peripheral IV cannulation and wound care were done according to established guidelines, reducing the risk of infection (21). It is also possible that the sample size or duration of the study may not have been large enough to detect significant associations. However, further research is needed to confirm these findings and determine the effectiveness of interventions to minimize these risk factors.

Owing to time constraints and lack of availability, blood cultures were omitted as the diagnostic criterion for neonatal sepsis in our setup. This can serve as a possible limitation to our study

We have suggested several measures for the prevention, early diagnosis and expeditious management of neonatal sepsis.

1)Following appropriate hygiene measures i.e. use of sanitizers and proper handwashing technique (22) and use of sanitizers by doctors and attendants, regular monitoring and changing of diapers and dignity sheets and making sure that the neonate's clothes are clean and dry at all times.

2) Regular laboratory evaluation of CRP levels and blood cultures in all septic patients to determine the cause of sepsis and in order to optimize the antibiotic treatment (16).

3) Timely initiation of culture sensitive antibiotic therapy in neonates to minimize mortality and morbidity associated with neonatal sepsis.

As a result of this study, quantitative CRP levels and blood cultures have now become routine investigations in our setup, especially for neonates in the postop setting. Whether or not this affects neonatal mortality requires further assessment.

5. CONCLUSION:

The importance of prompt diagnosis of sepsis in post-op neonates should never be underestimated, especially in high-risk populations, such as low birth weight newborns, or those presenting with fever prior to surgery. Surgical wound severity, hygienic measures and duration of peripheral IV catheterization failed to show any significant association with late-onset sepsis, although new trends might be delineated if subsequent studies employing a greater sample population from more than one tertiary care hospital are carried out as part of the Quality Improvement Project for Neonatal Care in Pediatric Surgery. Being a multi-faceted domain of pediatric care, the topic of neonatal sepsis warrants further research, as it is found to have a direct link with neonatal mortality and outcome. Recognition of relevant and clinically tangible risk factors for neonatal sepsis will go a long way in improving the dismal state of affairs in pediatric care in low-income polities by paving the way for the employment of efficacious preventive measures

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