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**ORIGINAL ARTICLE**

# Risk Factors of Neonatal Sepsis in DHQ Hospital Skardu

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## ABSTRACT

**Background:** Sepsis is a substantial cause of newborn illness and death. Few aspects of sepsis' clinical impact and risk factors are thoroughly recognized. Late-onset sepsis is linked to healthcare-associated infections and affects newborns older than seven days.
**Aim:** To evaluate the clinical outcome and risk variables related to newborn sepsis at the DHQ hospital Skardu in Pakistan.
**Methods:** A quantitative retrospective institution-based chart review was carried out at DHQ Hospital Skardu with a sample size n=225.
**Results:** 164(72.9%l) of the 225 evaluated newborn charts were for newborns less than 7 days old, and 144(64%) were for males. Meconium aspiration syndrome involved forty newborns, or 17.8%, while abnormal respiratory symptoms affected twenty-nine infants or 12.9%. Among newborns diagnosed with neonatal sepsis, therapy resulted in complete recovery for 189(84%) infants, death for 9(4%) infants, and transfer of care to other hospitals for 13(5.7%) infants. Meconium aspiration syndrome and respiratory distress syndrome contributed to the poor prognosis of newborn sepsis (AOR = 0.1989 [0.059-0.664] and AOR = 0.258 [0.072-0.900], respectively).
**Conclusion:** The clinical prognosis for newborn sepsis at DHQ hospital Skardu was worse than desirable. RDS and meconium aspiration syndrome were the most accurate indicators of a poor prognosis in newborn sepsis. It is hypothesized that improved prenatal care, early diagnosis and treatment of neonatal illnesses or abnormalities, and the provision of essential newborn care to all newborns through the end of the neonatal period will all contribute to improved neonatal outcomes.
**Keywords:** Risk factors, treatment, Sepsis, Neonatal, DHQ hospital, Sakrdu, Pakistan

## INTRODUCTION

Neonatal sepsis is a kind of systemic infection that often makes its presence known during the first 28 days of a newborn's life[1]. It is also one of the top causes of sickness and death in babies. The following is the definition of neonatal sepsis that was agreed upon at the international pediatric consensus conference in the year 2020[2]. A systemic inflammatory reaction syndrome that develops during the initial 28 days of a child's life in the context of or as a consequence of a presumed or confirmed infection accompanied by or without associated bacteremia and is confirmed by a positive blood culture.

A wide variety of systemic diseases collectively referred to as "sepsis" can affect newborns. These diseases can manifest as anything from septicemia and meningitis to pneumonia and osteomyelitis, and even rheumatoid arthritis and urinary tract infections[3]. Newborns are particularly susceptible to these diseases. Both gram-positive and gram-negative bacteria have been linked as potential triggers of sepsis in infants[4,5].

If a newborn child is less than seven days old when they get sepsis, this is considered to be an early onset of the condition.If signs of sepsis do not appear until after the age of 8 days has passed, this condition is said to have developed at a later age[5].If the neonate's health improves during therapy and there are no negative side effects, such as convulsions, meningitis, shock, deafness, or blindness, then the outcome may be considered a success. On the other hand, if the neonate's health does not improve after receiving treatment, then the outcome was unfavourable[6]. Negative outcomes include a neonate that does not improve after getting therapy, that develops issues, that passes away, that refuses to receive more medical care, and is transferred to another hospital.

Early-onset (EONS) and late-onset (LONS) variants of neonatal sepsis are distinguished from one another by the timing of the development of the first symptoms. The majority of instances of early-onset neonatal sepsis occur in the first week of a newborn's life, most often during the first 24 hours of life. On the other hand, late-onset neonatal sepsis often does not show any symptoms until beyond the eighth day of a newborn's life and is identified after delivery[5,6].

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Some diagnostic procedures, such as a complete WBC count and differential, blood cultures, urine cultures, and lumbar punctures for cell counts and cultures, are used in the process of diagnosing sepsis. To eliminate the possibility of an infant having early-onset sepsis, other factors such as maternal illness, protracted membrane rupture, and premature birth are taken into consideration[1,6].

In infants, a mild infection may be indicated by one or more of the following signs and symptoms that are not unique to the illness. The presence of symptoms such as fever or hypothermia, drowsiness, a weak cry, a refusal to suckle, poor perfusion, a prolonged capillary refill time, hypotonia, an absence of neonatal reflexes, a prominent fontanel, bradycardia, tachycardia, respiratory distress, apnea and gasping respiration, hypoglycemia, and metabolic acidosis are all indications that something is serious about the baby.

The place of birth, prematurity, reduced birth weight, complex or instrument-assisted delivery, and minimal appearance pulse grimace activity respiration (APGAR) rankings are all possible causes for the sudden onset of sepsis. Premature membrane rupture (PROM), fever, chorioamnionitis, duplicated vaginal examination, meconium-stained amniotic fluid, and nutrition comprised of tainted meals. Other risk factors include being hospitalized, undergoing surgery, or acquiring an infection while a patient is in the hospital may all lead to a condition known as slow-onset sepsis[6,7]. This condition is a medical emergency.

It is possible to prevent sepsis nearly totally if a timely diagnosis, cautious use of antimicrobial medicine, and intensive supportive care are administered. Penicillin (Benzylpenicillin, Ampicillin, or Cloxacillin) plus an aminoglycoside, most often Gentamicin[8,9], are the antibiotic combinations that are used the most frequently in the treatment of septic shock.

According to the World Health Organization (WHO), sepsis is one of the most common causes of illness and death in newborns across the world. In 2012, sepsis was responsible for around 12% of the 2.9 million fatalities that occurred in neonates[10]. The developing world accounts for ninety-nine point nine percent of all of this fatalities[11].In Africa, sepsis is the leading cause of death for newborns, accounting for 28% of all newborn fatalities[12], while infectious diseases are responsible for 68%[13] of all baby deaths. In Pakistan, sepsis is the underlying cause of 5% of neonatal deaths[14].

There was a considerable amount of research on the risk factors of sepsis but there was no research on neonatal sepsis in Skardu. At DHQ hospital Skardu, Pakistan, the subject of this research was newborn sepsis, and its clinical outcomes as well as the risk factors connected with it were going to be investigated.

In order to lower the chance of the neonate acquiring sepsis, this study helps to increasing mother antenatal care use and also assist detect indicators of risk during both prenatal and postnatal periods and apply the proper therapies.

## METHODOLOGY

**The setting of study and duration:** A quantitative retrospective institution-based chart review was carried out at the DHQ Hospital Skardu Hospital between the 30th of April and 30th of May in year 2021. It is possible to find it in the city of Skardu, which is located in the GilgitBaltistan province of Pakistan.About 700km far from Islamabad.The hospital's inpatient treatment, outpatient care, and operating room care are each overseen by their separate departments. The hospital also provides care for patients outside of the facility. Since it has a total of more than 250 beds, it can serve about 20,000 patients at the same time. Each year, the DHQ Hospital Skardu provides treatment for around 550 newborns who have been identified as having sepsis. There were a total of 15 beds available in the neonatal intensive care unit, in addition to 4 medical professionals and 11 nursing staff members. By applying the following assumptions to a computation of a single population percentage, we were able to arrive at a final sample size of 225. These assumptions are as follows: prevalence (P) = 50%, confidence level (CI) = 95%, and margin of error (W) = 5%. Since there are less than 10,000 people in total, this was achieved by the use of an appropriate formula.

**Measurement:** To facilitate the gathering of information and the registration process, a systematic checklist was used. The construction of the checklist was based on a comprehensive analysis of the pertinent previously published research. The checklist includes things like the socioeconomic position of the mother and baby, the risk factors of both the mother and the newborn, and health service-related variables that contribute to an unfavorable result of sepsis. Four distinct data collectors and one supervisor worked together to compile the information, after which the supervisor swiftly sent it to the researcher who had requested it. A full-day-long orientation and training session was held before the time when data was being gathered. This session took place before the time when the data was being collected. Both data collectors and supervisors were invited to participate in this session.

Based on an analysis of linked literature regarding the risk factors of newborn sepsis, a semistructured data annotation tool was created. The application and database tool was split into two components the first part was made up of maternal features, and the second part was made up of neonatal variables. Neonatal features included birth injury, resuscitation at birth, sex, maternal age, birth weight, and APGAR scores at the first and fifth minutes.

Age of the mother, marital status, educational attainment, employment status, parity, method of delivery, a quantity of prenatal care, hypertensive disorders, bleeding disorders, and PROM were some of the maternal variables.

Information was entered into SPSS version 25. Using Pearson's chi-squared test, the relationships between independent and dependent variables were analyzed. Binary and multivariate logistic regression analyses were also used to estimate the risk of newborn sepsis. Lastly, tables and charts of the data were shown to illustrate the distribution of cases. Before starting to gather data, the DHQ hospital Skardu Research Ethics Board granted the present research approval letter. The management system then gave its blessing for the study to start.

## RESULTS

**Socio-demographic data:** In all, 225 newborn records with sepsis were analyzed during this study. 115(51.1%) of the moms were between the ages of 19 and 29 years old, 144(64%) of the total were males, 164(72.9%) were less than 7 days old, 133(59.1%) lived in rural areas, and the total number of babies was 164 (Table 1).

Table 1: Neonatal-related risk factors for sepsis inDHQ HospitalSkardu2021

| Variable | Frequency | %age |
|---|---|---|
| **Gender** | | |
| Male | 144 | 64 |
| Female | 81 | 36 |
| **Age of infant** | | |
| 0–7 days | 164 | 72.9 |
| 8–28 | 61 | 27.1 |
| **Birth weight (g)** | | |
| <1500 | 7 | 3.1 |
| <2500 | 71 | 31.6 |
| 2500–4000 | 143 | 63.6 |
| >4000 | 4 | 1.8 |
| **Resuscitation** | | |
| Yes | 8 | 3.6 |
| No | 217 | 96.4 |
| **APGAR score** | | |
| <3 | 4 | 1.8 |
| 4–6 | 69 | 30.7 |
| >7 | 152 | 67.6 |
| **Birth injury** | | |
| Yes | 4 | 1.8 |
| No | 221 | 98.2 |
| **IV line medication** | | |
| Gentamycin + ampicillin | 203 | 90.2 |
| Ceftriaxone + genta | 20 | 8.9 |
| Vancomycin + ceftazidim | 2 | 0.9 |
| **Out come** | | |
| Improved | 189 | 84 |
| Death | 9 | 4 |

**Neonatal-related risk factors for sepsis:** 169 out of 225 newborns (75.1%) were admitted to the hospital because they had an early start of sepsis. Out of the total, 71(31.6%) had a low birth weight, 173 (76.9% of them) were term (37–42 weeks), 8(3.6%) were presented with meningitis, 8(3.6%) had a history of birth asphyxia, and 73(32.4% of them) were neonates with an APGAR score of less than six. The majority of the neonates, 203 (90.2%), were given treatment with ampicillin and gentamycin. After finishing the therapy, around 89(84%) showed signs of improvement, however, 9(14%) passed away (Table 1).

**Maternal-related risk factors for neonatal sepsis:** The majority of the 124 mothers were multigravid, accounting for 55.1% of the total. A history of urinary tract infections was present in just nine out of the 95.1% of pregnant women who had ANC treatment. In all, 47 women had a fever at some point throughout their pregnancies, 12(5.9%) gave birth to multiples, 2(0.9%) had cervical cerclage, and 4(1.8%) had previously experienced complications during pregnancy. 61 women had cesarean sections, accounting for 27.9% of the total, and 133 women who did so, accounted for 59.1%. Among individuals who participated in the study, 47 (or 20.9%) had a history of PROM, and 29 (or 12.9%) reported having had a PROM that lasted longer than 12 hours. Antibiotic treatment was provided to 43 (19.1%) of the moms who were identified as having PROM. It's estimated that 20.4% of deliveries include a woman whose labor lasted far longer than she had planned. Women who had a history of chorioamnionitis made up 34 (15.1%), while women who had meconium aspiration syndrome made up 40 (17.8%) of the whole sample. Women who had obstructed labor made up 28(12.4%) of the total sample (Table 2).

Table 2: Mother risk factors predisposed for neonatal sepsis during gestation

| Variable | Frequency | %age |
|---|---|---|
| **Age of the mother (years)** | | |
| <18 | 14 | 6.2 |
| 19–29 | 115 | 51.1 |
| 30–34 | 67 | 29.8 |
| >35 | 29 | 12.9 |
| **No. of pregnancy** | | |
| Primi gravid | 97 | 43.1 |
| Multi gravid | 124 | 55.1 |
| Grand multi Para | 4 | 1.8 |
| >24 h | 8 | 3.6 |
| **Twin pregnancy** | | |
| Yes | 12 | 5.3 |
| No | 213 | 94.7 |
| **Maternal infection hx (n = 205)** | | |
| Yes | 4 | 1.8 |
| No | 201 | 89.3 |
| **Mode of delivery** | | |
| SVD | 147 | 65.3 |
| Instrumental | 17 | 7.6 |
| C/S | 61 | 27.1 |
| **PROM (217)** | | |
| Yes | 47 | 20.9 |
| No | 170 | 75.6 |
| **PROM > 12 h (n = 207)** | | |
| Yes | 29 | 12.9 |
| No | 178 | 79.1 |
| **PROM intrapartum antibiotic (n = 203)** | | |
| Yes | 43 | 19.1 |
| No | 60 | 71/1 |
| **Duration of labor (n = 174) (h)** | | |
| <8 | 51 | 22.7 |
| 8-18 | 69 | 30.7 |
| 18-24 | 46 | 20/4 |
| **Obstructed labor hx (n = 222)** | | |
| Yes | 28 | 12.4 |
| No | 194 | 86.2 |
| **Chorioamnionitis hx (n = 186)** | | |
| Yes | 34 | 15.1 |
| No | 152 | 67.6 |
| **Meconium hx (n = 183)** | | |
| Yes | 40 | 17.8 |
| No | 143 | 63.6 |
| **Foul lochia (n = 180)** | | |
| Yes | 10 | 4.4 |
| No | 70 | 75.6 |

Manifestations of newborn sepsis in the clinic These infants had a history of fever in 71% of cases, and tachypnea was documented in 29.12% of those cases. The temperature of the skin of 43 newborns, which is 19.1% of the total, was below normal, and 74 of them, which is 32.9% of the total, were not receiving enough to eat. Test results from diagnostic procedures and laboratories for babies who have been diagnosed with sepsis Gram-negative bacteria were identified in 39 of the 225 different kinds of samples that were analyzed (17.3 percent). Although 142 WBC were identified in the CBC profile obtained from the CSF in 63.1% of cases, 6.7% of cases had a WBC count of 5 cells/L or more, 4.5% of cases had glucose levels that were lower than 40mg/dL, and 2.7% of cases had protein levels that were higher than 45mg/dL (Table 3).

Table 3 Neonatal sepsis diagnostic test results

| Variables | Frequency | Percent |
|---|---|---|
| **Culture and gram stain result** | | |
| Gram-negative | 39 | 17.3 |
| Not done | 186 | 82.7 |
| **Lumbar puncture result about WBC (20) (8.9%)** | | |
| Clear | 10 | 4.4 |
| Cloudy | 6 | 2.7 |
| Bloody | 4 | 1.8 |
| **Lumbar puncture result about WBC (20) (8.9%)** | | |
| 0–5 cells/µL | 5 | 2.2 |
| >5 cells/µL | 15 | 6.7 |
| **Glucose (20) (8.9%)** | | |
| <40 mg/dL | 10 | 4.4 |
| >40 mg/dL | 10 | 4.4 |
| **Protein (20) (8.9%)** | | |
| <45 mg/dL | 6 | 2.7 |
| >45 mg/Dl | 14 | 6.2 |
| **Gram stain (20) (8.9%)** | | |
| Gram-negative | 20 | 8.9 |
| **WBC result in CBC profile** | | |
| <4 billion cells/L | 5 | 2.2 |
| 5–10.5 billion cells/L | 54 | 24 |
| >10.5 billion cells/L | 142 | 63.1 |
| No CBC profile | 24 | 10.7 |
| X-ray results in Normal finding | 5 | 2.2 |
| No X-ray | 220 | 97.8 |

Indicators of newborn sepsis on a clinical level and an examination of the major variables were carried out with the use of a bivariate analysis. The concluding multivariate analysis investigated the relationship between the poor prognosis of baby sepsis and the components that were shown to be significantly associated with the bivariate analysis ($p<0.05$). The prognosis for newborn sepsis was much poorer regardless of whether the infant had a history of meconium aspiration syndrome or respiratory distress syndrome.

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Table 4: Factors associated with clinical outcome of neonatal sepsis

| Factors | <2500 | >2500 | Asphyxia | Respiratory distress | Skin color | APGAR score | Onset of illness | Iv line medications | Place of birth | Maternal fever | NG tube feeding | Meconium aspiration |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clinical outcome | 60 | 129 | 3 | 186 | 129 | 60 | 153 | 36+Gentamycin +Ceftriaxone | Health institution | Yes | Yes | Yes |
| | | | | | | | | | Home | No | No | No |
| Percentage | 76.9% | 87.8% | 37.5% | 85.7% | 90.2% | 73.2% | 87.9% | 70.6% | 83.6% | 84.2% | 87.0% | 87.4% |
| | 18 | 18 | 5 | 31 | 14 | 22 | 21 | 15+Gentamycin + Ampicillin | N/A | N/A | N/A | N/A |
| Percentage | 23.1% | 12.2% | 62.5% | 14.3% | 9.8% | 26.8% | 12.1% | 29.4% | N/A | N/A | N/A | N/A |
| Odds Ratio | 0.465 | 1 | 1 | 0.296 | 0.329 | 0.953 | 2.227 | 3.571 | 0.308 | 4.846 | 13.862 | 0.299 |
| Confidence Interval | 0.226-0.957 | 0.023-0.440 | N/A | 0.142-0.618 | 0.155-0.701 | 0.447-2.032 | 1.049-4.728 | 1.373-9.289 | 0.085-1.112 | 1.110-21.163 | 1.850-103.87 | 0.131-0.683 |
| p-value | 0.038 | 0.009 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |

A very poor prognosis is expected for infants who have both sepsis and RDS. Compared to newborns who did not have the illness, those who did have respiratory distress syndrome had a likelihood of a bad outcome that was 74.2% higher (AOR 0.258: 0.072, 0.930). A substantial correlation was found between meconium aspiration syndrome and a bad prognosis in patients with sepsis. Neonates who had a history of meconium aspiration syndrome had an odds ratio of 0.198 (range: 0.059–0.664) of having a poor neonatal outcome, which was 80.2% higher than the odds ratio for neonates who did not have a history of meconium aspiration syndrome (Table 4).

## DISCUSSION

Neonatal sepsis is a prominent cause of morbidity and death among newborns[1]. Neonatal sepsis is a systemic infection that affects babies who are less than 28 days old. It encompasses a wide variety of systemic illnesses that may affect infants, such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and infections of the urinary tract[2].

According to the result of this study premature membrane rupture, fever, chorioamnionitis, repeated vaginal exams, meconium-stained amniotic fluid, the consumption of tainted foods, cervical cerclage, the location of the birth, premature birth, low birth weight, difficult or instrument-assisted delivery, and low appearance pulse grimace activity respiration (APGAR) scores are all risk factors for the early onset of sepsis. Other risk factors include the consumption of contaminated foods. Being hospitalized, undergoing surgery, or acquiring an infection while a patient is in the hospital may all lead to a condition known as slow-onset sepsis[6,8]. This condition is a medical emergency.

According to the findings of this research, babies that were treated had an increased likelihood of survival that was 84% greater. A study of infant sepsis was conducted in Debrezeyt, Pakistan[8], and another research investigated the causes of neonatal death due to infections[15]. Both studies came to similar conclusions. It was found that the mortality rate from sepsis was 5% of hospital-based data in Pakistan[14], 18.1% in Uganda[16], 14.5% in Sudan[13] and 51% in Egypt[13]. In Egypt, sepsis mortality was the highest.

Through their research, the researchers were able to demonstrate a link between newborn sepsis and a bad clinical outcome brought on by RDS. The infant's probability of having a negative outcome was elevated by 74.2% when there was a history of respiratory distress syndrome in the mother. Tachypnea was the determining factor for a bad outcome of sepsis (in 69.4% of cases), according to investigations that were done in Uganda[16] and Sudan[18]. These studies produced findings that were comparable to one another. This was a result of the medical personnel not having a sufficient understanding of the syndromes, early warning symptoms not being correctly diagnosed, and mothers not arriving at the hospital on time.

There was a significant correlation between the occurrence of meconium aspiration syndrome and the clinical outcome of sepsis. The likelihood of a negative outcome being experienced by a neonate was elevated by 80.2% when there was a previous diagnosis of meconium aspiration syndrome. According to research carried out in Uganda[16], infants who were diagnosed with meconium aspiration syndrome had a 2.5 times higher risk of having poor outcomes than infants who did not have a history of meconium aspiration. This underscores the need of following up on instances of meconium aspiration carefully and methodically. It can be possible that pediatricians and nurses are not as acquainted with babies as they should be to recognize the warning indications of meconium aspiration.

## CONCLUSION

In this particular research, there were major successful outcomes of newborn sepsis. The presence of respiratory distress syndromes and meconium aspiration syndrome were the primary contributors to a poor prognosis in newborn sepsis patients. It is recommended that to improve neonatal outcomes, the following should be done. Essential newborn care should be provided to all newborns; appropriate follow-up should be arranged until the end of the neonatal period. Early detection and management of neonatal infections or problems should be performed.

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1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.
4. All authors agree to be responsible for all aspects of their research work

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