

Systematic Review

Prevalence, Risk Factors and Predictors of Mortality Outcome in Neonatal Sepsis in KSA: Systematic Review

Abstract:

The systemic reaction to infection in newborn infants during the first 28 days of life has been referred to as neonatal sepsis. Global health issues include neonatal sepsis. Furthermore, newborn sepsis contributes significantly to morbidity and mortality in underdeveloped nations. This study examined the prevalence, risk factors, aetiology, death rate, and outcomes of neonatal sepsis in newborns in the Kingdom of Saudi Arabia. On the same subject, a thorough search of the literature was done using online databases like PubMed, Embase, and Google Scholar. After removing 45 duplicates, a total of 119 articles were found in the initial systematic search. 25 studies were removed after title and abstract screening on 74 study papers. Only 16 papers out of 49 total items that underwent full-text evaluation met the requirements for inclusion in this meta-analysis. We took research that were released between January 1997 and December 2021. We only looked for English-language studies during our search. Neonatal sepsis is a major public health problem due to its rising occurrence; therefore, it is crucial to look at its epidemiology, risk factors, and clinical characteristics. Since gluten is now well recognised as a precipitating factor, current research is helping to better understand the other aspects of this syndrome.

Key words: neonatology, epidemiology, mortalityantenatal care, KSA, NeonateSepsis.

Introduction:

Systemic response to bacterial, fungal, and protozoal infection is known as sepsis [1]. A bloodstream infection in newborn babies under 28 days old is referred to as neonatal sepsis. It is a significant disease-causing factor in 1–10 out of every 1000 live births, and it affects 15–50% of neonates, especially preterm newborns [2, 3]. A systemic inflammatory response to an infection is one more definition of NS. Although improvements in neonates' care have increased survival, sepsis is

still remains one of the most frequent leading cause of morbidity and mortality among neonates, especially in developing countries [4]. The clinical presentation of neonatal sepsis can be subtle and variable depending on the age of the patient and the causative organism [5]. The diagnosis of NS based on early clinical signs can be misdiagnosed with other diseases including respiratory distress syndrome, pneumonia and intracranial hemorrhages that has common nonspecific symptoms tachycardia, fever, and drowsiness [6]. The accurate diagnosis of NS is only based on positive results of sterile body fluid and/or blood culture but always takes a long time (48 to 72 hr)[7]. The classification of neonatal sepsis is based on the time of onset. According to the time of presentation, neonatal sepsis is divided into two groups: Sepsis with early onset (EOS) and late-onset onset (LOS). The terms EOS and LOS are used to describe sepsis in newborns that occurs at or before 72 hours of life (some experts prefer seven days) and at or after 72 hours of life, respectively [7]. (EOS), which is often brought on by maternal vertical transmission of organisms from the female genitourinary system to the neonate or foetus. These viruses can enter the uterus, cervix, and vagina, as well as the amniotic fluid. As they move through the vaginal canal during delivery or while still in the womb, newborns can also contract an infection. Group B streptococcus (GBS), Escherichia coli, coagulase-negative Staphylococcus, Haemophilus influenza, and Listeria monocytogenes are typical bacterial infections causing EOS. Chorioamnionitis, GBS colonisation, delivery before 37 weeks, and prolonged membrane rupture lasting longer than 18 hours are maternal risk factors that increase the risk of neonatal sepsis. In contrast, late-onset sepsis (LOS), which is typically brought on by pathogen infection during the hospital care course, is typically spread through contact with healthcare personnel or other caregivers after delivery. A portion of LOS could also be brought on by a vertically transmitted infection that manifests later than expected. Infants who require the insertion of intravascular catheters or other invasive operations that disturb the mucosa are more likely to develop LOS. [7]

According to the WHO, neonatal sepsis results in 1 million annual deaths (or 10% of all deaths in children under the age of five), with 42% of these deaths occurring within a week of birth. The leading causes of newborn deaths in the globe are thought to be preterm birth (28%) severe infections (26%) and suffocation (23%)[8], however it was recorded that incidence of neonatal bacterial sepsis may vary from one country to another as well as within the same country. In developing countries, neonatal mortality resulting from all different causes is approximately 34 per 1000 live births, occurring mainly in the first week of life, whereas it is only 5 per 1000 live births in developed countries [6].

There are numerous risk factors for developing neonatal sepsis, such as low birth weight, prolonged rupture of membranes over 24 hours, unsafe place of delivery or non-sterilized delivery, chorio-aminonitis, perinatal asphyxia, maternal pyrexia, and prolonged labor

Gram-positive bacteria were discovered to be the most common isolated organisms in LOS with regard to the causal organism [9]. At the same time, infants with EOS who were born underweight had a higher prevalence of gram-negative bacteria [10]. Additionally, it was noted that the chance of developing newborn sepsis was greatly increased following a caesarean section delivery [11]. Despite being delivered by caesarean section, babies usually experience a lengthy hospital stay and a delayed start to breastfeeding [12]. Delayed nursing after caesarean section (CS) delivery can deprive the newborn of colostrum's anti-pathogenic protective action [13].

Study Rational:

Despite the availability of new treatment options for this illness, neonatal sepsis remains a significant cause of neonatal mortality and morbidity and is the main reason for neonatal admission to the neonatal intensive care unit (NICU).

Due to the clinical importance of this topic and the scarcity of data related to it in Saudi Arabia, this study aimed to identify the incidence of neonatal sepsis, causative organisms and their antibiotics susceptibility.

Study Objectives:

This study aims to discuss and illustrate the prevalence, pattern, risk factors and Predictors of Mortality Outcome in Neonatal Sepsis in KSA.

Materials and Methods:

Study Design: systematic review.

Study duration: Data will be collected during the period from 1– 29 May, 2022.

ILR is a technique for compiling previously published studies with the aim of synthesizing suggestion on a subject; it is frequently utilized in the health disciplines to identify novelties then discover new approaches to health services, enabling the utilization of evidence-based health care, guaranteeing high quality services, and enhancing patient welfare and safety. There are six sequential stages that requisite to be followed: Explanation of the study issue; inclusion and exclusion criteria; sample definition; evaluation of included studies; findings interpretation; and presentation of the ILR synthesis

The papers that had the same goal as our study were reviewed in depth after searching and defining the sample. Following data collection, the information was grouped in a table, allowing the profile of the articles to be described and the main points were highlighted.

Due to their reputation as reliable databases, PubMed and EBSCO Information Services were preferred as the exploration databases for the papers utilized in the study. One of the biggest online digital libraries, PubMed was created by the National Center for Biotechnology Information (NCBI), a division of the National Library of Medicine of the United States. The article was created using subjects relating to prevalence, pattern, risk factors and predictors of mortality outcome in neonatal sepsis in KSA. The topics and summaries of the established papers were scrutinised.

The subjects were selected for addition founded on their applicability to the research, which must have at least one of the following subjects; neonatology, epidemiology, mortalityantenatal care, KSA, NeonateSepsis.

Exclusion criteria: All additional papers, recurring researches, and reviews of research which do not possess one of these themes as their major end were disregarded.

Statistical analysis: The data will not be analysed by any programme. The information was taken from a specified form that included the research topic, author's designation, aim, executive summary, results, conclusions, and outcomes. To guarantee rationality in addition to reducing errors, the results of each affiliate were double-revised.

In order to ensure that the research we contained within the study are applicable to the goal line of our study and to avert or diminish slips in the results, studies were double-reviewed during the article selection process.

Results:

Search results and characteristics of included studies:

A total of 119 articles were extracted from the initial systematic search, and 45 duplicates were removed. Title and abstract screening were implemented on 74 study articles, and 25 studies were excluded. Of all, 49 items underwent full-text assessment, and only 16 studies met the inclusion criteria in this systematic review.

All of these studies were conducted in Saudi Arabia but in different cities and years regarding neonatal sepsis its prevalence, etiologies, risk factors and mortality outcome. Summary of study characteristics is presented in Table 1.

Table 1: Summary of study characteristics

Author, Publishing Year	Study Objective	Methodology	Study Outcome
<p>Dr. Abdulhadi Husun Al-Mazroea (2017) [14]</p>	<p>Analyze the bacteriological and clinical characteristics of 80 premature newborns.</p>	<p>80 preterm newborns were the subject of a case-controlled study at Almadina Almunawara, Saudi Arabia. The included newborns were split into two equal groups: the first group consisted of 40 preterm neonates who were admitted to the NICU with sepsis, which was confirmed by clinical and laboratory tests; the second group consisted of 40 healthy preterm neonates.</p>	<p>An increased risk of newborn sepsis is linked to preterm labour and CS delivery. Gram positive bacteria, including CONS and staph aureus, were the most common isolates in our hospital. Klebsiella pneumoniae led the gram-negative bacteria, followed by E coli, Acenobacter, and pseudomonas (10%).</p>
<p>Ali H. Almudeer, MD., et al. (2020) [15]</p>	<p>This study aims to describe the epidemiology of early onset sepsis (EOS) and its associated risk factors in a tertiary healthcare centre in the south of KSA.</p>	<p>retrospective review of the medical records of neonates diagnosed with EOS at King Fahad Central Hospital (KFCH), Jazan, KSA. Data on the incidence, causative organisms, and related risk factors for EOS were collected.</p>	<p>the KFCH in the Jazan region has a greater incidence of EOS than other clinical settings in KSA. Reevaluating prenatal care services in the area may be necessary if preterm birth weight and low birth weight are found to be potential risk factors for infants with EOS dying young.</p>
<p>Bader Hasan Sobaih., et al. (2014) [16]</p>	<p>The study's main objective was to ascertain the overall prevalence of neonatal sepsis in very low birth weight (VLBW) infants born at one of Riyadh's university hospitals.</p>	<p>All children with very low birth weights (500 to 1500 grammes) who were delivered at King Khalid University Hospital (KKUH) in Riyadh between January 1999 and December 2007 were included in a retrospective analysis. NICU database and medical record databases were used for data collection after receiving ethics permission. Before starting antibiotics, all blood and/or CSF cultures were obtained. In this investigation, only initial bouts of sepsis</p>	<p>preventing and controlling sepsis must be given top attention because the risk of newborn sepsis in VLBW infants was high (48%) and there were significant rates of both EOS and LOS.</p>

		were taken into account.	
Hanan H. Balkhy, MD., et al. (2009) [17]	To examine the risk of device-associated bloodstream infection (BSI) in a neonatal intensive care unit at Riyadh.	a prospective surveillance research was conducted in 2006 and 2007 in Riyadh, Saudi Arabia, to assess the risk of device-associated bloodstream infection (BSI).	For umbilical catheter-associated BSI, the incidence per 1000 device-days was 10.5 and for central line-associated BSI, it was 8.2. In comparison to the rates provided by the American National Healthcare Safety Network hospitals, both rates were greater with more umbilical catheter and less central line utilisation ratios. Over the course of the trial, BSI rates decreased as more stringent infection control procedures were implemented. An independent risk factor for device-associated BSI was a prolonged device duration.
MS HASAN., et al. (2011) [18]	assess the risk factors of neonatal sepsis among the studied sample.	A total of 50 cases with established sepsis and 50 cases with no established sepsis were included as cases and controls, respectively. Between the first of October 2002 and the last day of March 2003, the study was conducted at the Chittagong Medical College Hospital's Child Health Department.	Maternal risk factors for newborn sepsis include intrapartum fever, strong-smelling alcohol, young mothers (under 20 years old), low socioeconomic status, extended labour, and UVE and Primi mothers. Prematurity, newborn resuscitation, and a low APGAR score all significantly increased the risk of sepsis. It was discovered that maternal irregular Antenatal check-up, prematurity, resuscitation at birth, and maternal intrapartum fever are the main risk factors in the development of neonatal sepsis when these risk factors' relative influences were analysed over neonatal sepsis in order to discover their predictive values.
Nazim Faisal Hamid., et al. (2021) [19]	study aims to determine the association amongst birth weight, gestational age,	A systematic search in PubMed, Web of Science, Science Direct, and EBSCO databases, was conducted. The reviewers screened the extracted literature to include	The study discovered a link between the likelihood of newborn sepsis and both neonatal and maternal variables as potential independent risk factors. Additionally, researchers found

	type of delivery, and risk of neonatal sepsis in Saudi Arabia	the studies that met the inclusion criteria.	that whereas caesarean delivery was linked to a higher risk of neonatal infection, birth weight, gestation, and vaginal deliveries were not.
A. Dawodu., et al. (1997) [20]	The purpose is to provide further information in the changing pattern of NNS in the Middle East.	Sixty-one cases of neonatal septicaemia (NNS) identified by positive Mood cultures during surveillance of infection at King Fahd Hospital of the University in Khobar, Saudi Arabia	NNS occurred in 4.9 out of every 1000 live births (LB). Birth weight-specific sepsis rates among inborn babies ranged from 2 per 1000 live births for newborns weighing more than 2500 g to 150 per 1000 live births for those weighing less than 1500 g. Foetal discomfort, a poor Apgar score at 5 mm, the need for artificial breathing, and umbilical catheterization were all major risk factors for septicaemia. Identical results were found in babies whose moms had pre-eclampsia. The most common Gram-positive isolate in both "early" (48 h) and "late" (448 h) onset septicaemia was staphylococci.
Asindi A. Asindi., et al. (1999) [21]	To determine the prevalent bacterial agents of neonatal septicemia and their antimicrobial susceptibility	During that time, any newborn with a positive blood culture was prospectively examined. The susceptibility of each isolate to several antibiotics was examined.	According to this study, Group B Streptococcus is more common in Western countries than in our environment, where Klebsiella pneumoniae is the most common bacterial cause of neonatal sepsis. For the empirical therapy of neonatal sepsis in our institution, a combination of gentamicin and cefotaxime is advised; ampicillin will no longer be used as is customarily done. There are suggested control measures to reduce nosocomial infection.
Abdulrahman Al-Matary., et al. (2019) [22]	To identify the risk factors, laboratory profile, microbial profile, mortality	A retrospective study was conducted using the neonatal intensive care unit (NICU) database in King Fahad Medical City (KFMC), Riyadh, Saudi Arabia. All	Sepsis continues to pose a severe threat to the health of newborns, thus coordinated efforts are required to identify the range of risk factors as well as the clinical characteristics of EOS and LOS in

	and complications, mortality causing organisms and antimicrobial susceptibility patterns of neonatal sepsis at a tertiary care hospital.	neonates born in KFMC with clinically diagnosed sepsis in the NICU were included in this study.	order to apply effective treatment techniques. Additionally, our study underlines that using aminoglycosides is preferable to using wide spectrum antibiotics, which are currently used more frequently.
Abdulaziz S. Alrafiah., et al. (2016) [23]	This study aimed to identify the incidence of neonatal sepsis, causative organisms and their antibiotics susceptibility.	This cross-sectional study included neonates who were born in KAMC-R and had positive blood cultures during the year of 2014 within the first 90 days of life in King Abdulaziz Medical City in Riyadh (KAMC-R)	The majority of neonatal sepsis cases in our hospital were caused by gram-positive bacteria, with CONS being the most isolated organism. However, gram-negative bacteria were associated with higher rates of mortality.
Majeda S. Hammoud., et al. (2017) [24]	To investigate the incidence and the pattern of causative organisms of culture-proven earlyonset sepsis (EOS) in Arab states in the Gulf region.	This 2-year prospective study was conducted in Kuwait, Saudi Arabia, the United Arab Emirates, and five neonatal care centres. A uniform data collection form was used to collect data prospectively. A single potentially pathogenic organism growing from blood or cerebrospinal fluid in babies within 72 hours of delivery was referred to as EOS, and clinical and laboratory results that were compatible with infection were used to diagnose the condition.	The prevalence of EOS and the distribution patterns of the pathogenic microorganisms in the Arab Gulf States are comparable to those in Western nations prior to the advent of intrapartum antibiotic prophylaxis. In the Arab state context, efforts should be made to enhance intrapartum antibiotic prophylaxis, which could prevent a significant proportion of GBS infections.
DuhaSabeeh Jumah&Mea 'adKadhum Hassan (200	to determine the predictors of outcome in neonates with	A prospective study was carried out to determine the predictors of outcome in neonates with sepsis	In contrast to neonates with positive blood cultures for Proteus and Enterobacter aeruginosa, where only 7.9% and 11.1% of

7) [25]	sepsis admitted to neonatal care unit.	admitted to neonatal care unit at Basrah Maternity and Children Hospital over six months (from the first of November 2004 till the end of April 2005).	neonates died, the highest mortality was linked to positive blood cultures for Pseudomonas aeruginosa and Staphylococcus aureus, where all neonates died (100%) and klebsiella spp. and Escherichia coli, respectively. Neonatal patients with thrombocytopenia, neutropenia, and a Creactive protein level below 10 mg/dl had a statistically significant increased mortality. Body weight, gestational age, thrombocytopenia, neutropenia, positive blood cultures for klebsiella spp., prolonged capillary refilling time, sclerema, and signs of dehydration were found to be predictive factors of the outcome of death in neonatal sepsis after regression analysis of various neonatal and maternal variables, haematological, and microbiological tests.
Gamal Allam., et al. (2015) [26]	The objective of this study was to investigate single nucleotide polymorphism (SNP) in the interleukin (IL)-1 β -31 T/C, IL-6 -174 G/C, tumor necrosis factor α (TNF- α) -308 G/A, and interferon γ (IFN- γ) +874 A/T genes for their possible association with susceptibility to early onset sepsis (EOS) in Saudi newborn	After meeting the inclusion requirements, 205 newborn babies aged 1-2 days were sequentially included in the study (as per the research protocol). The Chelex-100 technique was used to recover DNA from filter sheets. Taqman 5' nuclease allelic discrimination was used to genotype the cytokines SNP. We employed an ELISA kit, or enzyme-linked immunosorbent assay, to evaluate the levels of cytokines.	In EOS patients, circulation levels of IL-1, IL-6, TNF, and IFN were considerably (p 0.001) higher than in suspected and sepsis-free comparison groups. In Saudi newborns, the IL-1 -31C, IL-6 -174G, TNF -308G, and IFN +874A alleles were linked to EOS. In conclusion, examination of the levels of cytokines and SNP for the four examined genes can be utilised to predict how sepsis will progress in infants.

	infants.		
Fahad Abdullah Al-Zamil (2008) [27]	to determine the incidence and pattern of bacteremia in pediatric group at a tertiary hospital in Riyadh, Saudi Arabia.	This retrospective study was conducted at the Department of Pediatrics, College of Medicine, King Khalid University Hospital, Riyadh in the period of January 2003 to January 2005. Positive culture was found in 259 patients aged below 15 years with a total of 8244 admissions in the period.	Staphylococcus aureus is the most common isolated pathogen. The most common primary infections are respiratory tract infection and septic meningitis. Klebsiellapneumoniae and E. coli are the most common isolated Gram-negative organisms.
R A Kilani, M Basamad. (2000) [28]	To determine the pattern of proven bacterial sepsis in a neonatal intensive care unit	retrospectively reviewed the medical records of all infants who had positive blood cultures during a 2-year period in the NICU at a university hospital in Riyadh, Saudi Arabia.	Overall, 10.2% of NICU admissions had proven-bacterial sepsis (PBS). PBS occurred at rates of 19%, 41%, and 49%, respectively, in infants with low birth weights (LBW), very low birth weights (VLBW), and extremely low birth weights (ELBW). In 21% of all sick neonates, bacterial sepsis relapsed many times. The most frequent contaminant causing late-onset sepsis (LOS) was Coagulase Negative Staphylococcus (CONS) (50%) and the most frequent contaminant causing early-onset sepsis (EOS) was Escherichia coli (29%) (EOS). In 50% of the EOS episodes and 29% of the LOS episodes, gram-negative bacteria (GNB) were the causative agents. Only 14 out of the PBS, or 11%, were EOS. There were 10 newborns (10.4%) with bacterial meningitis. The overall neonatal mortality rate associated with PBS was 9%, or 22% of all neonatal fatalities.

A Doronjski, et al. (2015) [29]	To examination of incidence of neonatal sepsis and determination of risk factors.	The survey was conducted as retrospective - prospective study and included 239 preterm infants (born before 37 weeks of gestation) who were treated in Neonatal Intensive Care Unit (NICU) in Institute for Child and Youth Health Care of Vojvodina during one year (January 1st, 2012 to December 31st, 2012).	Education of employees, use of checklists and sterile sets for blood sampling, permanent control of false positive blood cultures, as well as regular and routine monthly reports are crucial for successful reduction of contamination rates.
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Discussion:

The incidence of neonatal sepsis has been increased worldwide [30, 31], especially developing countries. Also, sepsis is a major risk factor neonatal mortality in more than third of all neonatal deaths annually and a significant risk for disease morbidity as well as the admission to the NICU [32]. Our estimates confirm that neonatal sepsis is an important contributor to neonatal morbidity in KSA.

In this study we aimed to discuss the burden of neonatal sepsis in Saudi Arabia in the last years.

The incidence estimated by Ali H. Almudeer, MD., et al [15], was 4.44 per 1000 live births with EOS in their retrospective study in Jazan between May 1, 2012 and April 31, 2019. A two-year prospective evaluation of EOS in five hospitals in the KSA and other Arab Gulf states was reported by Hammoud et al. Between King Abdul Aziz Hospital in KSA and Al-Sabah Maternity Hospital in Kuwait, their sample's incidence of EOS ranged from 0.4 per 1000 live births to 2.6 per 1000 live births [24]. In other investigations carried out in KSA, tertiary healthcare facilities were examined for EOS and LOS. In a retrospective study carried out in King Fahad Medical City in Riyadh, Al-Matary et al. revealed a number of newborns who had been diagnosed with neonatal sepsis. According to their research, between January 2011 and December 2015, there were 298 diagnoses of neonatal sepsis, with 33 (11.1%) instances being labelled as EOS.[22].

In older studies done in KSA, the frequency of neonatal septicaemia of 5 per cent observed in the infants admitted for special care during the study period is similar to reports from other intensive care units [34, 35]. These results are higher than those estimated from the earlier studies. This may be because the development in the care units and antibiotic usage as well.

Higher percent was obtained in Riyadh (9%) and confirm that major systemic infection is still an important cause of morbidity among high risk infants admitted for special care. The incidence of septicaemia of 4.9/ 1000 live births (LB) among inborn population is within the range of 1-5.7/1000 LB reported from other perinatal care centres in the West and Saudi Arabia. [36] A much higher figure of 6-12/1000 LB has been reported from Riyadh" and other developing countries. [37, 38, 39] The variation in the incidence probably reflects differences in the population characteristics and the prevalence of the predisposing factors.

In another cross-sectional study done by Abdulaziz S. Alrafiah., et al. [23] included neonates who were born in KAMC-R and had positive blood cultures during the year of 2014 within the first 90 days of life. They found that among 85 neonates with positive blood cultures 43 (51%) had documented sepsis in their charts. Out of these 43 neonates 17 (40%) had early-onset sepsis and 26 (60%) had late-onset sepsis.

Many studies were done previously regarding the risk factors of neonatal sepsis in different parts of KSA. The medical records of all children who had positive blood cultures throughout a 2-year period in the NICU at a university hospital in Riyadh, Saudi Arabia, were retrospectively evaluated in a prior study by R AKilani et al [28] in Riyadh, KSA. Low, extremely low, and very low birth weights were discovered to be risk factors for neonatal sepsis. PBS occurred at rates of 19%, 41%, and 49%, respectively, in infants with low birth weights (LBW), very low birth weights (VLBW), and extremely low birth weights (ELBW). In 21% of all sick neonates, bacterial sepsis relapsed many times. In a similar study done by Bader Hasan Sobaih., et al. [16], two hundred and twenty five of the VLBW infants in this study developed neonatal sepsis with an overall incidence of 48%. This high figure is similar to that reported by Haque et al [40], 2 decades ago done in VLBW infants in the same unit. This result was also reported by MS HASAN., et al. [18]

Also device-associated bloodstream infection (BSI) is a considerable risk factor which was discussed in Hanan H. Balkhy MDs' [17] among a sample of neonatal intensive care unit at Riyadh, Saudi Arabia, during 2006 and 2007. The incidence per 1000 device-days was 8.2 for central line-associated BSI and 10.5 for umbilical catheter-associated BSI. Both rates were higher with more umbilical catheter and less central line utilization ratios compared with those reported by the American National Healthcare Safety Network hospitals.

In a study published in 2015 by ADoronjski., et al. [29] in which they discussed the main risk factors of neonatal sepsis among 239 preterm infants (born before 37 weeks of gestation) who were treated in Neonatal Intensive Care Unit (NICU) The main risk factors for sepsis were prelabor rupture of membranes, low

gestational age, low birth weight, mechanical ventilation, umbilical venous catheter placement, and abdominal drainage. Prematurity is reported as risk factor for neonatal sepsis in MS HASAN., et al. [18]. In their study prematurity (gestational age < 37 weeks) had a significant association ($P < 0.016$) with the development of sepsis. Also it was seen in other observation that justified the inverse relationship of sepsis and gestational age. [41, 42] Abdulrahman Al-Matary [22] reported that, for both neonates with EOS and LOS prematurity was the major neonatal risk factors for sepsis 16 (48.5%), 214 (80.8%); respectively. Multiparity and delivery by caesarean section were the top maternal risk factors of both EOS and LOS. Neonates with LOS had high CRP, Total WBC count and thrombocytopenia compared to EOS neonates.

In another study Gamal Allam., et al. [26] studied the associations between cytokine gene polymorphisms and the development, course, and outcome of sepsis and they reported that a total of 205 newborn infants aged 1-2 days were consecutively enrolled onto the study having met the inclusion criteria.

Considering the gestational age as a risk factor for neonatal sepsis, a case controlled study done by Abdulhadi Husun Al-Mazroea [14] in Ohud general hospital in Almadina Almunawara. 80 preterm newborns were included in the study and were split into two groups: the first group consisted of 40 preterm neonates admitted to the NICU with sepsis, which was determined by clinical and laboratory tests, and the second group consisted of 40 healthy preterm neonates. Neonatal sepsis group members' gestational ages and Apgar scores were significantly lower than those in the healthy group. When compared to the normal group, the newborn sepsis group's respiratory rate was substantially higher. In comparison to the normal group, the newborn sepsis group had a considerably increased neutrophil and IT count. However, the NS group's platelet count was lower than that of the normal group. A comparable systematic review and meta-analysis was carried out in Ethiopia by Belachew et al., (2020) [45] to examine the connection between gestational age and newborn sepsis. They reported that preterm neonates were 3.36 times more vulnerable to developing neonatal sepsis than term newborns.

MS HASAN., et al. [18] divided the neonatal sepsis risk factors into neonatal and maternal factors, however (T-1 & T-3), Prematurity, APGAR scores, resuscitations were only the significant neonatal factors found to be associated with neonatal sepsis. Among the maternal risk factors study shows that the attack rates of sepsis increased significantly with neonates born to mothers less than 20 years old ($P < 0.003$), in Primi ($P < 0.029$) in poor income group family ($P < 0.004$) and those mothers took irregular antenatal checkup ($P < 0.046$). But no previous study could be found to support these factors. Prolonged labor > 24 hrs is a recognized risk factor for neonatal sepsis. [43] We also observed significant ($P < 0.008$) association between this factor and sepsis.

Regarding the culture isolated etiology of neonatal sepsis in the different studies, The most prevalent culture isolate among neonatal sepsis group were gram positive bacteria as CONS (27.5%) and staph aureus (20%). The gram negative bacteria were klebsiella Pneumonia (20.8%) followed by E coli (15%) then Acenobacter (10%) and pseudomonas (10%) in AbdulhadiHusun Al-Mazroea [14], while in another study, around 60% of EOS were due to Group B Streptococcus infections followed by E. coli. [24] Similarly, GBS infection was reported to be the leading cause of EOS among American populations, followed by E. coli infections. [44] In another study, gram positive pathogens were the leading organisms retrieved in 87.4% of LOS which matched with most published reports all over the world. Staphylococcus Epidermidis was the most common single infecting organism in LOS (63.8%). [16] Unlike most of the reports regarding EOS commonest pathogens (which are gram negative organisms representing maternal flora). In a study done by Asindi A. Asindi., et al. [21] identifies Klebsiella pneumoniae as the leading bacterial agent of neonatal sepsis in our environment in contrast with Western countries where Group B Streptococcus is predominant. Based on in vitro susceptibility test results, a combination of gentamicin and cefotaxime is recommended; and no more conventional use of ampicillin, for empirical treatment of neonatal sepsis in the hospital. Following GBS as the most prevalent infection in EOS neonates, Escherichia coli was found in another study's findings. Staphylococcus spp., Klebsiella, and Pseudomonas aeruginosa were the most prevalent microbes in LOS neonates. In comparison to LOS 24, which accounts for 11.3% of all LOS, EOS 5 has a higher mortality rate from newborn sepsis (15.2% from the whole EOS). Amikacin had a high susceptibility among all Gram-negative bacteria. Amikacin and gentamycin are effective against non-fermenting gram-negative bacteria such P. aeruginosa and Acinetobacter. Gentamycin had an effect on all Gram-positive bacteria. Floconazole was responsive to thirteen isolates of Candida albicans; 85% of them.[22]

The survival rate of infants with neonatal sepsis varies from place to another according to many variations including the high levels of health care. A high survival rate was obtained by Bader Hasan Sobaih., et al [16] , which is around 88%, is comparable to international figures [46], reflecting the good quality of care provided to those infants.

In A. Dawodu's [20], the case fatality rate of 23 per cent in this study is comparable to recent published results [47], but higher mortality have been reported from other units including Riyadh. These findings suggest that neonatal septicaemia is still associated with significant mortality. The main-stay of therapy of established sepsis includes full intensive care support and appropriate antibiotics based on the local sensitivity of the pathogens. [48]

The predictors of death rates and outcome were discussed by DuhaSabeehJumah et al. [25]. A high death rate of 44.2 percent was observed; Radhy H. reported a similar high figure for Basrah (Iraq) in 2001 (43.5 percent). Similar outcomes were attained in Abha (Saudi Arabia) by Asindi A et al. (44%)[21] and in Mexico (43.9%) by Rodriguez-Weber, et al. [50] However, other writers found lower fatality rates, such as the 19.3% found in the study by Ezechukwze C, et al. in Nigeria. [51], Koutouby A et al. in the United Arab Emirates (26%)[52], Stall B. in the United States (28%)[20], and Dawodu A et al. in Al-Dammam (Saudi Arabia) (28%) According to [21], there are numerous explanations for these variations in newborn sepsis death rates between nations, including social, regional, and racial factors, use of ventilators, incubators, different microorganisms and use of different antibiotics[52].

Conclusion:

Our study shows a high prevalence of neonatal sepsis with variable etiologies and risk factors in different cities. With growing incidence and because it's a serious problem with a high morbidity and mortality rate, neonatal sepsis is becoming a main public health concern; thus, investigating its epidemiology, risk factors, etiology and mortality outcome rate is of great importance. Identifying pre-term birth weight and low birth weight as possible risk factors of early mortality of infants with EOS and LOS may necessitate the need for reassessment of antenatal care services in the region.

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