Systematic Review

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

Abstract:

Neonatal sepsis is the term that have been used to describe the systemic response to infection in newborn infants during the first 28 days of life. Neonatal sepsis is a worldwide health problem. Additionally, neonatal sepsis causes a great burden of morbidity and mortality in developing countries. This paper aimed at exploring the epidemiology of the neonatal sepsis in newborn , including its prevalence, associated risk factors, etiology and mortality rate and outcome in KSA. An extensive search of the literature was conducted from electronic databases such as PubMed, Embase, and Google Scholar about the same topic. 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 meta-analysis. We extracted studies published from January 1997 to December 2021. Our search was limited to studies published in English. With growing incidence, neonatal sepsis is becoming a main public health concern; thus, investigating its epidemiology, risk factors and clinical features is of great importance. It is now well known that gluten is a precipitating factor, and the research being conducted at present is adding to the understanding of other components of this condition.

Key words: neonatology, epidemiology, mortality antenatal care, KSA, Neonate Sepsis.

Introduction:

Sepsis is defined as a systemic reaction to bacterial, fungal and protozoal infection [1]. Neonatal sepsis refers to an infection involving the bloodstream in newborn infants less than 28 days old. It is a serious cause of diseases in about1-10 per 1000 live births also it results in 15-50% of neonates particularly in preterm infants [2, 3]. Another definition of NS is a systemic response of inflammation to an infection. 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: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis in neonates at or before 72 hours of life (some experts use seven days), and LOS is defined as sepsis occurring at or after 72 hours of life [7]. (EOS) typically caused by maternal vertically transmitted organisms to the neonate from the female genitourinary system to the newborn or the fetus. These pathogens can ascend the vagina, the cervix, and the uterus, and can also infect the amniotic fluid. Neonates can also become infected in utero or during delivery as they pass through the vaginal canal. Typical bacterial pathogens for EOS include Group B streptococcus (GBS), Escherichia coli, coagulase-negative Staphylococcus, Haemophilus influenza, and Listeria monocytogenes. Maternal factors that increase the risk of neonatal sepsis include chorio-amnionitis, GBS colonization, delivery before 37 weeks, and prolonged rupture of membranes greater than 18 hours, while, late-onset sepsis (LOS) usually caused by pathogens infection during the hospital care course usually occurs via the transmission of pathogens from the surrounding environment after delivery, such as contact from healthcare workers or caregivers. A percentage of LOS may also be caused by a late manifestation of vertically transmitted infection. Infants requiring intravascular catheter insertion, or other invasive procedures that disrupt the mucosa, are at increased risk for developing LOS. [7]

The WHO reports that neonatal sepsis causes 1 million deaths per year (10% of all deaths in children under the age of five), with 42% of these deaths happening one week after birth. Preterm delivery (28%), serious infections (26%), and asphyxia are considered to be the top direct causes of neonatal death worldwide (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

Regarding the causative organism, gram-positive bacteria were found to be the most prevalent isolated organisms in LOS [9]. At the same time, gram-negative pathogens were more common among underweight infants at birth with EOS [10]. Also it was reported that cesarean section delivery was significantly related to the risk of occurrence of neonatal sepsis [11]. Although newborns delivered via cesarean section overcome the vaginal bacteria, they frequently have a prolonged hospital stay and a delayed start to breastfeeding [12]. Delayed breastfeeding in CS deliveries can deprive the neonate of colostrum's protective effect against various pathogenic microbes that are harmful to the newborn [13].

Study Rational:

Neonatal sepsis is a major pediatric health care problem despite the availability of new modalities in the management of this disease and still an important cause of neonatal mortality and morbidity and it's the major cause for neonatal admission in 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, mortality antenatal care, KSA, Neonate Sepsis.

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
Dr. Abdulhadi Husun Al-Mazroea (2017) [14]	Study the clinical and bacteriological profile of 80 preterm neonates.	**case controlled study conducted at Almadina Almunawara, Saudi Arabia on 80 preterm neonates. The included neonates were divided into 2 equal groups, the first groups included 40 preterm neonates directed to neonatal intensive care unit (NICU) with diagnosis of sepsis that proved was with clinical and laboratory investigations and the second group included 40 healthy preterm neonates.**	Preterm pregnancy and CS delivery is associated with higher risk for neonatal sepsis. Gram positive bacteria were the most prevalent type of isolates in our hospital including CONS and staph aureus. The gram negative bacteria were klebsiella Pneumonia followed by E coli then Acenobacter and pseudomonas (10%).
Ali H. Almudeer, MD., et al. (2020) [15]	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.	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.	study shows a higher incidence of EOS in KFCH in the Jazan region compared to similar clinical settings in KSA. Identifying pre-term birth weight and low birth weight as possible risk factors of early mortality of infants with EOS may necessitate the need for reassessment of antenatal care services in the region.
Bader Hasan Sobaih., et al. (2014) [16]	The aim of the study was to determine the overall incidence of neonatal sepsis in very low birth weight (VLBW) infants born at one of university hospitals in Riyadh, Saudi Arabia for the period 1999 to 2007, and	A retrospective study of all very low birth weight (500grams to 1500 grams) infants born at King Khalid University Hospital (KKUH) in Riyadh over a 9-year period from January 1999 to December 2007 were included. Data were collected from medical records and NICU database after obtaining ethics approval. All cultures were taken (blood and/or CSF) prior to initiation of antibiotics. Only first episodes of sepsis	The rate of neonatal sepsis in VLBW infants was high (48%) with high rates of EOS as well as LOS which necessitates a high priority to prevent and control sepsis in our unit.

	identify the incidences and commonest isolated pathogens in both early and late onset episodes of sepsis in this group of infants.	were considered in this study. The main outcomes are total incidences of sepsis, incidence of early and late onset sepsis, and the causative pathogens for each type of sepsis.	
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 study, to examine the risk of device-associated bloodstream infection (BSI) in a 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. Concurrent with implementation of more strict infection control practices, BSI rates declined over the course of the study. Prolonged device duration was an independent risk factor for device-associated BSI.
MS HASAN., et al. (2011) [18]	assess the risk factors of neonatal sepsis among the studied sample.	**A total number of 50 cases were enrolled as case having established sepsis and 50 cases were matched as control having no established sepsis. This study was done in Child Health Department of Chittagong Medical College Hospital from 1st October 2002 to 31st March 2003.**	maternal intrapartum fever, foul smelling liquor, young mother (< 20 yrs), poor income group, prolonged labor, UVE & Primi mother can be designated as maternal risk factors for neonatal sepsis. Among neonatal factors, prematurity, resuscitation at birth & low APGAR score carried the significant risk of developing sepsis. Relative influence of these risk factors when analyzed over neonatal sepsis in detecting their predictive values, it was found 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.
Nazim Faisal Hamid., et al. (2021) [19]	study aims to determine the association amongst birth weight, gestational age, type of delivery, and risk of neonatal sepsis in Saudi Arabia	A systematic search in PubMed, Web of Science, Science Direct, and EBSCO databases, was conducted. The reviewers screened the extracted literature to include the studies that met the inclusion criteria.	This study found that both neonatal and maternal factors as potential independent risk factors to have an association with the risk of neonatal sepsis. We also observed that birth weight, gestational, and vaginal deliveries are not associated with a higher risk of neonatal sepsis, while cesarean delivery was associated with greater risk.
A. Dawodu ., et al. (1997) [20]	The purpose is to provide further information in the changing pattern of NNS in the Middle East. It is also to document the perinatal risk factors for NNS among infants under special care using a case control method.	**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 from September 1983- September 1988 were studied to evaluate the local pattern of pathogens and the risk factors for sepsis using a case control analysis.**	The incidence of NNS was 4.9 per 1000 live births (LB). Among inborn infants, birth weight specific sepsis rate ranged from 2 per 1000 liveboras among infants with birth weight > 2500 g to 150 per 1000 liveboras in those weighing < 1500 g. Factors significantly associated with septicaemia were foetal distress, low Apgar score at 5 mm, and requirement for mechanical ventilation and umbilical catheterization. Similar findings were obtained with infants whose mothers had pre-eclampsia. Staphylococci were the major Gram-positive isolate occurring hi both 'early' (< 48 h) and 'late' (448 h) onset septicaemia.
Asindi A. Asindi., et al. (1999) [21]	To determine the prevalent bacterial agents of neonatal septicemia and their antimicrobial susceptibility in Abha Maternity Hospital, Saudi Arabia, during	**Any newborn with a positive blood culture during the period was prospectively studied. All isolates were tested for antimicrobial susceptibility.**	This study thus 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

	the years 1996-98.		ampicillin, for empirical treatment of neonatal sepsis in our hospital. Control measures for limiting nosocomial infection are suggested.
Abdulrahman Al-Matary., et al. (2019) [22]	To identify the risk factors, laboratory profile, microbial profile, mortality and complications, mortality causing organisms and antimicrobial susceptibility patterns of neonatal sepsis at a tertiary care hospital.	**A retrospective study was conducted using the neonatal intensive care unit (NICU) database in King Fahad Medical City (KFMC), Riyadh, Saudi Arabia. All neonates born in KFMC with clinically diagnosed sepsis in the NICU were included in this study.**	Concerted efforts are needed to determine the spectrum of risk factors and the clinical characteristics of EOS and LOS in order to implement appropriate treatment strategies as sepsis remains to be a serious danger to neonatal wellbeing. Moreover, our study emphasizes that use of aminoglycosides is much agreeable as compared to the broad spectrum antibiotics which are more rampantly used nowadays.
Abdulaziz S. Alrafiaah., 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.	**Five neonatal care units participated in this 2-year prospective study in Kuwait, the United Arab Emirates, and Saudi Arabia. Data were collected prospectively using a standardized data collection form. EOS was defined as the growth of a single potentially pathogenic organism from blood or**	The incidence of EOS and the patterns of the causative organisms in the Arab states in the Gulf region are similar to those in developed countries before the era of intrapartum antibiotic prophylaxis. Efforts should be made to improve intrapartum antibiotic prophylaxis in the Arab state setting, which could avert large numbers of GBS infections.

		cerebrospinal fluid in infants within 72 h of birth, with clinical and laboratory findings consistent with infection.	
Duha Sabeeh Jumah & Mea'ad Kadhum Hassan (2007) [25]	to determine the predictors of outcome in neonates with sepsis admitted to neonatal care unit.	**A prospective study was carried out to determine the predictors of outcome in neonates with sepsis 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).**	Highest mortality was associated with positive blood culture for Pseudomonas aeruginosa and Staphylococcus aureus, where all neonates died (100%), followed by klebsiella spp. and Escherichia coli (71.1%) and (48.5%) respectively in comparison with neonates who have positive blood culture for Proteus and Enterobacter aeruginosa where only 7.9% and 11.1% of neonates died respectively. A statistically significant higher mortality was reported in neonates having thrombocytopenia, neutropenia and Creactive protein ≥10 mg / dl. Regression analysis of different neonatal and maternal variables, hematological and microbiological tests, revealed that body weight, gestational age, thrombocytopenia, neutropenia, positive blood culture for klebsiella spp., prolonged capillary refilling time, sclerma and signs of dehydration are predictive factors of the outcome of death in neonatal sepsis.
Gamal Allam., et al. (2015) [26]	The objective of this study was to investigate single nucleotide polymorphism (SNP) in the interleukin (IL)-1β -31 T/C, IL-6 -174 G/C, tumor necrosis factor α (TNF-α) -308	**A total of 205 newborn infants aged 1-2 days were consecutively enrolled onto the study having met the inclusion criteria (as per the research protocol). DNA was extracted from filter papers using the Chelex-100 method. The cytokines SNP were genotyping using Taqman 5' nuclease allelic**	the circulating IL-1β, IL-6, TNF-α, and IFN-γ were significantly ($p < 0.001$) elevated in EOS patients compared to suspected and sepsis-free control groups; and IL-1β -31C, IL-6 -174G, TNF-α -308G, and IFN-γ +874A alleles were associated with EOS in Saudi infants. In conclusion, analysis of cytokines concentrations and SNP for the four tested genes can be

	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 infants.	**discrimination. For cytokine measurements we used the commercially available Enzyme-Linked Immunosorbent Assay (ELISA) kit.**	used as a predictor of sepsis outcome in newborns.
Fahad Abdullah Al-Zamil (2008) [27]	to determine the incidence and pattern of bacteremia in pediatric group at a tertiary hospital in Riyadh, SaudiArabia.	**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 the incidence of proven-bacterial-sepsis (PBS) was 10.2% of NICU admissions. The incidence of PBS in low-birth-weight (LBW), very low-birth-weight (VLBW), and extremely low-birth-weight (ELBW) infants were 19%, 41%, and 49% respectively. Multiple episodes of bacterial sepsis occurred in 21% of all infants infected. Coagulase negative Staphylococcus (CONS) (50%) was the most common infecting organism causing late onset sepsis (LOS) and Escherichia coli (29%) the most common causing early onset sepsis (EOS). Gram negative bacteria (GNB) were the infecting organisms in 50% of the EOS episodes and 29% of LOS episodes. Only 11% (14) of the PBS were EOS. Only 10 (10.4%)

			infants had bacterial meningitis. The overall PBS related mortality was 9%, representing 22% of all neonatal deaths.
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.

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. While Hammoud et al. reported a two-year prospective investigation of EOS in five hospitals in KSA and other Arab states in the Gulf region. The incidence of EOS in their sample varied between 0.4 per 1000 live births in King Abdul Aziz Hospital in KSA to 2.6 per 1000 live births in Al-Sabah Maternity Hospital in Kuwait [24]. Other investigations conducted in KSA investigated both EOS and LOS in tertiary healthcare facilities in the kingdom. Al-Matary et al. conducted a retrospective study in King Fahad Medical City in Riyadh and reported a number of neonates diagnosed with neonatal sepsis. In their findings, there were 298 diagnoses of neonatal sepsis between January 2011 and December 2015, with 33 cases (11.1%) classified 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. Alrafiaah., 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. In a previous retrospective study done by R A Kilani., et al [28] in Riyadh, KSA, they 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. They found that low and very low and extremely low birth weight at the time of birth is risk factor for neonatal sepsis. The incidence of PBS in low-birth-weight (LBW), very low-birth-weight (VLBW), and extremely low-birth-weight (ELBW) infants were 19%, 41%, and 49% respectively. Multiple episodes of bacterial sepsis occurred in 21% of all infants infected. 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.BalkhyMDs' [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 puplished in 2015 by A Doronjski., 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] AbdulrahmanAl-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. Multiparty and delivery by caesarean section were the top maternal risk factors of both EOS and LOS. Nneonates 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. The study included 80 preterm neonates subdivided into 2 groups, the first groups included 40 preterm neonates admitted to NICU with sepsis proved with clinical and laboratory investigations and the second group included 40 healthy preterm neonates. The gestational age and Apgar score were lower in neonatal sepsis group than normal group with a significant difference. The respiration rate was significantly increased in neonatal sepsis group than normal group. A significantly higher count of neutrophil and IT were found in the neonatal sepsis group in comparison with normal group. However, platelets count was lower in NS group than normal group. Belachew et al., (2020) [45] performed a similar systematic review and meta-analysis in Ethiopia to assess the relationship between neonatal sepsis and gestational age. They reported that preterm neonates were 3.36 times more vulnerable to developing neonatal sepsis than term newborns.

MS HASAN., et al. [18] devided the neonatal sepsis risk factors into neonatal and maternal factors, however (T-1 & T-3), Prematurity, APGAR score 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 e" 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 Abdulhadi Husun 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. Another study results showed that in the EOS neonates, GBS was the most common pathogen followed by Escherichia Coli. In LOS neonates, the common organisms were Staphylococcus spp., Klebsiella and Pseudomonas aeruginosa. Mortality rate of neonatal sepsis is higher in EOS 5 (15.2%) from total EOS compared to LOS 24 (11.3%) from total LOS. All Gram-negative bacteria were sensitive to Amikacin. Gram-negative non-fermenting bacteria, such as P. aeruginosa and Acinetobacter were sensitive to amikacin and gentamycin. All Gram-positive bacteria were sensitive to gentamycin. Among thirteen Candida albicans isolates, 85% were sensitive to fluconazole. [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]

Duha Sabeeh Jumah., et al. [25] discussed the predectors of mortality rates and outcome. A high mortality rate was reported about (44.2%), the same high result was reported in Basrah (Iraq) by Radhy H. in 2001 (43.5%)[49], similar results were obtained in Abha (Saudia Arabia) by Asindi A et al, (44%)[21] and by Rodriguez-weber, et al in Mexico (43.9%)[50], while lower mortality rates were detected by other authors as that carried out by Ezechukwze C, et al in Nigeria (19.3%)[51], by Koutouby A et al, in UAE (26%)[52], Stall B. in USA (28%)[20], and by Dawodu A et al, in Al-Dammam (Saudi Arabia) (28%)[21], these differences in mortality rate in neonatal sepsis among different countries may be explained by many factors e.g: socioeconomic, geographical 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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