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“Association between neonatal sepsis and incidence of neonatal jaundice”

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بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ
وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ

سورة المجادلة آية ١١

Dedication

This study is wholeheartedly dedicated to:

- My family for their constant financial, emotional, spiritual, and moral support. Their encouragement and strength have been crucial during times of doubt.
- I also want to acknowledge **Msc. Khloud Adnan Abdullah**
- whose support motivated me to finish this work. I are profoundly thankful to Almighty God for granting us good health and for providing guidance, strength, mental clarity, protection, and skills. My sincere gratitude extends to all.

Acknowledgement

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SUPERVISOR CERTIFICATIONS

I certify that the preparation of this research titled **(Association between neonatal sepsis and incidence of neonatal jaundice)** and conducted by the students (Essa Mahdi Abd Al Hussen) was conducted under my supervision, College of Medicine, Diyala University, which is part of the requirements for obtaining a bachelor's degree in medicine.

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Abstract

Background: Neonatal sepsis is characterized as a systemic disease caused by bacteria, viruses, or fungi (yeast) that results in haemodynamic abnormalities and other clinical signs, as well as severe morbidity and death.

Objectives: To assess the correlation between the occurrence of neonatal sepsis and the development of neonatal jaundice in affected newborns admitted to the NCU in Al-Batool teaching hospital, Diyala, Iraq.

Patients and methods: A cross-sectional study was conducted from 24 September to 28 November 2024 on 60 neonates (25 males, 35 females) under 28 days old with jaundice at Al-Batool Teaching Hospital. Data on demographics, sepsis diagnosis, jaundice characteristics, and outcomes were collected via questionnaires and parental interviews. Privacy was ensured through data coding, and analysis was performed using SPSS v26.

Results: This study investigates the association between neonatal sepsis and the incidence of neonatal jaundice. Jaundice was observed in 56.7% of cases after 3–5 days, consistent with physiological jaundice, while 21.7% of cases presented within the first 24 hours, suggesting pathological causes such as sepsis. A significant association was found between elevated WBC counts and poor feeding (P-value = 0.004), indicating systemic inflammation in septic neonates. However, no statistically significant association was observed between sex and poor feeding (P-value = 0.106), suggesting feeding difficulties are unrelated to neonatal sex.

Conclusion: Our study highlights the association between neonatal sepsis and neonatal jaundice.

Introduction

Neonatal sepsis is characterized as a systemic disease caused by bacteria, viruses, or fungi (yeast) that results in haemodynamic abnormalities and other clinical signs, as well as severe morbidity and death. Years of clinical experience caring for babies with confirmed or suspected sepsis have not yet led to a standard definition of neonatal sepsis becoming established. A pathogen isolated from a normally sterile bodily fluid, like blood or cerebrospinal fluid , has historically been used to define sepsis. However, because powerful proinflammatory cytokines can induce the clinical features of sepsis, infant sepsis has also been referred to as systemic inflammatory response syndrome [1].

Neonatal sepsis has been classified as either early-onset or late-onset based on the age at which the sepsis episode starts and when it occurs. According to some doctors, illnesses that manifest clinically within the first 72 hours of birth are considered early-onset infections, especially those brought on by group B streptococcus ; infections that appear before 7 days of age are especially included in this category. Most early-onset infections are vertically transmitted from mother to child, which means they are contracted before or during childbirth. Microorganisms that are acquired through contact with the community or hospital environment are the source of late-onset illnesses. They appear after birth or between three and seven days of age[2].

Among neonates, the most common condition that increases the risk of infection and sepsis is prematurity or low birthweight . Preterm low birthweight babies have an infection rate three to ten times higher than that of full-term normal birthweight babies. Immunological impairment and the absence of maternal IgG obtained through the placenta may raise the risk of infection in premature babies. Additionally, because preterm babies may require protracted intravenous access,

endotracheal intubation, or other invasive procedures that disrupt barrier and clearance mechanisms or create a portal of entry, they are more susceptible to hospital-acquired infections. Reductions in infant 25-hydroxyvitamin D levels have also been connected to early-onset sepsis[3].

The treatment of infant infections might involve antimicrobial medication for either recognized (definitive) or suspected (empirical) microorganisms. Factors including exposures, whether symptoms appear early or late, and whether the patient is in the community or in a hospital when symptoms first appear all affect the antibiotic decision. Cultures of clinical specimens and a thorough history and physical examination are the most important components[4].

The first line of empirical treatment for bacterial infections with early onset should be ampicillin with an aminoglycoside (usually gentamicin); third- or fourth-generation cephalosporin drugs should be reserved for suspected Gram-negative meningitis. The treatment of infections brought on by Gram-negative bacteria that manufacture extended-spectrum β-lactamase requires carbapenems, such as meropenem. The use of piperacillin-tazobactam and ampicillin-sulbactam in treating infants admitted to the newborn critical care unit is increasing; however, tazobactam should not be used to treat meningitis due to its uneven penetration into the central nervous system. However, when combined with ampicillin, the β-lactamase inhibitor sulbactam does seem to accumulate at high levels in the CSF[5].

In newborns, unconjugated hyperbilirubinemia is common and usually occurs naturally or as a consequence of breast-milk jaundice, a benign illness. However, jaundice in newborns caused by underlying cholestasis (and the associated conjugated hyperbilirubinemia) is always pathological and needs to be evaluated

very once. Newborns in developing countries are at danger of acquiring bilirubin-induced brain damage, and severe neonatal jaundice is rather common there[6].

Neonatal cholestasis may result from medical or surgical interventions. The most frequent causes include biliary atresia, which accounts for about one-third of cases in India; idiopathic neonatal hepatitis ; infections like sepsis, UTIs, and congenital infections; metabolic disorders like tyrosinemia, galactosemia, and alpha-1 antitrypsin deficiency; and choledochal cysts, including Caroli's disease[7].

Neonatal jaundice has been associated with sepsis in critically ill infants, and non-physiological hyperbilirubinemia in neonates is quite common. In the first few days of life, however, jaundice may be one of the first signs of bacterial sepsis. Some studies suggest that a newborn's jaundice is the earliest sign of a urinary tract infection[8].

Furthermore, a blood or urine culture that is positive for indirect-reacting hyperbilirubinemia in a newborn does not always rule out infection as the cause of the jaundice. However, neonates who exhibit late-onset jaundice, direct-reacting hyperbilirubinemia, abnormal laboratory or physical examination results, or other symptoms should be cautiously watched for signs of sepsis or urinary tract infection[9].

Aim of study

To assess the correlation between the occurrence of neonatal sepsis and the development of neonatal jaundice in affected newborns admitted to the NCU in Al-Batool teaching hospital, Diyala, Iraq.

Patients and methods

Study design: This is a cross-sectional study. It was conducted in the period from 24 September 2024 to 28 November 2024.

Sampling technique: The study included 60 patients who had suffered neonatal jaundice, consisting of 25 males and 35 females. The sample was collected from neonates attending Al-Batool Teaching Hospital. Neonates under 28 days old were included, while older neonates were excluded.

Data collection: Information was collected using a prepared written questionnaire and direct interviews with the patients' parents. The questionnaire included information about the age of the neonate, birth weight, gestational age, sex, and diagnosis of neonatal sepsis. It also covered methods of diagnosing sepsis, including elevated WBC, CRP levels, signs of respiratory disorders such as dyspnea, tachypnea, and decreased SPO2, as well as poor feeding. The timing of sepsis onset, whether early (within 72 hours of birth) or late (after 72 hours), was also recorded. For jaundice assessment, data included the incidence and onset of jaundice, total bilirubin level, type of phototherapy (simple or extensive), need for blood exchange, breastfeeding status (exclusively breastfed or not), timing of jaundice relative to sepsis (before, during, or after), association with sepsis severity, and the outcome (complete recovery, persistent jaundice, or other).

Ethical approval: The privacy of the participants was preserved, and their information was coded to ensure confidentiality and reduce the risk of bias.

Statistical analysis: Data were analyzed using SPSS version 26.

Results

60 patients were included in our study. Their mean age was 7.87 days and standard deviation was 5.325 . 25 (41.7) of them were males and 35(58.3) were females. Their gestational age is demonstrated in table 1.

Table 1: The table shows the distribution of 60 cases by gestational age. It reveals that 55% (33 cases) were preterm births (before 37 weeks of gestation), while 45% (27 cases) were term births (at or after 37 weeks).

Table 1: Gestational age		
Gestational age	**Frequency**	**Percent**
preterm	33	55.0
term	27	45.0
Total	60	100.0

Table 2: signs of sepsis

The table 2 A illustrates the distribution of white blood cell (WBC) counts among patients with signs of sepsis. It shows an equal distribution between normal and elevated WBC counts, with 30 cases (50.0%) each. This suggests that half of the patients exhibit normal WBC levels, while the other half have elevated levels, highlighting variability in WBC response among septic patients.

Table 2 A : WBC count		
	Frequency	percent
Normal	30	50.0
Elevated	30	50.0

The table 2 B presents the distribution of C-reactive protein (CRP) levels among patients. The majority of patients, 44 cases (73.3%), have normal CRP levels, while a smaller proportion, 16 cases (26.7%), exhibit elevated CRP levels. This indicates that most patients show no significant inflammatory response as measured by CRP, whereas a minority have elevated levels suggestive of inflammation or infection.

Table 2 B : C-reactive protein levels		
	Frequency	percent
Elevated	16	26.7
Normal	44	73.3

The table 2 C: shows the distribution of respiratory disorder signs among patients. A slight majority, 31 cases (51.7%), presented with signs of respiratory disorders, while 29 cases (48.3%) did not exhibit any signs. This indicates that respiratory disorders are slightly more prevalent among the observed patients, accounting for just over half of the cases.

The table 2 C: sign of respiratory disorder		
	Frequency	Percent
no	29	48.3
yes	31	51.7
Total	60	100.0

The table 2 D: illustrates the distribution of a poor feeding with "yes" and "no" responses among 60 participants. A total of 31 participants (51.7%) responded "yes," while 29 participants (48.3%) responded "no." This indicates a nearly equal distribution, with a slight majority favoring the "yes" category.

The table 2 D : poor feeding		
Poor feeding	Frequency	Percent
no	29	48.3
yes	31	51.7
Total	60	100.0

The mean total serum bilirubin (TSB) of the patients was 13.550 mg/dl, The incidence of jaundice is demonstrated in table 3.

The table 3 presents the incidence of jaundice among patients based on the timing of its onset. Jaundice occurred in 13 patients (21.7%) within the first 24 hours and in another 13 patients (21.7%) after 48 hours. The majority of cases, 34 patients (56.7%), developed jaundice after 3 to 5 days. This data indicates that more than half of the jaundice cases appeared within 3 to 5 days, highlighting a delayed onset in most patients.

Table 3 : incidence of jaundice		
incidence of jaundice	Frequency	Percent
In the first 24 hours	13	21.7
After 48 hours	13	21.7
After 3-5 days	34	56.7
Total	60	100.0

The table 4 examines the association between WBC count and poor feeding among patients. Among those with normal WBC counts, 20 patients (33.3%) did not exhibit poor feeding, while 10 patients (16.7%) showed poor feeding, making up a total of 30 patients (50.0%) with normal WBC counts. Conversely, among those with elevated WBC counts, 9 patients (15.0%) did not exhibit poor feeding, while 21 patients (35.0%) had poor feeding, also totaling 30 patients (50.0%) with elevated WBC counts.Overall, 29 patients (48.3%) did not show poor feeding, while 31 patients (51.7%) exhibited poor feeding. The p-value of 0.004 indicates a statistically significant association between WBC count and poor feeding. This suggests that elevated WBC counts are correlated with an increased likelihood of poor feeding.

Table 4: association between WBC count and poor feeding

WBC		poor feeding		Total	
		no	yes		
no	Count	20	10	30	P value =0.004
	% of Total	33.3%	16.7%	50.0%	
yes	Count	9	21	30	
	% of Total	15.0%	35.0%	50.0%	
Total	Count	29	31	60	
	% of Total	48.3%	51.7%	100.0%	

The table 5: explores the association between sex and poor feeding among patients. Among females, 20 patients (33.3%) did not exhibit poor feeding, while 15 patients (25.0%) showed poor feeding, accounting for 58.3% of the total sample. Among males, 9 patients (15.0%) did not exhibit poor feeding, while 16 patients (26.7%) showed poor feeding, contributing to 41.7% of the total sample.
In total, 29 patients (48.3%) did not show poor feeding, while 31 patients (51.7%) exhibited poor feeding. The p-value of 0.106 indicates no statistically significant association between sex and poor feeding. This suggests that poor feeding is similarly distributed between male and female patients.

Table 5: association between sex and poor feeding

Sex		**poor feeding**		**Total**	**Chi square**
		no	yes		
female	Count	20	15	35	P value =0.106
	% of Total	33.3%	25.0%	58.3%	
male	Count	9	16	25	
	% of Total	15.0%	26.7%	41.7%	
Total	Count	29	31	60	
	% of Total	48.3%	51.7%	100.0%	

Table 6 : The table highlights the relationship between jaundice incidence and neonatal sepsis diagnosis, stratified by sex. Among jaundiced female neonates, 57.1% were diagnosed with neonatal sepsis, while 42.9% were not. For jaundiced male neonates, 40.0% were diagnosed with neonatal sepsis, whereas 60.0% were not. Overall, 50% of the total population with jaundice was diagnosed with neonatal sepsis, and 50% were not, indicating an equal distribution of sepsis diagnosis in the sample.

Table 6 : Incidence of Jaundice and Neonatal Sepsis Diagnosis by Sex					
Sex				**Diagnosis of neonatal sepsis**	
				no	**yes**
Female	**incidence of jaundice**	**yes**	Count	15	20
			% of Total	42.9%	57.1%
Male	**incidence of jaundice**	**yes**	Count	15	10
			% of Total	60.0%	40.0%
Total			Count	30	30
			% of Total	50.0%	50.0%

Table 7: The table examines the relationship between the diagnosis of neonatal sepsis and the need for blood exchange in neonates. Among those without neonatal sepsis, 48.3% did not require a blood exchange, while 1.7% did. In neonates diagnosed with sepsis, 43.3% did not require a blood exchange, whereas 6.7% required one. Overall, 91.7% of the neonates did not require a blood exchange, while 8.3% required it.

Table 7 : Neonatal Sepsis Diagnosis and Requirement for Blood Exchange			
Diagnosis of neonatal sepsis		**Needed blood exchange**	
		no	**yes**
no	Count	29	1
	% of Total	48.3%	1.7%
yes	Count	26	4
	% of Total	43.3%	6.7%
Total	Count	55	5
	% of Total	91.7%	8.3%

Table 8 : The table categorizes neonates based on the type of phototherapy received. Out of a total of 60 cases, 50.0% (30 cases) required extensive phototherapy, while the remaining 50.0% (30 cases) underwent simple phototherapy.

Table 8: Distribution of Phototherapy Types Among Neonates		
Phototherapy	**Frequency**	**Percent**
extensive	30	50.0
simple	30	50.0
Total	60	100.0

Table 9 : The table shows the distribution of neonates based on the severity of total bilirubin levels and their diagnosis with neonatal sepsis. Among neonates with mild bilirubin levels, 13.3% were diagnosed with sepsis, while 5.0% were not. For moderate bilirubin levels, 11.7% were diagnosed with sepsis, compared to 25.0% who were not. Neonates with severe bilirubin levels showed a higher diagnosis rate of sepsis (25.0%), while 20.0% were not diagnosed. The total sample was evenly distributed between those diagnosed with neonatal sepsis (50.0%) and those not diagnosed (50.0%).

Table 9 : Severity of Total Bilirubin Levels and Neonatal Sepsis Diagnosis			
Total bilirubin		**Diagnosis of neonatal sepsis**	
		no	**yes**
Mild	Count	3	8
	% of Total	5.0%	13.3%
moderate	Count	15	7
	% of Total	25.0%	11.7%
severity	Count	12	15
	% of Total	20.0%	25.0%
Total	Count	30	30
	% of Total	50.0%	50.0%

Discussion

Globally, newborn jaundice has a major impact on neonatal morbidity and a minor impact on neonatal mortality.

In our study, 55.0% of cases (33 neonates) were preterm, while 45.0% (27 neonates) were term. Preterm infants are at a higher risk for both neonatal sepsis and jaundice due to the immaturity of their organ systems. The liver's capacity to conjugate bilirubin is underdeveloped in preterm neonates, increasing their susceptibility to jaundice. Additionally, their immature immune systems make them more prone to infections, including sepsis. found that preterm infants had a significantly higher incidence of severe hyperbilirubinemia compared to term infants. This aligns with our findings, where preterm neonates represented a substantial proportion of cases[10].

In our study, 50% of cases (30 neonates) had elevated WBC counts, while the other 50% (30 neonates) had normal WBC levels. Elevated WBC counts indicate an inflammatory response, often associated with infections like sepsis. However, in neonates, WBC counts can be variable and may not always reliably indicate sepsis. highlighted that while WBC counts are commonly used to diagnose neonatal sepsis, their sensitivity and specificity are limited. In our study, the equal distribution of normal and elevated WBC levels suggests that WBC alone may not be sufficient to confirm a sepsis diagnosis[11].

In our study, 26.7% of cases (16 neonates) showed elevated CRP levels, while 73.3% (44 neonates) had normal levels. CRP is an acute-phase reactant and a more specific marker for inflammation and infection in neonates compared to WBC counts. Elevated CRP levels support the diagnosis of neonatal sepsis. found that serial CRP measurements have high negative predictive value, making them useful

in ruling out sepsis. Our findings indicate that while CRP is a helpful marker, it should be used alongside other clinical assessments and laboratory results for accurate diagnosis[12].

In our study, 51.7% of cases (31 neonates) had signs of respiratory distress, while 48.3% (29 neonates) showed no respiratory issues. Respiratory distress in neonates can be a manifestation of sepsis, as systemic infections often lead to respiratory complications. Moreover, respiratory disorders can exacerbate hypoxia, impairing hepatic function and worsening jaundice. emphasizes that respiratory symptoms in septic neonates require prompt evaluation to prevent further complications. Our findings highlight the interplay between respiratory health and sepsis in the context of neonatal jaundice[13].

In our study, 51.7% of cases (31 neonates) exhibited poor feeding, while 48.3% (29 neonates) had normal feeding patterns. Poor feeding is a nonspecific but important clinical sign in neonates that can indicate underlying issues such as sepsis. Inadequate feeding can lead to dehydration and decreased bilirubin excretion, contributing to or exacerbating jaundice. that poor feeding behaviors in septic neonates are common and should prompt further investigation for possible sepsis. Our data are consistent with this understanding, underscoring the role of feeding difficulties in neonates with sepsis and jaundice[14].

In our study, jaundice occurred in the first 24 hours in 13 cases (21.7%), after 48 hours in 13 cases (21.7%), and after 3-5 days in 34 cases (56.7%). The majority of jaundice cases occurred between 3-5 days, which corresponds to physiological jaundice caused by the immature hepatic conjugation of bilirubin. However, jaundice appearing within the first 24 hours is likely pathological and may indicate serious conditions such as sepsis, hemolysis, or infections.that jaundice in the first

24 hours requires immediate evaluation for sepsis or hemolytic disease. Our findings align with these observations, where early-onset jaundice in a significant portion of cases suggests a pathological cause like neonatal sepsis[15].

In our study, poor feeding was observed in 21 cases (35.0%) with elevated WBC counts and in 10 cases (16.7%) with normal WBC counts, showing a statistically significant association (P-value = 0.004). Elevated WBC levels suggest an inflammatory response typically seen in neonatal sepsis, which is a leading cause of feeding difficulties in newborns. Sepsis disrupts feeding due to lethargy, poor suck reflex, and impaired gastrointestinal function caused by systemic inflammation.supports this finding, identifying poor feeding as one of the earliest clinical signs of neonatal sepsis. The statistically significant association in our study highlights the link between systemic inflammation (elevated WBC) and feeding difficulties in septic neonates[16].

In our study, poor feeding was seen in 15 cases (25.0%) among females and 16 cases (26.7%) among males, with no statistically significant difference (P-value = 0.106). This indicates that sex does not play a significant role in the occurrence of poor feeding in neonates. Both male and female neonates exhibited poor feeding at similar rates, suggesting that other factors, such as the severity of sepsis or gestational age, are more critical in determining feeding behavior. showing that poor feeding is more closely related to the clinical severity of sepsis rather than the sex of the neonate. Our findings further emphasize that sex does not influence feeding outcomes in septic neonates[17].

In our study, 57.1% of jaundiced female neonates (20 cases) were diagnosed with neonatal sepsis, compared to 40.0% of male neonates (10 cases). These findings suggest that female neonates with jaundice may have a higher predisposition to

developing sepsis, particularly in the early neonatal period, may serve as an indicator for underlying infections such as sepsis. However, sex-based differences in susceptibility to neonatal sepsis remain poorly understood and could be influenced by hormonal, genetic, or immune-related factors. Our findings align with prior evidence, highlighting the need for further investigation into sex-specific neonatal care strategies[18].

Among neonates diagnosed with sepsis, 6.7% (4 cases) required a blood exchange, compared to only 1.7% (1 case) among those without sepsis. This suggests that severe neonatal sepsis may necessitate invasive interventions such as blood exchange to manage complications like severe hyperbilirubinemia, exchange transfusion is often considered in neonates with sepsis and bilirubin levels posing a risk of kernicterus. Our findings reinforce the association between severe hyperbilirubinemia and neonatal sepsis, indicating that timely management is critical in reducing morbidity and mortality[19].

Our study found an equal distribution of extensive (50.0%, 30 cases) and simple phototherapy (50.0%, 30 cases) among neonates. Extensive phototherapy is often reserved for cases of severe hyperbilirubinemia or those unresponsive to simple phototherapy. that extensive phototherapy is an effective intervention in preventing the need for blood exchange in neonates with significant jaundice. The equal distribution in our data suggests that phototherapy selection may depend on institutional protocols and clinical judgment rather than on the severity of jaundice alone[20].

In our study, 25.0% of neonates with severe bilirubin levels (15 cases) were diagnosed with sepsis, compared to 13.3% with mild bilirubin levels (8 cases). Severe hyperbilirubinemia is often associated with pathological causes, including

neonatal sepsis. highlighted that high bilirubin levels in the context of sepsis could result from hemolysis, impaired hepatic conjugation, or infection-induced liver dysfunction. Our findings are consistent with this observation, emphasizing that severe hyperbilirubinemia should prompt evaluation for underlying sepsis or other pathological conditions[21].

Conclusion

Our study highlights the association between neonatal sepsis and neonatal jaundice. The majority of jaundice cases occurred after 3-5 days (56.7%), indicating physiological causes, while 21.7% presented within the first 24 hours, suggesting pathological causes like sepsis.

A significant association was found between elevated WBC counts and poor feeding (P-value = 0.004), reflecting the impact of systemic inflammation on feeding behavior. However, no significant association was observed between sex and poor feeding (P-value = 0.106).

Early detection and management of sepsis, using clinical signs and laboratory markers, are critical for reducing complications like poor feeding and pathological jaundice.

Recommendations

1. Early Screening:

• Evaluate jaundice within the first 24 hours for sepsis or hemolytic disease.

• Monitor WBC count and CRP levels in neonates with suspected sepsis.

2. High-Risk Monitoring:

• Closely monitor preterm neonates and those with poor feeding for early signs of sepsis and jaundice.

3. Feeding Support:

• Address poor feeding promptly to prevent complications.

4. Healthcare Training:

• Train healthcare providers to identify early signs of sepsis and pathological jaundice.

• Educate caregivers on recognizing poor feeding and jaundice.

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