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Frequency of Urinary Tract Infections (UTI) in Neonates with Indirect Hyperbilirubinemia

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ABSTRACT

Background: A significant percentage of neonatal hospital admissions are caused by neonatal jaundice, one of the most prevalent clinical disorders during the neonatal era. Some newborns may experience pathological jaundice because of underlying illnesses like infections, even though the majority of instances are physiological. One significant but frequently disregarded cause of indirect hyperbilirubinemia in neonates is urinary tract infection (UTI). Jaundice is frequently the only sign of a UTI, which can cause a delay in diagnosis if the necessary tests are not carried out. **Methodology:** Over the course of six months, this descriptive cross-sectional study was carried out in a tertiary care hospital's pediatric ward and neonatal intensive care unit (NICU). Non-probability consecutive sampling was used to include 151 infants with indirect hyperbilirubinemia. A standardized proforma was used to record demographic and clinical information such as age, gender, gestational age, and birth weight. Under aseptic conditions, sterile catheterization was used to collect urine samples, which were then examined using urine microscopy and culture. SPSS version 25 was utilized for data entry and analysis. For categorical variables, frequencies and percentages were computed, and associations between variables were evaluated using the Chi-square test, where a p-value of less than 0.05 was deemed statistically significant. **Results:** 94 (62.3%) of the 151 newborns were male, and 57 (30.7%) were female. While 122 neonates (80.8%) showed no signs of a urinary tract infection, 29 neonates (19.2%) developed a UTI. Escherichia coli was the most frequently isolated organism (65.5%), followed by Proteus mirabilis (10.4%) and Klebsiella pneumoniae (24.1%). Preterm and low birth weight neonates had a slightly higher prevalence of UTI, but the differences were not statistically significant. **Conclusion:** According to the study, infants who arrive with indirect hyperbilirubinemia are comparatively likely to have urinary tract infections. Neonates with chronic or unexplained jaundice should be screened for urinary tract infections to help with early identification and avoid consequences.

INTRODUCTION

One of the most prevalent clinical disorders that babies encounter is neonatal jaundice, which continues to be a leading cause of newborn hospitalization.[1] Jaundice is thought to occur in the first week of life in about 60% of term neonates and up to 80% of preterm neonates.[2] The majority of instances are caused by physiological factors, such as accelerated fetal red blood cell disintegration and immature hepatic bilirubin metabolism. However, jaundice may indicate underlying medical issues in some newborns, necessitating more testing.[3]

The most prevalent kind of newborn jaundice is called indirect hyperbilirubinemia, which is defined by high blood levels of unconjugated bilirubin. Persistent or inexplicable indirect hyperbilirubinemia may be a sign of underlying conditions such hemolytic illness, metabolic abnormalities, endocrine problems, or infections, even though physiological jaundice is often benign and self-limiting. Urinary tract infections (UTIs) are becoming more well acknowledged as a significant but sometimes disregarded infectious cause of newborn jaundice.[4,5]

One of the most prevalent bacterial illnesses in infants and young children is urinary tract infection. UTIs in neonates can present with a variety of symptoms, including poor feeding, irritability, lethargy, vomiting, fever, or failure to thrive. Sometimes jaundice is the only symptom that

appears, which might cause a delayed diagnosis if the necessary tests are not carried out.[6,7]

Numerous studies have shown a link between urinary tract infections and newborn jaundice.[8,9] According to the suggested mechanism, high serum bilirubin levels are caused by bacterial endotoxins interfering with the conjugation and elimination of bilirubin in the liver. Depending on the study design and diagnostic standards, the reported prevalence of UTI among neonates with indirect hyperbilirubinemia varies from roughly 6% to 20% across various populations.[10,11]

Because delayed diagnosis and treatment can lead to major problems such chronic kidney disease, hypertension, and renal scarring later in life, early detection of urinary tract infections is crucial. Thus, checking for UTIs in newborns who exhibit extended or unexplained jaundice may be crucial to enhancing neonatal outcomes. The goal of the current investigation was to ascertain how common urinary tract infections were in newborns with indirect hyperbilirubinemia.

METHODOLOGY

To ascertain the prevalence of urinary tract infections in neonates presenting with indirect hyperbilirubinemia, a descriptive cross-sectional study was carried out in the pediatric department and neonatal intensive care unit (NICU) of a tertiary care teaching hospital from 29th August 2024 to 28th February 2025. After receiving Institutional Review Board (IRB) approval, the study was conducted over a six-month period. The study comprised 151 neonates in total. Using the WHO sample size calculator, the sample size was determined to be 151 at a 95% confidence interval and 5% margin of error, based on an expected frequency of 11.5% of UTI in neonates with prolonged jaundice in a study carried out in Peshawar, Pakistan.[12] All neonates who met the inclusion criteria during the study period were enrolled until the necessary sample size was reached using a non-probability sequential sampling procedure.

After receiving informed agreement from their parents or guardians, the study comprised 28-day-old or younger neonates with indirect hyperbilirubinemia who were admitted for assessment or treatment of jaundice. The study excluded newborns with congenital defects, hemolytic disorders such Rh or ABO incompatibility, conjugated hyperbilirubinemia, or those who had taken antibiotics before being admitted.

Relevant demographic and clinical data, such as age, gender, gestational age, birth weight, feeding history, and maternal history, were recorded using a systematic data collecting proforma. Every newborn was given a thorough clinical checkup to evaluate their overall health and find any indications of infection or other jaundice-related conditions. To verify indirect hyperbilirubinemia and assess serum bilirubin levels, blood samples were collected.

Urine samples were obtained using sterile catheterization under stringent aseptic settings to reduce contamination in order to identify urinary tract infections. Urine microscopy, culture, and sensitivity tests were performed on the collected urine samples in the hospital laboratory. A single pathogenic organism growing in urine culture was considered significant bacteriuria.

Version 25 of the Statistical Package for Social Sciences (SPSS) was used to enter and analyze all of the data. While qualitative factors like gender, gestational age category, and the presence of a urinary tract infection were displayed as frequencies and percentages, quantitative variables like age, birth weight, and bilirubin levels were represented as mean and standard deviation. The association between categorical variables was evaluated using the Chi-square test, and a p-value of less than 0.05 was deemed statistically significant. All participants' information was kept private during the study, and the information gathered was only utilized for research.

RESULTS

This study examined the frequency of urinary tract infections (UTI) in 151 infants with indirect hyperbilirubinemia. Below is a summary of the research population's clinical and demographic features.

With 94 (62.3%) males and 57 (30.7%) females among the 151 neonates, the male-to-female ratio was almost 1.6:1. The majority of neonates (89, or 58.9%) presented during the first week of life, according to age at presentation. Nineteen neonates (12.6%) appeared after the age of 14 days, whereas forty-three (28.5%) did so between the ages of 8 and 14. In terms of gestational age, 48 (31.8%) neonates were born prematurely, and 103 (68.2%) were born at term. Ninety-nine (65.6%) neonates were born weighing more than 2,500 grams, whereas fifty-two (34.4%) were born weighing less than 2,500 grams. (Table 1).

Table 1

Demographic Characteristics (n=151)

Variable		Frequency (n)	Percentage (%)
Gender	Male	94	62.3
	Female	57	37.7
Age at Presentation	≤7 days	89	58.9
	8–14 days	43	28.5
	>14 days	19	12.6
Gestational Age	Term	103	68.2
	Preterm	48	31.8
Birth Weight	<2500 g	52	34.4
	≥2500 g	99	65.6

29 neonates (19.2%) had a urinary tract infection, whereas 122 neonates (80.8%) showed no signs of a UTI on urine culture (Table 2). According to these results, a urinary tract infection was present in about one out of every five infants with indirect hyperbilirubinemia.

Table 2

Frequency of Urinary Tract Infection in Neonates with Indirect Hyperbilirubinemia

UTI Status	Frequency (n)	Percentage (%)
UTI Present	29	19.2
UTI Absent	122	80.8
Total	151	100

Escherichia coli was the most frequently isolated bacterium on urine culture, accounting for 19 (65.5%) of the 29 newborns with confirmed UTIs. Next in line were

Proteus mirabilis in 3 instances (10.4%) and Klebsiella pneumoniae in 7 cases (24.1%) (Table 3).

Table 3
Bacterial Isolates in Neonates with UTI (n = 29)

Organism	Frequency (n)	Percentage (%)
Escherichia coli	19	65.5
Klebsiella pneumoniae	7	24.1
Proteus mirabilis	3	10.4

Twelve (21.1%) of the 57 female neonates were diagnosed with a urinary tract infection, whereas 17 (18.1%) of the 94 male neonates had a UTI (Table 4). There was no statistically significant correlation between gender and UTIs, according to the Chi-square test ($\chi^2 = 0.21$, $p = 0.64$). Thirteen (27.1%) of the 48 preterm newborns and sixteen (15.5%) of the 103 term neonates were diagnosed with UTI. Preterm newborns seemed to have a higher prevalence, although the difference was not statistically significant ($p = 0.08$).

Of the 99 neonates weighing more than 2,500 grams, 15 (15.2%) were diagnosed with a urinary tract infection (UTI), while 14 (26.7%) of the 52 neonates weighing less than 2,500 grams had a UTI. There was no statistically significant correlation between low birth weight and UTI ($p = 0.09$).

Table 4
Stratification of UTI According to Gender

Gender	UTI Present	UTI Absent	Total
Male	17	77	94
Female	12	45	57
Total	29	122	151

DISCUSSION

A significant percentage of neonatal hospital admissions are caused by neonatal jaundice, one of the most prevalent clinical disorders during the neonatal era. Neonates exhibiting inexplicable or prolonged hyperbilirubinemia should also be evaluated for pathological diseases, including as infections, even if physiological jaundice accounts for the majority of instances. It is becoming more widely acknowledged that urinary tract infections (UTIs) are a significant but often disregarded cause of newborn jaundice. Neonates with UTIs may exhibit nonspecific symptoms, and in certain situations, jaundice may be the only clinical sign of infection, according to numerous research.[13]

The goal of the current investigation was to ascertain how common urinary tract infections were in newborns with indirect hyperbilirubinemia. Nearly one in five neonates with indirect hyperbilirubinemia had an underlying urinary tract infection, according to our study's 19.2% UTI prevalence. This result emphasizes how crucial it is to think about UTI as a possible cause of newborn jaundice, especially when other causes are not obvious.

Our findings are in line with a number of other research investigations that found similar rates of UTI in infants who were jaundiced. Among neonates with persistent jaundice, a Lahore research found a UTI prevalence of 18.57%, which is much the same as the frequency we found.[14] Given the similarities between these results, it is possible that, in comparable clinical situations, the prevalence of UTI in neonates with indirect hyperbilirubinemia may be rather high.

Similarly, 11.5% of newborns with prolonged jaundice had a urinary tract infection, according to another cross-sectional study done in Peshawar.[15] The relationship between newborn jaundice and urinary tract infection is supported even though the prevalence reported in that study was lower than that seen in the current investigation. discrepancies in study populations, diagnostic criteria, sampling strategies, and inclusion criteria may account for discrepancies in prevalence across studies.

Different UTI frequencies among jaundiced infants have also been found by a number of additional studies. According to earlier studies, the prevalence of UTI in newborns exhibiting jaundice varies significantly among populations, ranging from 5.8% to 21%.[16] This broad range can be the result of variations in screening methods, clinical procedures, and regional epidemiological trends.

The idea that urinary tract infections are a significant underlying cause of newborn jaundice is further supported by the finding that 12.5% of neonates in another study assessing infants with unconjugated hyperbilirubinemia had a UTI diagnosis.[17] The therapeutic importance of screening for infection in newborns with unexplained hyperbilirubinemia is further highlighted by the fact that population-based investigations have shown that 3.6% to 18% of jaundiced infants may have a positive urine culture.[18]

The demographics of newborns with indirect hyperbilirubinemia were also assessed in our study. Male neonates made up 62.3% of the cases in the current study, whilst female neonates made up 37.7%. Previous investigations have revealed similar gender distributions. For example, Muhammad et al. found that male neonates accounted for 58.6% of those with persistent jaundice, indicating a marginally greater incidence of neonatal jaundice in male infants.[19] Although the precise mechanism is still unknown, the larger percentage of males may be related to biological factors impacting bilirubin metabolism.

Our study found no statistically significant difference between male and female newborns when looking at the relationship between gender and UTIs. This result is in line with some previous research that found comparable rates of infection during the newborn period in both genders. However, it's crucial to remember that because of anatomical characteristics like a shorter urethra, UTIs are typically more common in females during later infancy and childhood.

Another factor examined in this investigation was gestational age. Although the difference was not statistically significant, we found that the prevalence of urinary tract infections was somewhat greater in preterm infants than in term neonates. Because of their underdeveloped immune systems and extended hospital stays, preterm newborns are typically thought to be more prone to infections. Higher infection rates among preterm

neonates have also been observed in a number of studies, albeit the correlation may differ based on the group under investigation.

Birth weight was investigated as a possible risk factor in addition to gestational age. Although the difference did not achieve statistical significance, our results showed that neonates with low birth weight had a higher frequency of UTIs than neonates with normal birth weight. Due to immature immune responses and higher exposure to invasive treatments during newborn care, low birth weight is known to be linked to an increased risk of infection.

The distribution of bacterial isolates that cause urinary tract infections was another significant factor assessed in this investigation. According to our findings, the majority of UTI cases were caused by Escherichia coli, which was the most frequently isolated bacteria. Numerous studies have found E. coli to be the most common pathogen in pediatric and newborn urinary tract infections, which is in line with this finding.[20]

Our investigation also found Proteus mirabilis and Klebsiella pneumoniae in addition to E. coli. These organisms are frequently identified as pathogens in newborn urinary tract infections. It is commonly known from the literature that gram-negative bacteria are more common in newborn UTIs, and this is because these organisms colonize the gastrointestinal system.

It is still unclear how urinary tract infections and neonatal hyperbilirubinemia are related pathophysiologically. But a number of theories have been put forth. According to one theory, the conjugation and excretion of hepatic bilirubin may be disrupted by bacterial endotoxins generated during illness. According to a different view, hemolysis brought on by an illness may raise bilirubin production, which would raise serum bilirubin levels.[21,22]

Additionally, illness may hinder the liver's ability to absorb bilirubin, which could result in an accumulation of unconjugated bilirubin in the blood. When a newborn has a urinary tract infection, several processes work together to cause indirect hyperbilirubinemia.

These discoveries have important clinical ramifications. Lethargy, irritability, poor feeding, vomiting, and temperature instability are some of the nonspecific symptoms that newborns with UTIs frequently exhibit. If clinicians do not consider infection in newborns presenting with jaundice alone, the diagnosis of UTI may be delayed since these symptoms may be faint or nonexistent.

Serious consequences, such as renal scarring, hypertension, and chronic kidney disease later in life, may arise from a neonatal urinary tract infection that is not identified and treated. Therefore, to avoid long-term kidney impairment, early detection and treatment are crucial.

The results of this study corroborate the suggestion that infants with chronic or unexplained indirect hyperbilirubinemia should have their urine examined, especially after other common reasons have been ruled out. Early urinary tract infection screening may aid in a timely diagnosis and suitable treatment.

The continuous controversy around routine UTI screening in infants exhibiting jaundice is another significant topic brought to light in the literature. While some researchers suggest selective screening based on clinical risk factors, others contend that all infants with persistent jaundice should get routine urine cultures. According to recent research, focused screening methods might be more suitable, especially for newborns who exhibit chronic jaundice or who don't react well to phototherapy.

Urine culture as a urinary tract infection diagnosis technique and the study's prospective design are among its strong points. However, there are a few restrictions to take into account. The results may not be as applicable to other populations because the study was limited to a single tertiary care facility. Second, the study's statistical power might have been impacted by the sample size's relative smallness.

Larger multicenter trials in the future would aid in elucidating the connection between urinary tract infections and infant hyperbilirubinemia. Furthermore, more research on the risk factors for UTI in jaundiced neonates could aid in identifying high-risk populations that would profit from regular screening.

The present study's overall results highlight the clinical significance of taking a urinary tract infection into account as a possible underlying cause of jaundice in newborns. In infants with indirect hyperbilirubinemia, early detection and proper treatment of UTI may help lower morbidity and enhance neonatal outcomes.

CONCLUSION

The current investigation showed that a major underlying cause of indirect hyperbilirubinemia in newborns is urinary tract infection. In this study, the prevalence of urinary tract infection among neonates with indirect hyperbilirubinemia was 19.2%, meaning that almost one in five neonates who presented with jaundice also had a UTI. In line with the bacterial profile documented in earlier research on infant urinary tract infections, Escherichia coli was the most frequently isolated pathogen, followed by Klebsiella pneumoniae and Proteus mirabilis.

Despite the fact that preterm and low birth weight neonates had a slightly higher incidence of urinary tract infections, this study did not find a statistically significant correlation between these variables with infection. Likewise, there was no discernible correlation between the research population's gender and the incidence of UTIs.

These results highlight the importance of urinary tract infection as a differential diagnosis when neonates exhibit chronic or unexplained indirect hyperbilirubinemia, especially after other frequent causes of neonatal jaundice have been ruled out. Prompt diagnosis and treatment can be facilitated by early screening using urine examination and culture, so avoiding potential problems such renal impairment, sepsis, and extended hospital stays.

In neonates with indirect hyperbilirubinemia, doctors are advised to keep a high index of suspicion for urinary tract infections and, where necessary, take into account suitable laboratory tests. Neonatal outcomes can be greatly enhanced by early detection and treatment of urinary tract infections, which also lowers morbidity linked to delayed diagnosis.

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