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FREQUENCY OF URINARY TRACT INFECTION IN NEONATES WITH SIGNIFICANT INDIRECT HYPERBILIRUBINEMIA OF UNKNOWN ETIOLOGY

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Abstract

Objective: *To determine frequency of urinary tract infection in neonates with significant indirect Hyperbilirubinemia of unknown etiology*

Study Design: *Cross sectional (observational) study*

Study place and period: *Department of Pediatric Medicine, Services Hospital, Lahore from 26-06-2025 to 25-09-2025.*

Methodology: *After meeting selection criteria 100 neonates were enrolled. Informed consent and demographic details were taken from parents. Level of serum bilirubin level was also noted. Mid-stream urine sample of neonates was obtained in sterile container. All samples were sent to the laboratory for assessment of urine complete examination and urine culture. Reports were assessed and presence of infection was noted. Urinary tract infection was labeled if pathogen was detection. All the data was entered and analyzed on SPSS version 25.*

Conclusion: *Based on the findings of this study, we conclude that the frequency of urinary tract infection among neonates presenting with significant indirect hyperbilirubinemia of unknown etiology is 28%.*

INTRODUCTION:

Hyperbilirubinemia is a condition defined as elevated serum or plasma bilirubin levels above the reference range of the laboratory, and it is due to disorders of bilirubin metabolism.[1] Depending on the form of bilirubin present in serum, hyperbilirubinemia can be further classified as unconjugated (indirect) or conjugated (direct).[1, 2] Neonatal hyperbilirubinemia, characterized by a yellowish discoloration of the skin, sclera, and mucous membranes, is a commonly benign condition observed in newborns during the initial days of life, affecting at least 60% of full-term and 80% of preterm neonates.[3] It is a transitional process attributed to the turnover of fetal red blood cells and the limited conjugation of bilirubin by the newborn's immature liver, followed by a natural decline over the ensuing weeks. Nevertheless, approximately one in ten newborns are at risk of developing clinically significant hyperbilirubinemia, defined as an unconjugated bilirubin concentration, with most prevalent risk factors being prematurity, hemolytic disease, perinatal infection, and exclusive breastfeeding.[4, 5]

Indirect hyperbilirubinemia is frequently encountered during neonatal period. Although it has different causes, in some cases it can't be explained. Previous studies have illustrated that jaundice could be a major sign of urinary tract infection in neonates.[6, 7] It is also noteworthy that hyperbilirubinemia, in the absence of accompanying symptoms or signs, can be the sole clinical manifestation of urinary tract infection in neonates. Understanding this relationship is crucial for appropriate clinical management in neonates presenting with

jaundice. [4, 8] Urinary tract infection is a potential cause of neonatal jaundice. Nevertheless, there remains a lack of consensus regarding appropriate screening practices for urinary tract infection in infants with hyperbilirubinemia. [4] It is controversial to test for urinary tract infection in patients with unexplained indirect hyperbilirubinemia in the first 2 weeks of life. Therefore, it has been suggested that the neonates with unexplained pathological jaundice should be tested for possible urinary tract infection.[9, 10]

Rationale of this study is to determine the frequency of urinary tract infection in neonates with significant indirect hyperbilirubinemia of unknown etiology. Urinary tract infection in neonates with hyperbilirubinemia can lead to significant morbidity as well as severe consequences. Literature showed that frequency of urinary tract infection varies in different studies, even in previously reported local studies. Therefore, to confirm the extent of problem in local population, we want to conduct this study and to implement findings in local setting. Therefore, we want to conduct this study to get evidence for local population and improve our practice by improving diagnostic and treatment protocols of neonates with indirect hyperbilirubinemia in neonates. So, the objective of this study was to determine the frequency of urinary tract infection in neonates with significant indirect Hyperbilirubinemia of unknown etiology.

METHODOLOGY

After approval from ethical review committee, this was cross sectional (observational) study which was carried out at department of Pediatric Medicine, Services Hospital, Lahore from 26-06-2025 to 25-09-2025.The sample size was calculated by using WHO sample size calculator. The total sample size was 100 patients taking percentage of urinary tract infection i.e. 11.5% in neonates with indirect hyperbilirubinemia[11] with 95% confidence level and 6.5% margin of error. All the patients were included by applying non-probability consecutive sampling technique.

Inclusion: Neonates with 1-28 days, both gender, diagnosed with indirect hyperbilirubinemia of unknown etiology were included in the study. Indirect hyperbilirubinemia was defined as presence of serum bilirubin level 5-15 mg/dl at birth, with yellow coloration of skin, belly pain and swelling on clinical examination. [11]

Exclusion: Neonates with congenital disorders including cleft lip and palate, neural tube defect, congenital heart disease, inborn error of metabolism and with maternal history of urinary tract infection were excluded.

Informed consent and demographic detail was taken from parents. After evaluating clinical parameters mid-stream urine sample of neonates was obtained using sterile container. All samples were sent to the laboratory of the hospital for assessment of urine culture and examination. Reports were assessed and presence of infection (pathogen) in urine sample was noted. If pathogen was detected in mid-stream urine sample of neonates on urine culture and examination or more than 10 leukocytes per high-power field (HFP),[12] then urinary tract infection was labeled as per operational definition. All this data was noted in proforma.

All the collected data was entered and analyzed on SPSS version 25. Mean and SD was used to present age (days), gestational age, birth weight, and Apgar score. Frequency and percentage was used to calculate gender, mode of delivery, place of delivery, residence, socioeconomic status, history of maternal diabetes, hypertension, meconium stained liquor, premature rupture of membranes, and urinary tract infection.

RESULTS

In this study, a total of 100 patients were included. The mean age was 16.76 ± 6.49 days, and the average birth weight was 2456.71 ± 274.76 grams. The mean APGAR scores at 1 and 5 minutes were 6.93 ± 1.38 and 8.11 ± 1.32, respectively, while the mean serum bilirubin level was 9.47 ± 2.66. Among the participants, 55 (55%) were male. Regarding maternal factors, a history of maternal diabetes mellitus, hypertension, meconium-stained liquor, and PROM was reported in 74% (n=74), 72% (n=72), 34% (n=34), and 18%

(n=18) of cases, respectively. Normal vaginal delivery occurred in 17% (n=17) of patients. Most deliveries (65%) took place in hospitals, and 53% of the patients belonged to urban areas. Additionally, 48% of the study population belonged to the middle socioeconomic class. **Table-I**

Table-I: Distribution of demographic and clinical factors of the patients

Parameters		Output
Age (Days)		16.76 ± 6.49
Gender	Male	55%
	Female	45%
Birth Weight (Grams)		2456.71 ± 274.76
Apgar at 1 minute		6.93 ± 1.38
Apgar at 5 minute		8.11 ± 1.32
H/o Maternal Diabetes	Yes	74%
	No	26%
H/o Maternal Hypertension	Yes	72%
	No	28%
H/o Meconium	Yes	34%
	No	66%
H/o premature rupture of membranes	Yes	18%
	No	82%
Mode of delivery	Normal vaginal delivery	17%
	Induction of Labor	43%
	C-Section	40%
Place of Delivery	Hospital	65%
	Clinic	34%
	Home	1%
Residence	Rural	39%
	Urban	53%
	Semi Urban	8%
Socioeconomic status	Low	41%
	Middle	48%
	High	11%
Serum Bilirubin level		9.47 ± 2.66

According to this study urinary tract infection was present in 28(28%) patients. **Figure-1**

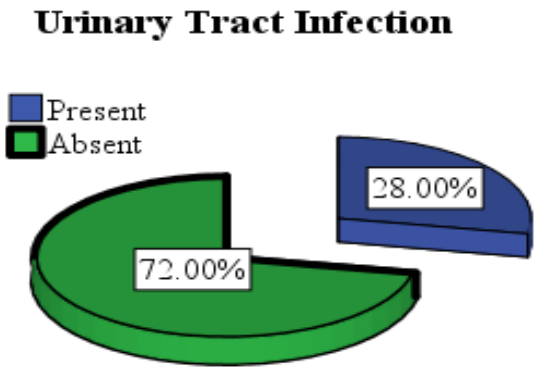


Figure-1: Frequency distribution of urinary tract infection

In infants aged ≤15 days, UTI was identified in 8 (21.1%) cases, while among those older than 15 days, it was observed in 20 (32.3%) cases (p=0.226). UTI was present in 14 (25.5%) male patients and 14 (31.1%) female patients (p=0.531). Among infants with a birth weight ≤2500 grams, 16 (28.6%) had UTI, compared to 12 (27.3%) among those weighing >2500 grams (p=0.886). For infants with a 5-minute APGAR score ≤7, UTI occurred in 9 (34.6%) cases, whereas in those with an APGAR score >7, UTI was found in 19 (25.7%) cases (p=0.382). Regarding maternal factors, only maternal hypertension showed a significant association with UTI; maternal diabetes, meconium-stained liquor, and PROM were not significantly related. UTI was present in 16 (22.2%) infants whose mothers had hypertension, compared to 2 (42.9%) infants without such history (p=0.039). Mode of delivery, place of birth, and socioeconomic status also demonstrated no statistically significant association with UTI. **Table-II**

Table-II: Comparison of demographic and clinical factors of the patients between urinary tract infection of the patient

		UTI		p-value
		Present n = 28	Absent n = 72	
Age Groups	≤ 15 days	8 (21.1%)	30 (78.9%)	0.226
	>15 days	20 (32.3%)	42 (67.7%)	
Gender	Male	14 (25.5%)	41 (74.5%)	0.531
	Female	14 (31.1%)	31 (68.9%)	
Birth weight (grams)	≤ 2500	16 (28.6%)	40 (71.4%)	0.886
	>2500	12 (27.3%)	32 (72.7%)	
APGAR at 5 minutes	≤ 7	9 (34.6%)	17 (65.4%)	0.382
	>7	19 (25.7%)	55 (74.3%)	
H/o maternal diabetes	Yes	22 (29.7%)	52 (70.3%)	0.516
	No	6 (23.1%)	20 (76.9%)	
H/o maternal hypertension	Yes	16 (22.2%)	56 (77.8%)	0.039
	No	12 (42.9%)	16 (57.1%)	
H/o Meconium	Yes	8 (23.5%)	26 (76.5%)	0.475
	No	20 (30.3%)	46 (69.7%)	

H/o PROM	Yes	3 (16.7%)	15 (83.3%)	0.237
	No	25 (30.5%)	57 (69.5%)	
Mode of delivery	Normal vaginal delivery	3 (17.6%)	14 (82.4%)	0.863
	Induction Labor	15 (34.9%)	28 (65.1%)	
	C-Section	10 (25.0%)	30 (75.0%)	
Place of Birth	Hospital	18 (27.7%)	47 (72.3%)	0.972
	Clinic	10 (29.4%)	24 (70.6%)	
	Home	0 (0.0%)	1 (100%)	
Residence	Urban	4 (10.3%)	35 (89.7%)	0.002
	Rural	20 (37.7%)	33 (62.3%)	
	Semi Urban	4 (50.0%)	4 (50.0%)	
SES	Low	11 (26.8%)	30 (73.2%)	0.380
	Middle	17 (35.4%)	31 (64.6%)	
	High	0 (0.0%)	11 (100%)	

DISCUSSION:

Hyperbilirubinemia is frequent in newborns. In some newborns, total serum bilirubin doesn't reach pathological levels while in others it may exceed physiological levels and requires treatment. Many well-known causes could be detected during routine investigation of neonates with significant hyperbilirubinemia while in others it may remain unexplained [12]. The association between neonatal jaundice and urinary tract infection (UTI) has been reported in previous studies [5, 13, 14].

Similar to our study in prospective research conducted by Abdelrheem et al., the incidence of urinary tract infection (UTI) in infants with jaundice was observed to be 25.7%[7]. A study by Ing Chen et al also showed that the the prevalence of UTI was 29%. There was a significantly higher male predominance in the UTI group, and patients with UTI also had a significantly longer duration of hospitalization compared to those without UTI [15]. A study by Chen et al. investigated afebrile, asymptomatic newborns admitted due to neonatal jaundice at Changhua Christian Children's Hospital, Taiwan, and found the rate of positive urine culture was 14.3% [16].

In 2021, an Egyptian study found that the frequency of urinary tract infection was reported in 11% in neonates with indirect hyperbilirubinemia.[6] Later on, in 2022, a study done in Pakistan found that the frequency of urinary tract infection was reported in 31.5% in neonates with indirect hyperbilirubinemia.[17] But later on, in 2024, the frequency of urinary tract infection was reported in 11.5% in neonates with indirect hyperbilirubinemia.[11] In India, frequency of urinary tract infection has been ranged from 9-18% in neonates with indirect hyperbilirubinemia.[18, 19]

One study by Lal Muhammad et al in Peshawar Pakistan resulted that the proportion of male patients was 58.6%, while the proportion of female patients was 41.4%. Among these 11.5% were found to have urinary tract infection [11]. A study by Ahmed Mahrous Kamal Baz et al showed lower incidence of UTI in neonates as compared to our study findings. The author reported that the incidence of UTI cases was 11% of jaundiced neonates [6]. Anand Gourishankaret al demonstrated that nearly 1 in 10 otherwise asymptomatic infants with jaundice have a UTI [20]. Several studies have provided evidence to support unconjugated hyperbilirubinemia as a significant and potentially the first presentation UTI in newborns [5, 21, 22]. The reported incidence of UTI in neonates with unexplained indirect hyperbilirubinemia ranged from 11% to 21.1% [6, 14].

The frequency of UTI among neonates differed from the results of our study and some previously published research. Moreover, we did not checked for the most common pathogen involved in urinary tract infection in neonates with the significant indirect hyperbilirubinemia of unknown etiology. Therefore, future studies are recommended in our setting to further validate these findings in addition to most common pathogen causing urinary tract infection in jaundiced neonates. Additionally, multicenter studies with larger

sample sizes are suggested to provide more robust and generalizable evidence.

CONCLUSION:

Based on the findings of this study, we conclude that the frequency of urinary tract infection among neonates presenting with significant indirect hyperbilirubinemia of unknown etiology is 28%. This frequency is high and not negligible. Therefore, we will add screening of neonates for urinary tract infection in routine investigations when neonate will present with significant indirect hyperbilirubinemia to detect it in early phases and manage the neonate accordingly to prevent hazardous consequences of urinary tract infection, which can lead to severe morbidity and even mortality.

CONFLICT OF INTEREST

No

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