



## Original Article

## Frequency of Urinary Tract Infection among Neonates with Persistent Jaundice at Lady Reading Hospital, Peshawar

Lal Muhammad<sup>1</sup>, Inayatullah Khan<sup>1</sup>, Afzal Khan<sup>1\*</sup>, Numan<sup>1</sup>, Saddam Hussain<sup>1</sup> and Sajid Ali<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Lady Reading Hospital, Peshawar, Pakistan

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**\*Corresponding Author:**

Afzal Khan  
 Department of Pediatrics, Lady Reading Hospital,  
 Peshawar, Pakistan  
[aksafi151@gmail.com](mailto:aksafi151@gmail.com)

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## ABSTRACT

Jaundice refers to yellow-orange discoloration of the skin and sclera, resulting from an excessive accumulation of bilirubin in the dermis and mucous membranes. Indirect neonatal hyperbilirubinemia is a prevalent and frequent etiology of jaundice, leading to the hospitalization of neonates in healthcare institutions worldwide. **Objective:** To determine the frequency of urinary tract infection among neonates with prolonged jaundice. **Methods:** The present study, a cross-sectional design, was carried out at the Department of Pediatrics, Lady Reading Hospital, Peshawar, from June 20th to December 20th, 2022. The study consisted of 87 infants, encompassing both genders, who presented with persistent jaundice. Two samples of clean urine were collected from neonates, with a time interval of many minimums of two hours between each collection. These samples were then sent to the hospital laboratory for diagnosing urinary tract infection. **Results:** The age range of participant neonates in this study ranged from 14 to 28 days, with a mean age of 20.597±4.50 days. The mean duration of complaint was also 18.20±4.077 days, and the mean weight was 2.855±0.27 Kg. 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. **Conclusions:** It is concluded that significant number (11.5%) of patients with persistent jaundice has urinary tract infection. It is likely a potential etiological factor contributing to neonatal unexplained prolonged indirect hyperbilirubinemia.

## INTRODUCTION

Jaundice is a medical condition characterized by the yellow-orange discoloration of the skin and sclera, resulting from an excess of bilirubin in the skin and mucous membranes [1]. In neonates' jaundice, indirect neonatal hyperbilirubinemia (INH), is a common finding and frequent reason for neonatal hospitalization worldwide<sup>1</sup>. Physiologic jaundice typically manifests between days 2 to 4 after birth, reaches its peak around days 4 to 5, and resolves within a two-week period [2]. Physiologic jaundice is not observed within the initial 24-hours period. Likewise, the etiology of pathological un-conjugated hyperbilirubinemia is attributed to heightened bilirubin production, diminished bilirubin clearance, and increased

entero-hepatic circulation [3]. Pathological jaundice can manifest within the initial 24 hours of life and is characterized by a rapid escalation in bilirubin levels exceeding 0.2 mg/dl per hour or 5 mg/dl per day [3]. Urinary Tract Infection (UTI) represents one of the most prevalent bacterial infections in childhood [4]. This infection can impact either the upper urinary tract, referred to as pyelonephritis, or the lower urinary tract, referred to as cystitis<sup>4</sup>. Regrettably, discerning between pyelonephritis and cystitis based on clinical symptoms and signs, particularly in infants and young children, can be challenging, if not unfeasible [5, 6]. Consequently, these two conditions are commonly discussed collectively within

the context of UTI. The clinician faces substantial obstacles due to the high frequency, recurrence tendency, morbidity association, and difficulties in obtaining an uncontaminated urine specimen [7]. Breastfed infants have a higher prevalence of prolonged jaundice compared to formula milk fed infants, as indicated by previous research [8]. Studies conducted in developed countries, specifically focusing on infants who are not breastfed, have suggested that a thorough investigation should be conducted for formula fed infants with prolonged jaundice [8]. Pashapour et al., conducted a study which revealed a 6% incidence of urinary tract infection in neonates with persistent jaundice [9]. Similarly, Harb et al., conducted a separate study which found an incidence of urinary tract infection in neonates with persistent jaundice as 8.9% [10]. The risk factors for urinary tract infection (UTI) in neonates with jaundice include early ( $\leq 10$  days) idiopathic neonatal jaundice, poor response to phototherapy, and prolonged hyperbilirubinemia with an unexplained etiology [1, 2]. Other risk factors include indirect hyperbilirubinemia in the first week of life, unconjugated hyperbilirubinemia, and the presence of unexplained pathological jaundice [2, 3]. Neonates with unexplained indirect hyperbilirubinemia in the first 2 weeks of life should be tested for UTI [5]. It is recommended to screen for UTI in neonates with prolonged hyperbilirubinemia and direct bilirubinemia. Additionally, neonates admitted with indirect hyperbilirubinemia should be evaluated for UTI, as the frequency of UTI is high in this population. The most common pathogens associated with UTI in neonates with jaundice are *Escherichia coli* and *Klebsiella pneumoniae* [11].

A comprehensive clinical evaluation is necessary for all infants with prolonged jaundice; yet, the specific criteria and scope of diagnostic procedures remain ambiguous. The identification of predisposing variables in Asian nations, such as Pakistan, is crucial in facilitating prompt diagnosis and treatment of jaundice, leading to enhanced results and decreased complications. For this purpose, we performed this study to ascertain the prevalence of urinary tract infection among early infants exhibiting prolonged jaundice at Lady Reading Hospital in Peshawar.

## METHODS

The present study, a cross-sectional design, was carried out at the Department of Pediatrics, Lady Reading Hospital, Peshawar, spanning from June 20th, 2022 to December 20th, 2022. The study included a total of 87 neonates, encompassing both genders, who presented with persistent jaundice. The selection process adhered to strict inclusion criteria. The study used a non-probability consecutive sampling method, and the sample size was

determined using the WHO sample size software. A 95% confidence interval, 5% margin of error, and an estimated frequency of urinary tract infection of 6% in neonates with prolonged jaundice were considered [9]. Upon obtaining approval from the ethics committee, IRB No; 128/LRH/MTI dated 28 May 2021, study was commenced and patients who met the predetermined inclusion criteria were enrolled in the study. During study obtained informed consent from the parents, so ensuring confidentiality and confirming the absence of any risks to the patient during their participation. We collected basic demographic data from the patients, including age, gender, duration of complaint, and weight as measured on a weighing scale. Two samples of mid-stream urine were collected from neonates and sent to the hospital laboratory to test for the presence of urinary tract infection. The two samples were acquired at least two hours apart and were free from contamination. All laboratory studies were conducted under the supervision of a consultant microbiologist with post FCPS experience more than five years. Data pertaining to urinary tract infection, as defined operationally was recorded on a specially constructed form. The data were then analyzed using the statistical software SPSS version 21.0. Mean and standard deviation were used to measure quantitative characteristics such as age, duration of complaint, and weight. The frequency percentages of categorical variables, such as gender and urinary tract infection, were assessed.

## RESULTS

The age range of patients in this study ranged from 14 to 28 days, with a mean age of  $20.597 \pm 4.50$  days. The mean duration of complaint (jaundice) was also  $18.20 \pm 4.077$  days, and the mean weight was  $2.855 \pm 0.27$  Kg, as indicated in table 1.

**Table 1:** Mean  $\pm$  SD of patients according to age, duration of complaint and weight n=87

Demographics	Mean $\pm$ SD
Age (days)	20.597 $\pm$ 4.50
Duration of complaint (days)	18.20 $\pm$ 4.077
Weight (Kg)	2.855 $\pm$ 0.27

The distribution of patients by gender is presented in table 2, with males accounting for 58.6% and females comprising 41.4% of all included patients.

**Table 2:** Frequency and percentage of patients according to gender (n=87)

Gender	Frequency (%)
Male	51 (58.60)
Female	36 (41.4)
Total	87 (100)

A 11.5% was observed among patients to have urinary tract infection, as indicated in table 3.

**Table 3:** Frequency and percentage of urinary tract infection in neonates with persistent jaundice (n=87)

Urinary Tract Infection	Frequency (%)
Yes	10 (11.5)
No	77 (88.5)
Total	87 (100)

A total of 87 patients with persistent neonatal jaundice were studied and of them 11.5% were found to have UTI.

## DISCUSSION

Jaundice is widely recognized as a common disease in neonates. Approximately 60% of newborns born at full-term experience the development of jaundice [16]. Indirect hyperbilirubinemia is a prevalent phenomenon that is associated with a wide range of physiological and pathological situations. Infants in the neonatal period who have urinary tract infections (UTIs) may exhibit solely the symptom of jaundice. Urinary tract infection (UTI) investigations have been incorporated into the standard diagnostic evaluation of jaundice. The controversy surrounding the investigation of urinary tract infections (UTIs) in neonates with unexplained indirect hyperbilirubinemia of large magnitude has been noted [17]. Our study revealed that the prevalence of urinary tract infections (UTIs) among the infants with persistent jaundice in our sample was found to be 11.5%. The previous research has reported a range of 5.8% to 21% as the incidence rate of urinary tract infection (UTI) in infants with jaundice [18]. In prospective research conducted by Shaimaa S. Abdelrheem et al., the incidence of urinary tract infection (UTI) in infants with jaundice was observed to be 25.7% [19]. The study conducted by Deger I et al., revealed a lower but significant incidence of urinary tract infection (UTI) of 8% in large number of neonates admitted with indirect hyperbilirubinemia in a single center study [20]. According to a study conducted by Özcan et al., the incidence of urinary tract infection (UTI) was found to be 16.7% [18]. Tawfeek et al., in her study that UTI was the 3rd most common etiology of jaundice in neonates with persistent jaundice [21]. The first and common most risk factor was breastfeeding 32.7%, followed by ABO incompatibility 22%. The incidence of UTI was 20%. Similarly, Aygün et al., work shows breastfeeding, blood group incompatibility and urinary tract infection being the common causes of prolonged neonatal jaundice. The prevalence of these causes was 73%, 13% and 8% respectively [22]. Demographics of our patients were comparable to other studies. The age range of patients in our study ranged from 14 to 28 days, with a mean age of  $20.597 \pm 4.50$  days. Tawfeek et al., reported age range of 14 to 49 days with mean age of  $19.3 \pm 5.3$ . The mean duration of complaint in our study was also  $18.20 \pm 4.077$  days, and the

mean weight was  $2.855 \pm 0.27$  Kg. However, the mean weight of  $3.275 \pm 0.459$  was noted by Tawfeek et al., in her study. The distribution of patients by gender was males as 58.6% and females comprising 41.4% of all included patients. Similar distribution was observed by Tawfeek et al., study comprising of 58% males and 42% females' babies [21]. Regarding the prevalent isolated organisms, it was found that *E. Coli* is the commonest cultured bacteria in urinary tract infections and counted 45.5% in study conducted by Chen et al., *Enterococcus faecalis* (19.3%) was the next commonest followed by *Streptococcus agalactiae* (8.00%) and *Klebsiella pneumoniae* (6.8%). Other less common organisms were enterococcus species, staphylococcus aureus, enterobacter aerogenes, *Serratia marcescens*, *Enterobacter cloacae* and *Citrobacter koseri* [23]. Similarly, Sheaf et al., demonstrated coliforms organism being the commonest followed by *E. Coli* in neonates with UTI [24]. A potential constraint of the research lies in the absence of urine culture for all instances under investigation. Our approach involved doing urine analysis, which encompassed leukocyte esterase (LE) and nitrite tests, as well as microscopic examination to detect the presence of pyuria, for all newborns included in the study. The restriction in question was a result of the local policy in the NICU and microbiology laboratory, which dictates that urine culture should only be conducted in cases of sepsis, abnormal urine analysis, or pyuria. Nevertheless, the utilization of aseptic urinary catheterization technique has been found to enhance the specificity of urine sample collection. Additionally, the inclusion of aggregate urine analysis, which involves assessing the presence of leukocyte esterase (LE), nitrite, or pyuria (> 5 white blood cells per high-power field), has been shown to significantly increase the sensitivity for detecting urinary tract infections (UTIs) in infants below 60 days of age, with a reported accuracy of 99.4% according to a study conducted by Tzimenatos et al. [25]. The relationship between urinary tract infection (UTI) and jaundice in neonates is not yet fully understood, and further research is needed to investigate potential reasons [26]. Jaundice seems to be result of direct effect of bacteria, enhanced by its toxins and host response through pro-inflammatory cytokines. These bacteria also secrete hemolysin, which cause haemoglobin destruction and it, is then converted to bilirubin by liver enzymes [27].

## CONCLUSIONS

Our study concludes that a significant number of patients with persistent jaundice have urinary tract infections. Thus, it can be inferred that UTI may be a contributing factor to the occurrence of unexplained indirect hyperbilirubinemia in neonates. Hence, it is recommended

that neonates with persistent jaundice be screen for urinary tract infection (UTI) especially neonates with unexplained hyperbilirubinemia.

### Authors Contribution

Conceptualization: AK

Methodology: IK, N, SA

Formal analysis: LM, SH

Writing-review and editing: LM, IK, AK

All authors have read and agreed to the published version of the manuscript.

### Conflicts of Interest

The authors declare no conflict of interest.

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