Hyperbilirubinemia is common in newborns. Total serum bilirubin may not surpass physiological values in some neonates, but it may do so in others, at which point it requires treatment. During the regular evaluation of newborns with significant hyperbilirubinemia, several well-known causes might be identified, while others may go unnoticed (1). On the other hand, because of their immature immune systems, newborns are more likely to develop urinary tract infections (UTIs) in their first few months of life (2, 3). Although fever is a significant indicator of UTI in newborns, a considerable percentage of neonatal UTIs do not manifest with a fever or particular urinary tract symptoms. As a result, understanding non-specific signs and symptoms of newborn UTI is critical for identifying relevant cases that need an early diagnosis to avoid long-term complications (2).

The American Academy of Pediatrics (AAP) guidelines advocate urinalysis and urine culture in infants with conjugated hyperbilirubinemia (6). Furthermore, unconjugated hyperbilirubinemia may be a significant or the earliest manifestation of UTI (7, 8). Additionally, recent systematic reviews have evaluated the incidence of UTI in newborns with persistent jaundice (9, 10). Potentially, the direct effect of the UTI microorganisms on the structures and cells responsible for the secretion of conjugated bilirubin causes jaundice (11). It is possible to explore the potential factors affecting the type of pathogens responsible for UTI in neonatal hyperbilirubinemia.
that some factors may affect or determine the UTI-causing pathogens when neonates have concomitant hyperbilirubinemia; however, these factors have not been explored in previous studies. This study aimed to determine the potential factors influencing the type of pathogens responsible for UTI in neonatal hyperbilirubinemia.

**Materials and Methods**

**Participants and Study Design**

This cross-sectional study retrospectively evaluated newborns admitted to the neonatal ward of Bandar Abbas Children’s Hospital between 2016 and 2018. The participants’ informed consent was not required because of the retrospective nature of this research. The inclusion criteria were hyperbilirubinemia and positive urine culture. Urine cultures on catheterized samples ≥ 10⁵ and those on suprapubic ones with one-colony-forming unit were considered positive. Newborns with urinary tract anomalies were excluded from the study. Of the 683 evaluated medical records, 96 met the inclusion criteria.

The following data were extracted from the patients’ medical files:

- Demographics and anthropometrics: age, gender, gestational age, and birth weight
- Type of delivery: cesarean section (C-section) or normal vaginal delivery (NVD)
- Newborn’s feeding: breastfeeding or formula feeding
- Clinical manifestations: fever, poor feeding, and hyporeflexia
- Urine sampling method: suprapubic aspiration or catheterization
- Laboratory test results: total bilirubin and urine culture

**Data Analysis**

SPSS version 25.0 was used for data analysis. Mean, standard deviation, frequency, and percentage were used to describe the variables. The one-way analysis of variance (ANOVA) test was used to compare continuous variables between groups. The chi-squared and Fisher’s exact tests were used to compare categorical variables. P values ≤ 0.05 were considered significant in all statistical tests.

**Results**

Of the 96 neonates with hyperbilirubinemia and positive urine culture in this study, 63 (65.6%) were male and 33 (34.4%) were female. Their mean age was 13.60 ± 6.00 days. Most were born by C-section (61.5%) and received breastfeeding (93.8%). Fever, poor feeding, and hyporeflexia were present in 1%, 3.1%, and 2.1% of the newborns, respectively. Urine samples were mostly obtained by the suprapubic aspiration (85.4%). *Escherichia coli* was the most common pathogen isolated from the urine cultures (33.3%), followed by *Klebsiella* (24%) (Table 1).

Age, gender, gestational age, birth weight, type of delivery, newborn feeding, clinical manifestations, total bilirubin level, and urine sampling method were not associated with the type of pathogens isolated from urine culture ($P>0.05$) (Table 2).

**Discussion**

In this study, *E. coli* and *Klebsiella* were the most common microorganisms responsible for UTI in neonates with hyperbilirubinemia, which is in line with the findings of previous studies (10, 12-15). It has been suggested that jaundice associated with UTI may be caused by *E. coli* or other Gram-negative organisms hemolyzing the blood, which might lead to unconjugated hyperbilirubinemia (16). Moreover, we found that newborn feeding was not associated with the type of pathogens isolated from urine culture. In contrast, Hosseini et al found that formula-fed infants were more likely to have concomitant hyperbilirubinemia and UTI (17), while they did not

| Table 1. General Characteristics of the Study Participants |
|-----------------------------|-----------------------------|
| **Variables**               | **Values**                  |
| Age (days), mean (SD)        | 13.60 (6.00)                |
| Gender, No. (%)             |                             |
| Male                        | 63 (65.6)                   |
| Female                      | 33 (34.4)                   |
| GA (wk), mean (SD)          | 38.27 (2.09)                |
| Birth weight (g), mean (SD) | 3059.07 (506.32)            |
| Type of delivery, No. (%)   |                             |
| NVD                         | 37 (38.5)                   |
| C-section                   | 59 (61.5)                   |
| Newborn feeding, No. (%)    |                             |
| Breastfeeding               | 90 (93.8)                   |
| Formula feeding             | 3 (3.1)                     |
| Breastfeeding and formula feeding | 3 (3.1)                  |
| Clinical manifestations, No. (%) |                        |
| Fever                       | 1 (1.0)                     |
| Poor feeding                | 3 (3.1)                     |
| Hyporeflexia                | 2 (2.1)                     |
| Total bilirubin (mg/dL), mean (SD) | 11.65 (5.39)               |
| Urine sampling method, No. (%) |                  |
| Suprapubic aspiration       | 82 (85.4)                   |
| Catheterization             | 14 (14.6)                   |
| Urine culture results, No. (%) |                    |
| *Escherichia coli*          | 32 (33.3)                   |
| *Klebsiella*                | 23 (24.0)                   |
| *Citrobacter*               | 5 (5.2)                     |
| *Enterobacter*              | 11 (11.5)                   |
| Others                      | 25 (26.0)                   |

Abbreviations: N: number; SD: standard deviation; GA: gestational age; NVD: normal vaginal delivery; C-section: cesarean section.
explore the potential correlation of neonatal feeding with the type of pathogens responsible for UTI. This discrepancy may be attributable to the small number of newborns in our sample who received formula. On the other hand, there was no correlation between gender and type of pathogens in this study, which is in line with the findings of Hosseini et al (17).

Furthermore, gestational age, neonate’s age, birth weight, and total bilirubin levels were not linked to the type of urinary pathogens in our research. Besides, the delivery type was not associated with the isolated bacteria. These findings are consistent with those of the study by Hosseini et al (17). However, Rashed et al demonstrated different results (18). This discrepancy may be brought about by variations in maternal communicable infections or the difference in the quality of delivery in terms of hygiene between studies.

In the current study, clinical manifestations including fever, poor feeding, and hyporeflexia were not associated with the type of the responsible pathogen. These presentations may occur after a variety of illnesses caused by various bacteria and may represent infection-related unspecific consequences. Therefore, it would have been expected that there would be no link in this area.

As a common condition in newborns, hyperbilirubinemia is often benign and resolves spontaneously. About 60% of term and 80% of preterm neonates suffer from hyperbilirubinemia during the first week of life. A major cause of neonatal hyperbilirubinemia is physiologic jaundice. The diagnosis is determined after ruling out other significant causes such as hemolysis, infection, and metabolic disorders (19). Prolonged jaundice is defined as hyperbilirubinemia that persists beyond two weeks. Hemolysis, congenital glucuronyl transferase deficiency, hypothyroidism, bowel obstruction, metabolic diseases including galactosemia, and UTI may all result in prolonged unconjugated hyperbilirubinemia. Due to frequent phototherapy sessions and multiple blood samples taken from the newborn, prolonged icterus may be quite stressful for the parents (19).

The major limitation of the current study was its relatively small sample size. The sample size for each pathogen from urine culture was not sufficient for the comparison of some variables, and P-values are largely dependent on sample size.

**Conclusion**

*Escherichia coli* was detected in the majority of urine cultures from neonates with hyperbilirubinemia. The bacteria that cause UTI in newborns with hyperbilirubinemia were not associated with any of the relevant variables examined in this investigation. To ascertain the genuine association of...
the causative microorganisms with various parameters as well as their possible relationship with the occurrence of hyperbilirubinemia, large case-control studies including neonates with UTI and without hyperbilirubinemia may be beneficial.

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Competing Interests
The authors declare that they have no competing interests.

Ethical Approval
The research adheres to the principles of the Declaration of Helsinki and was given ethical clearance by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1400.208). The participants' informed consent was not required because of the retrospective nature of this research.

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