Original Article

Pattern of urinary tract infection in children with vesicoureteric reflux: Does breastfeeding reduce the occurrence of urinary tract infection?

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Abstract

Introduction: The protective factors against urinary tract infections (UTIs) in the setting of vesicoureteric reflux (VUR) remain poorly defined. Breastfeeding was suggested as a protective factor against UTI, but its role remains undetermined in this highly susceptible population.

Objectives: The objective of the study was to identify the pattern and risk factors of UTI and investigate the effect of breastfeeding on UTI occurrence in VUR children.

Materials and Methods: This was a mixed-method design, whereby the first part was a cross-sectional study that included children who were diagnosed with VUR and were assessed for their UTI pattern. The second part was a case–control study, which involved contacting the mothers of the children enrolled and questioning them about their breastfeeding pattern, and UTI development was assessed.

Results: Our study included 62 children with a median age of 4.4 (interquartile range = 21) months at diagnosis. Of those, 37 (60%) were male and 25 (40%) were female. Most UTIs occurred in the first 3 months of life, and the first episodes were more frequent in males. Constipation was significantly associated with the occurrence of UTI (relative risk [RR] =1.750 [95% confidence interval (CI): 1.231–2.489], $P = 0.003$). Children with breakthrough UTIs were more likely to have been breastfed for <9 months (odds ratio [OR] = 4.091 [95% CI: 1.287–13.002], $P = 0.015$) and to have been exclusively breastfed for <2 months (OR = 4.600 [95% CI: 1.337–15.823], $P = 0.012$).

Conclusion: Children with VUR are more susceptible to UTIs in their 1st year of life. Constipation is a major risk factor for UTI occurrence in VUR children and should be aggressively managed. Breastfeeding for longer durations showed promising protective features against breakthrough UTIs.

Keywords: Breakthrough urinary tract infection, breastfeeding, children, constipation, pediatric, urinary tract infections, vesicoureteric reflux

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INTRODUCTION

Vesicoureteric reflux (VUR) is a condition characterized by urine backflow from the bladder into the upper urinary tract. It is a relatively common medical condition in neonates, as the prevalence is estimated to be 25%–40%.[1] The clinical presentation of VUR differs from one child to the other; patients may be asymptomatic, or they might present with a urinary tract infection (UTI) and, consequently, nephropathy and chronic kidney disease.[1] VUR is considered a well-established risk factor for the development of UTIs, and the prevalence of UTI is approximately 31.1% in children with VUR.[2,3] In addition, UTIs are considered the most common serious bacterial infection in children, which leads to kidney damage if left untreated.[4]

Multiple studies determined several risk factors for the development of UTI in children including congenital anomalies of the kidney and urinary tract, uncircumcision, female gender, younger age, diabetes, and instrumentation of the urinary tract (urinary catheterization).[5,6] Edwards and Peters explained that risk stratification for UTI development should be conducted in the setting of VUR, particularly for severe VUR (Grades III to V), baseline renal scarring, and bladder and bowel dysfunction (BBD).[3] In addition, other studies have shown that these risk factors also apply to breakthrough UTIs in children on continuous antibiotic prophylaxis (CAP).[7] Finally, the protective factors against UTI in the setting of VUR remain poorly defined.

Some of the protective factors against UTIs that were described included CAP, male circumcision, and breastfeeding.[8-10] CAP is a widely recognized preventative measure against recurrent UTIs in children with VUR. A trial described that cotrimoxazole as CAP reduces the risk of recurrent UTIs after the first episode by half, especially in children aged between 2 months and 6 years. However, CAP does not protect against renal scarring, and due to the long-term exposure, it can induce the formation of antibiotic-resistant bacteria.[8] In addition, infant male circumcision was another well-described protective factor against UTIs. A systematic review concluded that circumcision reduces the risk of UTI by 90%.[9]

Breastfeeding was suggested as a cost-free, natural protective factor against UTIs, particularly during the first 6 months of life.[10] Breast milk contains a high concentration of various protective elements that provide immunity against respiratory infections, otitis, and sinus infections. Nonetheless, the association between breastfeeding and the reduction of UTIs is less established in infants with VUR.[11] Interestingly, Saudi Arabia has a high initiation rate of breastfeeding, which is over 90%; however, this rate drops gradually throughout the 1st year, leading to the discontinuation of exclusive breastfeeding and the introduction of mixed feeding.[12]

Our main research question is as follows: in children with VUR, does breastfeeding reduce UTI occurrence? This study hypothesizes that breastfeeding will reduce the incidence of UTI in children with VUR. This study will further explore the possible protective impact of breastfeeding on the occurrence of UTI in children with VUR. This association was poorly reported in the literature, and further investigation was recommended by other authors. The objectives of our study are to identify the pattern of UTI in children with VUR, to establish the risk factors for UTI development, and to determine the effect of breastfeeding on the reduction of UTI.

MATERIALS AND METHODS

Study participants

The study included all Saudi children aged from birth until 18 years who presented to a tertiary health-care hospital in Jeddah, Saudi Arabia, and were diagnosed with VUR. The list of children with VUR between January 2015 and December 2021 was obtained from the medical record department. We excluded patients who passed away in the first 2 months of life. A total of 62 children were enrolled in this study.

Study design

This study incorporated a mixed method, quantitative–quantitative design. The first part was a retrospective cross-sectional study, where all pediatric patients who were diagnosed with VUR were assessed for their UTI pattern and followed up from birth until the last entry in their medical records. On the other hand, the second part was a case–control study, where the cases were children with VUR who developed UTI (the outcome), whereas the controls were children who did not develop UTI. Those children were assessed for their breastfeeding pattern through a phone survey to determine the association between breastfeeding and UTIs.

Data collection methods

For the first part, the data were collected through the patients' medical records. The predetermined data collection sheet consisted of two sections: child-related questions and pregnancy-related questions. Exposure variables were specified as the following: VUR presentation, type and grade of VUR, age, presence of antenatal

hydronephrosis, congenital abnormalities, renal scarring at baseline, family history of VUR, toilet training age, chronic constipation, BBD, breakthrough UTIs, corrective surgery, UTI status, right kidney function, left kidney function. We defined constipation as difficult or painful stool passage or less than three bowel motions per week.[13] Children who were diagnosed with an overactive bladder, dysfunctional voiding, or underactive bladder as well as displaying urological symptoms such as dribbling, urinary frequency, dysuria, urinary retention, hesitancy, and avoidance of urination were said to have BBD.[14] For the other section, information regarding pregnancy including mode of delivery, birth weight, parity, multiple gestation, UTI during pregnancy, Premature rupture of membranes (PROM), oligohydramnios, and gestational age were gathered.

In the second part, phone surveys were conducted with the patients' mothers to ask about the breastfeeding pattern. Questions on the breastfeeding pattern were referenced from the Infant Feeding Practice Study.[15,16] Information on the mother's age, educational level, employment status, monthly income, breastfeeding status, type of feeding (breastfeeding, mixed, or formula), duration of any breastfeeding, duration of exclusive breastfeeding, and intensity of breastfeeding (50% or less, more than 50%) were collected. Duration of any breastfeeding was obtained by asking: "How long did you breastfeed your child." In addition, the duration of exclusive breastfeeding was obtained by asking mothers: "When did you first introduce any food or liquids other than breast milk to your child." Finally, data on breastfeeding intensity were obtained by asking: "Did breast milk feedings constitute more than half the milk feedings of your child?"[15,16]

Study outcomes

The main outcome of this study was the development of UTI. The diagnosis of UTI was established based on the presence of symptoms, including a body temperature >38°C, dysuria, urgency, malodorous urine, and the presence of a positive urine culture with a single uropathogenic growth $\geq 10^5$ CFU/mL in a clean-catch sample.[7] The occurrence of breakthrough UTI was also assessed as a second outcome. Data on breakthrough UTIs were collected by looking at the date of commencement and conclusion of CAP and whether the patient developed UTI during this period.

Statistical analysis

Data management and analysis were conducted using IBM SPSS program version 25. Simple descriptive statistics were reported as frequency and percentages for qualitative data and mean and standard deviation for quantitative data if it was normally distributed or median and interquartile range if data were skewed. The Chi-square test was used to study the relationship between risk factors and breastfeeding practices on the development of UTI, and the cutoff for statistical significance was $P < 0.05$. To further quantify the strength of the association, odds ratios (ODs) were calculated with 95% confidence intervals.

Ethical consideration

The Institutional Review Board of King Abdullah International Medical Research Center, Jeddah, Saudi Arabia, approved this study. IRB approval number: IRB/1486/22. Study number RSS22J/002/07.

RESULTS

Study participants (children group)

Our study included a total of 62 children, out of which 37 were male and 25 were female, with a median age of 4.4 (interquartile range [IQR] = 21) months. These children were categorized by their UTI status into two groups (with UTI and without UTI). All our male children were circumcised. Children diagnosed with VUR were older in the UTI group (6.4 months: IQR: 23.21) compared to those without UTI (4.4 months: IQR: 19.32). In terms of gender distribution amongst the two categories, there was an equal distribution in the UTI group, however, 77.3% of participants were males in the second group. Children diagnosed with antenatal hydronephrosis and congenital abnormalities were very similar in both the groups. All children had voiding cystourethrography performed as antenatal hydronephrosis follow-up and post-UTI. Of these children, 53% had bilateral VUR. There were 16 children with VUR Grades I–III (29%) and 40 children with Grades IV–V (71%). Bilateral VUR was more common in the UTI group 25 (64.1%) compared to no UTI group 8 (36.4%) (*P* value: 0.037). Severe grades (IV–V) of VUR were more common in both the groups. In the UTI group, 34 (85%) were full-term children compared to 15 (68%) in the no UTI group. Approximately one-third of the children in the UTI group had low-birth weight (<2.5 kg), whereas more than half of the children without UTI had a normal birth weight (≥2.5 kg) [Table 1].

Study participants (mother group)

Our study included all mothers of the 62 children with VUR with a mean age at birth of 28.9 (SD = 5.71) years. The mothers were categorized into two groups according to their children's UTI status (UTI vs. no UTI). Mothers of the children of both the groups were similar in terms of employment status, educational level, household monthly income, presence of medical conditions, and associated

prescription medication. The mothers who had UTI during pregnancy were 23% in the UTI versus 41% in the no UTI group [Table 2].

Urinary tract infection pattern

In Figure 1, 16 of the children with VUR presented with their first UTI attack during their first 3 months of life. The trend in the chart depicted that most first UTI attacks occurred in the 1st year of life and gradually decreased until there was a surge at 60 months. In Figure 2, the frequency of first UTI attacks in males during the first 3 months was 12 compared to five in females. At 12 months, the frequency of the first attack was significantly increased in females compared to males. Finally, the frequency of the first UTI attack was increasing gradually after the 1st year of life in females [Figure 2].

Urinary tract infection risk factors

The presence of renal scarring at baseline was similar in both the groups (relative risk [RR] = 1.108 [95% confidence interval (CI): 0.716–1.713]). Constipation was significantly associated with UTI development (RR = 1.750 [95% CI: 1.231–2.489], $P = 0.003$). The presence of BBD was similar

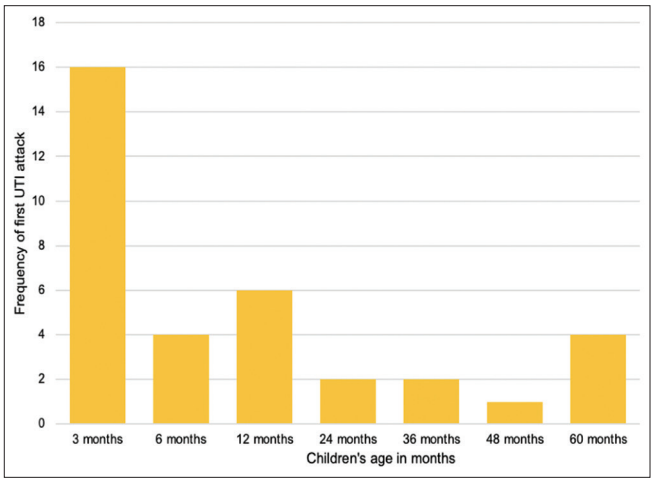

Figure 1: The frequency of first urinary tract infection attacks occurring in children based on their age

Table 1: Baseline clinical and demographic characteristics for children with vesicoureteric reflux

Characteristics	UTI group (*n*=40), *n* (%)	No UTI group (*n*=22), *n* (%)	*P*
Age at diagnosis (months), median (IQR)	6.4 (23.2)	4.4 (19.3)	0.897*
Gender			
Male	20 (50)	17 (77)	0.036
Female	20 (50)	5 (23)	
ANH			
Yes	22 (55)	11 (50)	0.706
No	18 (45)	11 (50)	
Congenital abnormalities			
Yes	20 (50)	10 (45)	0.732
No	20 (50)	12 (55)	
VUR presentation			
Hydronephrosis	24 (63)	21 (100)	0.001
Post-UTI	14 (37)	0	
VUR type			
Unilateral	14 (36)	14 (64)	0.037
Bilateral	25 (64)	8 (36)	
VUR grade			
Grades I–III	12 (32)	4 (22)	0.802
Grades IV–V	26 (68)	14 (78)	
Corrective surgery			
Yes	18 (45)	7 (32)	0.311
No	22 (55)	15 (68)	
Gestational age			
Term	34 (85)	15 (68)	0.120
Preterm	6 (15)	7 (32)	
Mode of delivery			
Spontaneous vaginal delivery	29 (73)	12 (55)	0.153
Cesarean section	11 (27)	10 (45)	
Birth weight (kg)			
<2.5	13 (33)	10 (45)	0.348
≥2.5	26 (67)	12 (55)	
Twins			
Yes	3 (7)	1 (4)	0.553
No	37 (93)	21 (96)	
Oligohydramnios			
Yes	2 (5)	1 (4)	0.715
No	38 (95)	21 (96)	

*The statistical procedure used was the Mann–Whitney *U*-test. IQR: Interquartile range, ANH: Antenatal hydronephrosis, VUR: Vesicoureteric reflux, UTI: Urinary tract infection

between both the groups (RR = 1.122 [95% CI: 0.674–1.868], $P = 0.685$). Regarding split renal function, the right kidney (RR = 1.03 [95% CI: 0.662–1.605], $P = 0.825$) and left kidney function (RR = 1.048 [95% CI: 0.679–1.618], $P = 0.833$) profiles were similar in both UTI and no UTI groups [Table 3].

Efficacy of breastfeeding: (Urinary tract infection status)

Both UTI and no UTI groups were comparable regarding the breastfeeding status, type of feeding, and breastfeeding intensity. Children with UTI were more likely to have been breastfed for <9 months (OR = 2.350 [95% CI: 0.777–7.110], $P = 0.127$); however, the association was not statistically significant [Table 4].

Efficacy of breastfeeding (Breakthrough urinary tract infection status)

We explored the effect of breastfeeding on the development of breakthrough UTI since all the children were on CAP. Children were categorized according to their breakthrough UTI status (breakthrough UTI vs. no

Table 2: Baseline clinical and demographic characteristics of mothers

Characteristics	UTI group (*n*=40), *n* (%)	No UTI group (*n*=22), *n* (%)	*P*
Age at birth (years), mean (SD)	28.6 (5.27)	29.7 (6.53)	0.469*
Educational level			
High school or less	19 (47)	9 (41)	0.618
Graduate or more	21 (53)	13 (59)	
Employment status			
Employed	11 (27)	5 (23)	0.681
Unemployed	29 (73)	17 (77)	
Household monthly income (SAR)			
<13,000	33 (83)	18 (82)	0.946
≥13,000	7 (17)	4 (18)	
Parity, median (IQR)	2 (2.0)	1 (1.3)	0.233**
Mothers with medical conditions			
Ye	11 (27)	7 (32)	0.720
No	29 (73)	15 (68)	
Mothers with medications			
Yes	8 (20)	4 (18)	0.862
No	32 (80)	18 (82)	
UTI during pregnancy			
Yes	9 (22)	9 (41)	0.127
No	31 (78)	13 (59)	
PROM			
Yes	6 (15)	2 (9)	0.507
No	34 (85)	20 (91)	

*The statistical test used was *t*-test, **The statistical procedure used was the Mann–Whitney *U*-test. PROM: Prolonged rupture of membranes, IQR: Interquartile range, UTI: Urinary tract infection, SD: Standard deviation

Table 3: Risk factors for urinary tract infection development

Risk factor	UTI group	No UTI group	Statistics
Renal scarring at baseline			
Yes	11 (38)	5 (31)	RR=1.108 (95% CI=0.716–1.713), *P*=0.654
No	18 (62)	11 (69)	
Constipation			
Yes	21 (53)	3 (14)	RR=1.750 (95% CI=1.231–2.489), *P*=0.003
No	19 (47)	19 (86)	
Bladder and bowel dysfunction			
Yes	5 (13)	2 (9)	RR=1.122 (95% CI=0.674–1.868), *P*=0.685
No	35 (87)	20 (91)	
Family history			
Yes	6 (15)	3 (14)	RR=1.039 (95% CI=0.628–1.720), *P*=0.884
No	34 (85)	19 (86)	
Toilet training			
Yes	28 (70)	15 (68)	RR=1.031 (95% CI=0.686–1.549), *P*=0.882
No	12 (30)	7 (32)	
Split renal function right kidney			
Renal function <45%	12 (39)	7 (37)	RR=1.030 (95% CI=0.662–1.605), *P*=0.825
Renal function ≥45%	19 (61)	12 (63)	
Left kidney			
Renal function <45%	14 (45)	8 (42)	RR=1.048 (95% CI=0.679–1.618), *P*=0.833
Renal function ≥45%	17 (55)	11 (58)	

CI: Confidence interval, UTI: Urinary tract infection, RR: Risk ratio

breakthrough UTI). Both the groups were similar in terms of breastfeeding status and type of feeding. Children with breakthrough UTI were more likely to have been breastfed for <9 months (OR = 4.091 [95% CI: 1.287–13.002], $P = 0.015$) and to have been exclusively breastfed for <2 months (OR = 4.600 [95% CI: 1.337–15.823], $P = 0.012$) [Table 5].

DISCUSSION

VUR is the most common urological abnormality identified on imaging in children presenting with UTI.[17,18] In Saudi Arabia, the prevalence of VUR is 41%–50% in patients with UTI, making it a significant risk factor for UTI development.[19,20] UTIs are considered the most prevalent, serious bacterial infections in children. They have multiple complications such as fever, urinary retention, and eventually renal function deterioration and scarring.[2]

Pediatric UTI cases account for 500,000 emergency visits and over 1 million outpatient visits annually.[21] Despite being a treatable infection, around 2%–3% of children with UTI require inpatient care contributing to increased health-care management expenses over the years. A study conducted in the US between 2000 and 2006 showed a 67% increase in mean hospitalization expenses and cumulative

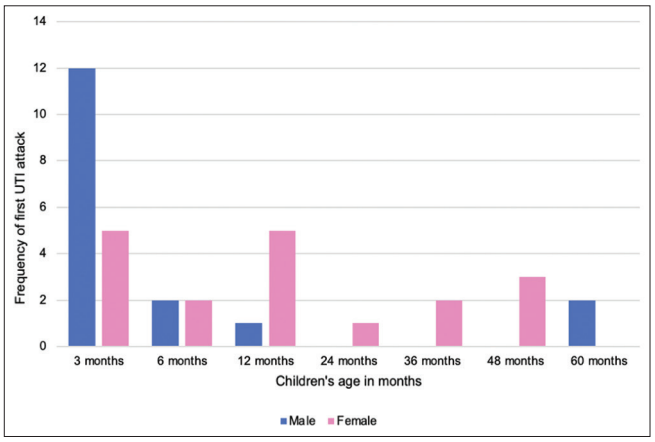

Figure 2: The frequency of first urinary tract infection attacks occurring in children based on their age and gender

Table 4: Effect of breastfeeding on urinary tract infection

Variable	UTI group (*n*=40), *n* (%)	No group (*n*=22), *n* (%)	Statistics
Breastfeeding status			
Yes	35 (88)	20 (91)	OR=0.700 (95% CI=0.124–3.946), *P*=0.685
No	5 (12)	2 (9)	
Type of feeding			
Exclusive	2 (5)	3 (14)	*P*=0.471
Mixed	33 (83)	17 (77)	
Formula	5 (12)	2 (9)	
Breastfeeding intensity			
50% or less	13 (39)	6 (35)	OR=1.192 (95% CI=0.353–4.018), *P*=0.777
>50	20 (61)	11 (65)	
Duration of breastfeeding			
<9 months	25 (66)	9 (45)	OR=2.350 (95% CI=0.777–7.110), *P*=0.127
9 months or more	13 (34)	11 (55)	
Duration of exclusive breastfeeding			
<2 months	25 (66)	12 (60)	OR=1.282 (95% CI=0.419–3.921), *P*=0.663
2 months or more	13 (34)	8 (40)	

OR: Odds ratio, CI: Confidence interval, UTI: Urinary tract infection

Table 5: Effect of breastfeeding on breakthrough urinary tract infection

Variable	Breakthrough UTI (*n*=30), *n* (%)	No breakthrough UTI (*n*=27), *n* (%)	Statistics
Breastfeeding status			
Yes	25 (83)	26 (96)	OR=0.192 (95% CI=0.021–1.764), *P*=0.111
No	5 (17)	1 (4)	
Type of feeding			
Exclusive	1 (3)	3 (11)	*P*=0.170
Mixed	24 (80)	23 (85)	
Formula	5 (17)	1 (4)	
Duration of breastfeeding (months)			
<9	21 (75)	11 (42)	OR=4.091 (95% CI=1.287–13.002), *P*=0.015
9 or more	7 (25)	15 (58)	
Duration of exclusive breastfeeding			
<2 months	23 (82)	13 (50)	OR=4.600 (95% CI=1.337–15.823), *P*=0.012
2 months or more	5 (18)	13 (50)	
Breastfeeding intensity			
50 or less	12 (50)	6 (26)	OR=2.833 (95% CI=0.830–9.668), *P*=0.092
>50	12 (50)	17 (74)	

UTI: Urinary tract infection, OR: Odds ratio, CI: Confidence interval

hospital expenses exceeding $520 million, which adds further to the burden on health care.[21] Recurrent UTIs are associated with frequent school absenteeism and excessive requests for parental leave.[21] Therefore, early UTI management and diagnosis are essential in preventing complications and difficulties.[22]

Our study confirms the results from prior studies. The first 6 months in the life of a child with VUR are crucial due to the higher risk of recurrent UTIs.[2] As children grow, their bladder control abilities mature, and this process is usually evident by the age of 5 years. As a result, BDD is usually diagnosed at this age after the completion of toilet training, particularly in the presence of symptoms suggesting lower urinary tract dysfunction (LUTS).[23] This explains the peak in the first UTI attacks at 60 months in Figure 1.

In our study, males had the highest frequency of first UTI attacks in the first 3 months, whereas females showed a peak at 12 months and a gradual increase between 24 and 48 months. This trend is similar in other studies.[21] Uncircumcised male infants younger than 3 months have a tenfold risk of developing UTI due to bacterial colonization beneath the foreskin.[21,24] In Saudi Arabia, the rate of circumcision is approximately 85%, and it is usually done in male infants up to 6 months of age.[25] After 12 months, females are more likely to develop UTI compared to males with a peak between 2 and 4 years corresponding to the toilet training age due to shorter urethras and the heavy colonization of the perineum.[26,27]

Numerous risk factors for the development of UTIs have already been identified in the literature, including uncircumcision, VUR, neurogenic bladder, lower urinary tract abnormalities, and constipation.[28,29] In addition, risk factors for the development of BT-UTIs in VUR patients were also studied. Female gender, uncircumcision, high-grade VUR, bilateral VUR, post-UTI presentation of VUR, younger age at first UTI, and presence of BBD were the most significant factors.[7,30] The results of our study were consistent with these findings. We found that female gender, VUR bilaterality, and constipation are significant risk factors for the development of UTI. Furthermore, our study demonstrated that chronic constipation had the most significant influence on the occurrence of UTI, since constipated children were 75% more likely to develop UTI than nonconstipated children. The possible pathological mechanism in this case is that the presence of hard feces can distend the rectum, leading to obstruction of bladder outflow. Loening-Baucke performed a randomized controlled trial, in which children with chronic constipation were managed with a regimen of disimpaction therapy, parental education, and maintenance treatment to recondition the child to normal bowel habits. This resulted in the disappearance of recurrent UTI in all children enrolled in the study, who did not have an anatomical abnormality. This further reiterated the importance of aggressive management of constipation to reduce the burden of urinary symptoms.[8]

On the other hand, the suggested protective measures included circumcision and CAP.[8,9] CAP has been shown to be effective in eradicating bacterial infections; the observed disadvantage was the increased bacterial resistance.[31] In addition, Meena *et al*. have suggested nonantibiotics alternatives such as cranberry products, probiotics, and D-mannose. Interestingly, two trials demonstrated that probiotics can be equally beneficial as antibiotic prophylaxis in preventing UTI recurrence in children with primary VUR without developing bacterial resistance; this could be due to the probiotic's effect on preventing uropathogen colonization in the urogenital tract. However, the accuracy of these claims is uncertain due to the low-quality evidence presented in the meta-analysis.[32]

Similarly, we aimed to explore the protective role of human milk as a natural and cost-effective option against UTIs. Breastfeeding is considered an ideal nutrition for healthy term infants up to 6 months of age; it contains numerous beneficial anti-infection bioactive components mainly within the colostrum, which is the milk produced during the 1st days of an infant's life. These components include immunoglobulins, cytokines, and hormones that interact with each other to provide passive immunity as well as stimulation to boost the infant's immune system's maturation.[11]

In our study, children who were breastfed for longer durations were less likely to develop UTI. First, our results have shown that children who were breastfed for <9 months were 2 times more likely to have UTI; however, the association was not statistically significant. This desired effect of breastfeeding was supported by a 2019 case–control study that succeeded to show that infants who were exclusively breastfed for 6 months had a 12% lower risk of UTI than partially breastfed 68% or bottle-fed 20%.[33] The same results were found by Mårild *et al*. who confirmed that even after weaning, a longer period of breastfeeding was documented with a lower risk of UTI.[10]

Second, it was found that children with breakthrough UTIs were four times more likely to have been breastfed for <9 months, which was statistically significant. In addition, children with breakthrough UTIs were

4.6 times more likely to have been exclusively breastfed for <2 months, and the association was strong. Interestingly, a 2020 case–control study has shown that infants who were exclusively fed commercial infant formulas before the age of 6 months were more vulnerable to acute pyelonephritis than breastfed or mixed-fed infants.[4] This suggests that not only breastfeeding is important but also the duration plays a very vital role in the protection against breakthrough UTIs. As a result, encouraging breastfeeding is recommended, at least during the first 6 months of life, when the infant's secretory immunoglobulin A (IgA) production is minimal; IgA is considered the first-line defense.[8] It should be noted that although 80% of the mothers in our study were mixed feeding compared to only 3% who were exclusively breastfeeding, around two-third of the mothers who mixed-fed their babies had breastfeed them with an intensity rate >50%. This provides a possible explanation to how the findings were achieved despite the lower percentage of exclusively breastfeeding mothers.

There were a few limitations in our study. First, the sample size is small; although we were able to retrieve all the medical records for the VUR patients, we could not include the outpatients' medical records because of data quality issues. Therefore, our statistical power and ability to observe significant associations were altered by our small sample size. Second, our study included all patients from birth until 18 years; therefore, it was challenging to collect baseline information which may result in recall bias.

To our knowledge, there have been no studies published describing the potential breastfeeding effect on UTI status among VUR children in general, especially in the Kingdom of Saudi Arabia. Therefore, we recommend conducting a prospective study to explore the effect of human milk and encouraging breastfeeding at least during the first 6 months of life. Regarding risk factor prevention, we recommend doing regular constipation screening programs for VUR patients, especially since constipation can be easily managed once identified.[8] On the other hand, failing to control constipation has serious repercussions in this population, including a higher risk of UTIs and, ultimately, kidney scarring.[29]

CONCLUSION

Children with VUR are more susceptible to UTIs in their 1st year of life. Constipation is a major risk factor for UTI development in children with VUR. Furthermore, our study showed that breastfeeding is a promising protective factor against UTIs in the setting of VUR. Therefore, we suggest further studies to confirm the effectiveness of breastfeeding in the prevention of UTIs.

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Conflicts of interest
There are no conflicts of interest.

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