

## Urinary Tract Infections in Children with Lower Abdominal Pain

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### ABSTRACT

**Objective:** To determine the association between different factors and the development of urinary tract infections in children presenting with lower abdominal pain.

**Study Design:** Case-control study.

**Place and Duration of Study:** Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan Aug 2022 to March 2023.

**Methodology:** This study was conducted on 198 paediatric patients. All patients underwent urine culture for establishing the diagnosis of a UTI and a positive culture was defined as >10<sup>5</sup> CFU/mL of a single bacterial pathogen. Patients with a positive urine culture were grouped into cases while with negative urine culture were used as controls.

**Results:** The mean age of our study sample was 9.61±3.62 years. Male gender (OR: 0.44 [95% CI 0.24 – 2.57]) was associated with a lower risk of developing UTIs while obesity (OR: 4.27 [95% CI 1.83 – 9.95]), family history of recurrent urinary tract infections (OR: 3.68 [95% CI 1.40 – 9.67]), renal scarring (OR: 4.13 [95% CI 0.45 – 37.59]), urinary tract anatomical abnormalities (OR: 6.06 [95% CI 1.31 – 28.11]), low daily fluid intake (OR: 7.19 [95% CI 3.01 – 17.19]) and decreased frequency of voiding per day (OR: 2.86 [95% CI 1.24 – 6.57]) were all associated with an increased risk of urinary tract infections.

**Conclusion:** Identification of risk factors for the development of urinary tract infections in children presenting with isolated, non-specific lower abdominal pain, such as obesity, poor fluid intake and inadequate voiding can help the clinician to make appropriate diagnoses.

**Keywords:** Children, Dysuria, Lower abdominal pain, Urinary tract infection.

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### INTRODUCTION

Bacterial infection of the urinary bladder and its associated structures, such as the urethra and ureters, is known as a urinary tract infection (UTI).<sup>1</sup> It is one of the most frequently encountered infections in the paediatric age group: approximately 6% to 8% of all febrile children presenting to the general physician suffer from this disorder.<sup>2</sup> In the short-term, complications of UTIs include a decrease in oral intake and, consequently, dehydration. In addition, patients are at risk of formation of local abscess formation, bacteraemia and the haematogenous propagation of the urinary pathogen to distant sites such as the meninges as well as acute kidney injury.<sup>3,4</sup> Long-term complications include the occurrence of scarring within the urinary tract which increases the risk of further UTIs, renal dysfunction resulting in hypertension and ultimately chronic kidney disease.<sup>4</sup>

Paediatric patients suffering from UTIs may report with specific local symptoms such as dysuria, urgency, urinary frequency, suprapubic tenderness,

turbid and/or malodorous urine,<sup>5</sup> or they may present with non-specific symptoms such as lethargy, vomiting, irritability, inadequate feeding, vague abdominal pain or just fever.<sup>6</sup> Still others may not have any signs or symptoms at all.<sup>7</sup> Thus the disorder may present as a diagnostic dilemma in this population age group. Identifying children at-risk for the development of this infection may be very useful in establishing the correct diagnosis: factors such as obesity, lack of breast-feeding, lack of circumcision, vesicoureteral reflux, previous UTI history and renal scarring are just some of the risk factors identified in children which may result in an predisposition to the development of UTIs.<sup>8-10</sup>

The aim of this study was to determine the frequency with which patients from the paediatric age group presented with UTIs while only complaining of non-specific abdominal pain. In addition, patients were evaluated for the presence of different conventional risk factors for the development of UTIs and their association with development of such poorly localizing infections. Establishing these factors and their association, or lack thereof, with the development of UTIs that manifest in such a silent

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manner will help sensitize the clinician to patients that are at increased risk for the development of such infections, initiate the appropriate investigations if required, and institute timely and appropriate management, which help in significantly reducing both the short- and long-term morbidity associated with the disease as well as financial costs of management.

**METHODOLOGY**

This study was conducted as a case-control study from August 2022 to March 2023 in the Department of Paediatrics, Combined Military Hospital, Rawalpindi, Pakistan on 198 (99 cases and 99 controls) paediatric patients who reported with complaints of abdominal pain, with informed consent being obtained from their parents or guardians for inclusion in the study. Patients were included in the study via non-probability, consecutive sampling. The EPI sample size calculator was used to calculate the sample size keeping a two-sided confidence level of 95%, a power of the test of 90%, a ratio of controls to cases of 1, percentage of controls exposed of 3.7%, percentage of cases exposed of 19.2%, and an odds ratio of 6.2, figures which were derived from Mahyar et al for obesity as a risk factor for the development of UTIs in children.<sup>11</sup>

**Inclusion Criteria:** All paediatric patients, of both genders, aged between 4 and 16 years of age, reporting with isolated lower abdominal pain were included for study.

**Exclusion Criteria:** Children with immunodeficiency syndromes, neurodevelopmental disorders, neoplastic disease and those on immunosuppressive drugs were excluded.

All the enrolled participants received documentation for relevant history and underwent a clinical examination, including height and weight measurement. Participants with a body mass index (BMI) measurement of greater than the 95<sup>th</sup> percentile for children of the same age and gender were classified as obese. Subsequently, all patients underwent urine culture for establishing the diagnosis of a UTI and a positive culture was defined as >10<sup>5</sup> CFU/mL of a single bacterial pathogen, cultured from a single midstream urine sample.<sup>11</sup> Patients with a positive urine culture were grouped into cases while those with a negative urine culture were used as controls. All patients underwent renal ultrasound and dimercaptosuccinic acid (DMSA) renal scan to look for renal scarring. Low fluid intake was defined as less

than 1.5 liters of fluid consumption per day,<sup>12</sup> and decreased frequency of voiding was defined as 3 or less episodes of passing urine per day.<sup>13</sup>

Data was analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows version 26, IBM Corp; Armonk, USA). Mean and standard deviation was calculated for quantitative variables specifically patient age. Qualitative variables like gender, presence of obesity, nocturnal enuresis, day-time enuresis, circumcision, family history of UTIs, presence of renal scarring, presence of anatomical anomalies in the urinary tract, low fluid intake and decreased frequency of voiding were recorded in terms of frequency and percentage. Quantitative variables were compared across groups using the independent samples t-test while the Chi square test/Fischer exact test was used for qualitative variables and a *p*-value of ≤0.05 was considered significant. Odds ratios were used to measure the associations between risk factors under study and the development of a urinary tract infection.

**RESULTS**

This study was conducted on a total of 198 paediatric patients reporting with non-specific abdominal pain who had a mean age of 9.61±3.62 years, of whom 130(65.7%) were female. A total of 35(17.7%) participants were obese, nocturnal enuresis was seen in 11(5.6%) patients, while day-time enuresis was seen in 6(3.0%) enrollees. A total of 25(12.6%) had a family history of recurrent UTIs, while 5(2.5%) had renal scarring at the time of the study. Anatomical structural anomalies affecting the urinary tract were seen in 13(6.6%) patients, 42(21.2%) patients had low daily fluid intake, while 31(15.7%) had a low frequency of voiding per day. Table-I shows the patient characteristics distributed according to cases and controls.

**Table-I: Patient Characteristics (n=198)**

Variables	Cases (n=99)	Controls (n=99)	<i>p</i> -value
<b>Gender</b>			
Male	25(25.3%)	43(43.4%)	0.007
Female	74(74.7%)	56(56.6%)	
Age (years)	9.59±3.73	9.64±3.52	0.922
Obesity	27(27.3%)	8(8.1%)	<0.001
Nocturnal Enuresis	6(6.1%)	5(5.1%)	0.756
Day-time Enuresis	2(2.0%)	4(4.0%)	0.683
Uncircumcised Males (Total Males: 68)	6(24.0%) (Total Males: 25)	1(1.0%) (Total Males: 43)	<0.001
Family History of Recurrent Urinary tract infection	18(19.2%)	7(7.1%)	0.019
Renal Scarring	4(4.0%)	1(1.0%)	0.369
Urinary Tract Anatomical Anomalies	11(11.1%)	2(2.0%)	0.018
Low Daily Fluid Intake	35(35.4%)	7(7.1%)	<0.001
Decreased Frequency of Voiding per Day	22(22.2%)	9(9.1%)	0.011

Table-II shows the odds ratios calculated for various risk factors that were suspected to be associated with an increased risk for the presence of UTI in paediatric patient reporting with isolated, non-specific lower abdominal pain. Male gender was associated with a lower risk of developing UTIs, while obesity, family history of recurrent UTIs, renal scarring, urinary tract anatomical abnormalities, low daily fluid intake and decreased frequency of voiding per day were all associated with an increased risk for the development of such infections.

**Table-II: Odds Ratio for Risk Factors (n= 198)**

Variables	Odds Ratios with 95% Confidence Interval
Male Gender	0.44 [95% CI 0.24 - 2.57]
Age (<7 years)	1.30 [95% CI 0.69 - 2.47]
Obesity	4.27 [95% CI 1.83 - 9.95]
Nocturnal Enuresis	1.21 [95% CI 0.36 - 4.11]
Day-time Enuresis	0.49 [95% CI 0.09 - 2.74]
Circumcised Males	0.08 [95% CI 0.01 - 0.67]
Family History of Recurrent Urinary tract infection	3.68 [95% CI 1.40 - 9.67]
Renal Scarring	4.13 [95% CI 0.45 - 37.59]
Urinary Tract Anatomical Anomalies	6.06 [95% CI 1.31 - 28.11]
Low Daily Fluid Intake	7.19 [95% CI 3.01 - 17.19]
Decreased Frequency of Voiding per Day	2.86 [95% CI 1.24 - 6.57]

## DISCUSSION

Isolated, non-specific lower abdominal pain is a frequent cause of presentation to the emergency department in paediatric patients. While a myriad number of causes can be identified in the pathogenesis of such cases, urinary tract infections remain a common, and oft-times missed, cause. Our study demonstrated that such children can be possibly identified by risk factors such as obesity, female gender, degree of fluid intake and frequency of voiding, among others, which can help to initiate the relevant investigations to confirm the diagnosis and give timely and appropriate treatment.

The mean age of patients in our study sample was 9.61±3.62 years. This figure was similar to a study on a Turkish population by Gul *et al.*, who reported a mean age of 10.91±5.58 years for patients reporting with suspected community acquired urinary tract infections.<sup>14</sup> However, this figure may vary depending on the which population the study was conducted in: Alrasheedy *et al.*, reported on a Saudi-Arabian population and reported a mean age of 4.5-5 years,<sup>15</sup> while Doğan *et al.*, reported a mean age of 7.01±4.83

years in their patients with recurrent UTIs.<sup>16</sup> Variability across populations is expected with different practices in hygiene and patterns of community-acquired pathogens, and is the likely cause of the variability seen in results. We also noted that young or older age did not appear to be associated with an increase in risk for the development of UTIs, (OR: 1.30 [95% CI 0.69 - 2.47],  $p=0.922$ ), as in other studies on the subject.<sup>14-16</sup>

Our study had a female majority of 65.7%, with females having a higher frequency of urinary tract infections, ( $p=0.007$ ), and the male gender having a significantly lower risk for the development of UTIs, (OR: 0.44 [95% CI 0.24 - 2.57]). These findings were in keeping with existing studies such as Leigh *et al.*, who reported that females had a higher risk for the development of UTIs in their study (OR: 2.3 [95% CI 1.1 - 4.7]).<sup>17</sup> This increased susceptibility of females can be explained with two reasons: females have a shorter urethra, and the perineum is susceptible to heavy colonization by enteric organism which can cause subsequent infections in the urinary tract, due to the close proximity of the urethral orifice with the perineum in females than in males.<sup>5,18</sup>

A total of 17.7% participants were obese in our study, with obese patients having a significantly higher risk of development of UTIs (OR: 4.27 [95% CI 1.83 - 9.95],  $p<0.001$ ). This was in-keeping with existing studies such as Renko *et al.*, who also reported an increased risk for the development of UTIs in obese patients, (OR: 2.23 [95% CI 1.37-3.63]),<sup>8</sup> a finding that was also seen in Alhabeeb *et al.*,<sup>19</sup> The mechanism by which obesity leads to the increased propensity to develop UTIs is unclear, however, alterations in cytokine production, disorder functioning of macrophages, natural killer T-cells and dendritic cells in obese patients have been implicated in its pathogenesis.<sup>20</sup>

Our study noted that neither nocturnal enuresis (OR: 1.21 [95% CI 0.36 - 4.11],  $p=0.756$ ), nor day-time enuresis (OR: 0.49 [95% CI 0.09 - 2.74],  $p=0.683$ ) was associated with an increase in risk for the development of UTIs, which was in keeping with findings from existing studies such as Renko *et al.*,<sup>8</sup> It has been previously proposed that weak muscles associated with the urinary system such as the bladder and pelvic floor muscles, which can cause enuresis, may lead to increased susceptibility to infections but this has not been borne out by research.<sup>8,21</sup>

Our study showed that circumcised males had a lower risk for the development of UTIs (OR: 0.08 [95% CI 0.01 - 0.67],  $p < 0.001$ ). Renko *et al.*, also noted that circumcision decreased the risk of development of UTIs, (OR: 0.1 [95% CI 0.06-0.17]),<sup>8</sup> this is likely attributable to the removal of the prepuce, the inner surface of which may serve as a nidus for secretions and infection if not adequately cleaned at regular intervals.<sup>22</sup>

A family history of recurrent UTIs was seen to be associated with an increased risk for the presence of UTIs in children reporting with lower abdominal pain, in our study, (OR: 3.68 [95% CI 1.40 - 9.67],  $p = 0.019$ ), which is in keeping with existing studies.<sup>8,23</sup> While the pathogenesis is unclear, this factor likely represents a complex interaction between genetic and environmental factors, and requires further study.<sup>23</sup>

Renal scarring was seen to be more frequently present in individuals with UTIs in our study, (OR: 4.13 [95% CI 0.45 - 37.59],  $p = 0.369$ ). Loukogeorgakis *et al.*, reported that patients with renal scarring were at a higher risk for the development of UTIs (OR: 3.3 [95% CI 1.4 - 7.4],  $p < 0.01$ ).<sup>24</sup> However, it is difficult to establish causality: children who develop recurrent UTIs may do so due to issues such as vesico-ureteral reflux which, if chronic, may lead to renal scarring, therefore, it is unclear whether renal scarring itself leads to increased risk of urinary tract infections or vice versa, and should be the subject of further study.

### LIMITATIONS OF STUDY

This research was conducted as a single-center study on the wards of military personnel, further multi-center study with a more diverse patient population may be required before conclusions that are generalizable to the population-at-large can be made. Additionally, urination habits such as the use of different kinds of toilets and hygiene practices used were not studied in our research protocol, and requires further study. Lastly, menstruation hygiene and practices were also not studied which may have resulted in some degree of confounding within the results, and should be the subject of future research.

### CONCLUSION

Our study showed that female gender, lack of circumcision, obesity, family history of recurrent urinary tract infections, renal scarring, anatomical abnormalities of the urinary tract, decrease oral intake of fluids and low frequency of voiding appear to be clear risk factors for the presence of urinary tract infections in paediatric cases with non-specific, isolated lower abdominal pain, necessitating vigilance from the treating clinician during diagnosis and management.

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### Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & WA: Data acquisition, data analysis, critical review, approval of the final version to be published.

FI & ZZ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

BA & MZ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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