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Clinical and Laboratory Assessment of the Severity of Urinary Tract Infections in Adolescent Girls Considering Vitamin D Status

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Abstract: Urinary tract infections in adolescent girls remain a significant pediatric and adolescent health concern because recurrent inflammatory episodes frequently contribute to chronic discomfort, metabolic disturbances, and progressive impairment of local antimicrobial defense mechanisms. The present study aimed to evaluate the clinical and laboratory severity of urinary tract infections depending on vitamin D status in adolescent girls. A total of 55 patients aged 10–18 years underwent comprehensive clinical, laboratory, microbiological, and ultrasonographic examination together with determination of serum 25-hydroxyvitamin D levels. The obtained findings demonstrated that vitamin D deficiency was associated with more severe and recurrent urinary tract infections accompanied by pronounced dysuric disorders, elevated inflammatory markers, anemia syndrome, disturbances of calcium metabolism, and increased prevalence of multidrug-resistant microbial associations. Girls with reduced vitamin D concentrations additionally exhibited higher rates of fungal colonization and persistent inflammatory activity, supporting the important immunomodulatory role of vitamin D in maintaining urothelial protection and antimicrobial resistance.

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1. Introduction

Although urinary tract infection (UTI) is one of the most common bacterial infections in children and adolescents in clinical practice and significant advances have been made in diagnostic and therapeutic methods, recurrent and complicated UTIs are still a major medical issue and are associated with chronic urinary incontinence, renal parenchymal damage and long-term renal impairment [1]. Urinary tract infections are especially threatening to adolescent girls as anatomic, hormonal and microbiologic factors facilitate ascending bacterial colonization, recurrent infections can slowly lead to chronic dysuric disorders, and formulating antimicrobial resistance with each infection can decrease quality of life and increase the risk of forming antimicrobial resistance. Many patients will have a variable clinical course, from asymptomatic bacteriuria to severe clinical symptoms with pyelonephritis and significant laboratory changes and systemic inflammatory responses [2].

In the past few years, the focus has been on metabolic and immunological factors that could have an impact on the risk of recurrent UTIs and vitamin D deficiency has become one of the most interesting, due to its wide immunomodulatory activity and its association with epithelial mechanisms. In addition to its classical role in calcium-phosphorus metabolism, vitamin D is involved in regulating innate and adaptive immune responses by inducing antimicrobial peptides (cathelicidins and β -defensins), influencing cytokine activity and maintaining mucosal barrier integrity. Thus, the low levels of 25-hydroxyvitamin D can affect the local antimicrobial defense of the urinary tract and facilitate the growth of pathogenic microflora and/or persistence of inflammatory activity [3].

Several modern pediatric studies have shown that children and young people with recurrent UTI tend to have lower levels of serum vitamin D than healthy individuals and hypovitaminosis D has been linked with higher incidence of resistant microorganisms, greater inflammatory response, and increased number of recurrent UTI [4].

Additionally, the chronic inflammatory response that follows repeated urinary tract infection could lead to iron metabolism and calcium homeostasis abnormalities, as well as to other metabolic dysfunctions, all of which could further worsen the inflammatory process and micronutrient deficiency in a vicious circle. Although increasing number of studies have been performed on the relationship between vitamin D and infectious diseases, there are still insufficient studies investigating the relationship between vitamin D status, microbiological characteristics, inflammatory markers and clinical-laboratory severity of UTIs in adolescent girls, especially recurrent cases of UTIs and inflammatory markers. Thus, vitamin D status in adolescent patients with UTI could be an important piece of information for prognosis and may be a useful element in personalized care and prevention in pediatric and adolescent care[5].

2. Materials and Methods

This clinical observational study involved adolescent girls with UTI who were treated and examined comprehensively in the departments of pediatric gynecology and pediatric urology at the Tashkent State Medical University (TSMU) multidisciplinary children's clinic. A single diagnostic protocol was used to obtain a uniform clinical and laboratory evaluation of disease severity and to assess the possible role of vitamin D status in UTI inflammatory activity, recurrence rates and microbiological features of UTIs. After inclusion criteria verification, a detailed clinical evaluation was performed, 55 girls (between 10-18 years old) were enrolled during the study period. Expanded medical history was obtained for all participants, which included a history of previous UTIs, UTI recurrence frequency, gynecological complaints, perinatal history, previous antibacterial treatment, and concomitant chronic diseases that might affect immune or metabolic function. Special emphasis was placed on signs that indicate the degree of involvement of the urinary tract such as dysuric disorders, lumbar pain, febrile episodes, weakness and systemic intoxication. The clinical manifestations, recurrence rate, laboratory inflammatory activity, and the ultrasonographic evidence of upper urinary tract involvement were used to define the severity of UTI [6].

Laboratory testing was conducted under standard conditions and comprised full blood count, including hemoglobin concentration and erythrocyte indices, white blood count and erythrocyte sedimentation rate. Biochemical analysis consisted of serum ferritin, serum 25-hydroxyvitamin D level, serum calcium concentration, and C-reactive protein measurements. Levels of 25(OH)D were measured by enzyme-linked immunosorbent assay (ELISA) methods as the serum vitamin D level is regarded as the most useful parameter to assess vitamin D status in clinical practice [7]. Based on the results obtained, patients were classified into groups of vitamin D deficient, deficient or normal serum vitamin D levels. General urinalysis, Nechiporenko test, bacteriological urine culture with

quantitative assessment of the growth of microorganisms and the assessment of sensitivity to antibacterial agents were performed as part of a comprehensive study of urine. Vaginal vestibular smears were also subjected to further microbiological examination to detect fungal colonization, association with other microorganisms and disturbances of local urogenital flora. Instrumental examination comprised ultrasonographic evaluation of kidneys, urinary bladder and pelvic organs with the indication of the absence of structural abnormalities and the presence of the signs characteristic of upper urinary tract inflammation and chronic recurrent infection [8].

The collected data were analyzed statistically with the SPSS version 26.0 software. Quantitative variables were presented as mean and standard deviation and categorical variables were analyzed by using χ^2 testing and odds ratio with corresponding confidence interval. Comparisons were made between study groups to determine the association between the severity of UTI and vitamin D status. The differences were considered statistically significant when $p < 0.05$.

3. Results

The clinical and laboratory analysis demonstrated that reduced serum vitamin D levels were highly prevalent among adolescent girls with urinary tract infections, and the severity of infectious manifestations progressively increased as the concentration of 25-hydroxyvitamin D decreased. Among the examined patients, only a relatively small proportion demonstrated normal vitamin D status, whereas the majority showed either insufficiency or pronounced deficiency, indicating that hypovitaminosis D may represent a common accompanying metabolic disturbance in adolescent girls suffering from recurrent urinary tract pathology. Patients with vitamin D deficiency more frequently presented with persistent dysuric complaints, recurrent inflammatory episodes, lumbar pain, fatigue, and manifestations of systemic inflammatory response compared with girls whose vitamin D concentrations remained within normal limits [9].

A particularly important observation involved the markedly higher frequency of recurrent urinary tract infections among girls with reduced vitamin D concentrations. Recurrent episodes occurring three or more times annually were significantly more common in patients with vitamin D deficiency, while girls with normal 25(OH)D values generally demonstrated milder clinical progression and lower inflammatory activity. In addition, laboratory analysis revealed that elevated C-reactive protein concentrations were predominantly observed in groups with deficiency and insufficiency of vitamin D, suggesting a stronger systemic inflammatory response and prolonged activation of immune pathways under conditions of impaired micronutrient status [10].

Anemia-related laboratory abnormalities also appeared considerably more frequent among patients with hypovitaminosis D. Lower hemoglobin and ferritin values were identified predominantly in girls belonging to vitamin D-deficient groups, which may reflect the combined influence of chronic inflammation, recurrent infection, and metabolic dysregulation. Simultaneously, disturbances of calcium metabolism were more pronounced in patients with severe vitamin D deficiency, where hypocalcemia occurred substantially more often compared with girls demonstrating adequate vitamin D status.

Table 1. Clinical and laboratory characteristics according to vitamin D status

Parameters	Vitamin D Insufficiency (n=30)	Vitamin D Deficiency (n=15)	Normal Vitamin D (n=10)
Mean 25(OH)D (ng/mL)	23 ± 2.1	18 ± 2.1	43 ± 5.1
Recurrent UTIs ≥3/year (%)	40%	67.4%	8%
Elevated CRP >5 mg/L (%)	72%	86%	20%
Anemia Syndrome (%)	70%	73%	12%

Hypocalcemia (%)	38%	73%	10%
Candida spp. Detection (%)	23%	53%	5%
Multidrug-resistant Strains (%)	17%	47%	4%

The data presented in Table 1 clearly demonstrate that the most severe and recurrent forms of urinary tract infections were predominantly observed in girls with vitamin D deficiency. Increased inflammatory markers, frequent anemia syndrome, disturbances of calcium metabolism, and higher prevalence of multidrug-resistant microbial strains collectively indicate that reduced vitamin D levels may contribute not only to impaired immune defense but also to broader metabolic instability associated with chronic infectious activity.

Microbiological investigations additionally revealed expansion of pathogenic microbial associations among patients with lower vitamin D concentrations. Although *Escherichia coli* remained the leading etiological pathogen, mixed bacterial-fungal associations and multidrug-resistant strains were identified considerably more frequently in girls with vitamin D deficiency [11]. Detection of *Candida* species and polymicrobial colonization suggests impaired local urothelial and mucosal defense mechanisms, potentially associated with weakened antimicrobial peptide activity under hypovitaminosis D conditions [12]. Overall, the obtained findings support the concept that vitamin D deficiency may significantly influence both the clinical severity and microbiological complexity of urinary tract infections in adolescent girls.

4. Discussion

The results obtained in the present study demonstrate a clear association between reduced serum vitamin D levels and the severity of urinary tract infections in adolescent girls, while the most unfavorable clinical and laboratory manifestations were predominantly observed among patients with pronounced vitamin D deficiency. Girls with lower concentrations of 25-hydroxyvitamin D experienced more frequent recurrent infections, higher inflammatory activity, greater prevalence of anemia syndrome, and increased occurrence of multidrug-resistant microbial associations, which together suggest that vitamin D deficiency may substantially influence both immune defense mechanisms and the chronicity of infectious processes within the urinary tract [13].

One of the most clinically significant findings was the markedly elevated recurrence frequency among girls with vitamin D deficiency, because repeated infectious episodes indicate not only incomplete bacterial eradication but also possible impairment of local antimicrobial resistance mechanisms. Contemporary immunological research has shown that vitamin D participates in activation of innate immune responses through stimulation of antimicrobial peptides such as cathelicidin and β -defensins, both of which contribute to protection of the urothelial epithelium against bacterial colonization and persistence [14].

Consequently, insufficient vitamin D levels may weaken mucosal defense capacity and create favorable conditions for recurrent infection, chronic inflammation, and microbial persistence within the urinary tract. The elevated C-reactive protein concentrations identified in girls with hypovitaminosis D additionally support the existence of enhanced systemic inflammatory activity under conditions of vitamin D deficiency. Persistent inflammatory stimulation may contribute to endothelial dysfunction, tissue irritation, and prolonged recovery periods, while simultaneously influencing iron metabolism and promoting development of anemia syndrome frequently observed in recurrent infectious diseases. The high prevalence of reduced ferritin and hemoglobin values among girls with vitamin D deficiency in the present study may therefore reflect the combined impact of chronic inflammation, recurrent infection, and metabolic imbalance rather than isolated hematological disturbance alone [15].

Particular attention should also be directed toward the microbiological findings because multidrug-resistant strains, mixed microbial associations, and fungal colonization were significantly more common in patients with low vitamin D concentrations. Such alterations may indicate disruption of normal uro-genital microbiota together with decreased epithelial immune stability. Previous pediatric investigations have similarly reported that vitamin D deficiency may alter local immune signaling pathways and impair regulation of inflammatory cytokines, thereby facilitating persistence of opportunistic microorganisms and increasing susceptibility to resistant infectious forms [16].

Another important aspect of the present results concerns the observed disturbances of calcium metabolism in girls with severe vitamin D deficiency. Since calcium participates in multiple cellular signaling and epithelial barrier processes, hypocalcemia may additionally contribute to impaired mucosal integrity and chronic inflammatory susceptibility. Taken together, these findings support the growing concept that vitamin D deficiency should not be considered merely a secondary metabolic abnormality in urinary tract infections, but rather an important pathogenic factor capable of influencing disease severity, recurrence frequency, inflammatory response, and microbiological behavior in adolescent patients.

5. Conclusion

The present study demonstrated that reduced serum vitamin D levels in adolescent girls with urinary tract infections are closely associated with a more severe, recurrent, and clinically complicated course of the disease, while the most pronounced pathological manifestations were identified in patients with confirmed vitamin D deficiency. Girls with hypovitaminosis D exhibited higher inflammatory activity, more frequent dysuric and pain syndromes, increased recurrence rates, disturbances of calcium metabolism, and significantly greater prevalence of anemia syndrome compared with patients who maintained normal vitamin D concentrations. These findings indicate that vitamin D deficiency may substantially influence not only immune resistance but also broader metabolic and inflammatory mechanisms contributing to persistence and progression of urinary tract infections during adolescence. An important outcome of this investigation was the identification of a relationship between low vitamin D status and unfavorable microbiological characteristics, including increased detection of multidrug-resistant microorganisms, bacterial-fungal associations, and opportunistic microbial colonization. Such findings support the concept that impaired vitamin D-mediated immune regulation may weaken local urothelial antimicrobial defense and facilitate chronic infectious activity. In addition, elevated inflammatory markers observed in girls with hypovitaminosis D suggest that vitamin D deficiency may contribute to prolonged systemic inflammatory response and incomplete resolution of infectious processes. The obtained results underline the clinical significance of assessing serum 25-hydroxyvitamin D levels in adolescent girls presenting with recurrent or complicated urinary tract infections. Evaluation of vitamin D status may provide additional prognostic information regarding disease severity, recurrence tendency, and inflammatory activity, thereby supporting more individualized therapeutic and preventive approaches. Overall, correction of vitamin D deficiency together with appropriate antimicrobial management and dynamic clinical monitoring may improve treatment effectiveness and reduce the risk of recurrent urinary tract infections in adolescent patients.

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