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Association of Serum Vitamin D Level with Symptomatic Urinary Tract Infection in Pregnant Women

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Abstract **Original Research Article**

Background: Urinary tract infections (UTIs) are the most common bacterial infections during pregnancy. Pregnant women in Bangladesh often suffer from UTIs due to a lack of knowledge regarding proper hygiene practices. Adequate vitamin D levels have the potential to enhance the innate immune response, thereby can reduce susceptibility to bacterial infections. Therefore, vitamin D deficiency in pregnant women could increase the risk of urinary tract infections. ***Aim:*** To determine the association between maternal serum vitamin D levels and urinary tract infection in pregnancy. ***Method:*** This was a case-control study among purposively selected pregnant women attending the inpatient and outpatient department of Obstetrics and Gynaecology, ICMH, Matuail, Dhaka. A total 80 pregnant women between 18-40 years of age were included in this study at their 6-28 weeks of gestation. Among them 40 women who had urinary tract infection, confirmed by presence of ≥105/HPF pus cell in urine routine microscopic examination and a positive urine culture report, were considered as the cases and the rest of the 40 age and gestational age-matched healthy pregnant women without UTI were enrolled as the controls. Aseptically, 5 mL of venous blood was drawn to measure maternal serum vitamin D levels. Statistical analysis was done using the latest version of analytic software SPSS, where required. ***Results:*** Among 40 case respondents, Escherichia coli was found to be the most prevalent (60.0%) cause of UTI, with an average maternal serum vitamin D level of 20.5±11.94 ng/ml among those cases. The overall mean (±SD) vitamin D level was much lower among the cases than the controls, 21.1±11.25 ng/mL and 27.9±9.58 ng/ml, respectively. This difference was found statistically significant p=0.004). Considering vitamin D level of 30 ng/mL as the cut-off value, odd's ratio calculation showed the mother with serum vitamin D level <30 ng/mL had 3.2 times more risk to develop UTI compared to those with vitamin D level ≥30 ng/mL (p=0.013; OR=3.157; CI95%=1.255-7.938). ***Conclusion:*** In conclusion, a low serum vitamin D level was commonly observed in pregnant women with urinary tract infections. Therefore, maternal serum vitamin D deficiency was found associated with urinary tract infections in pregnancy.

Keywords: Serum Vitamin D, Urinary Tract Infection, Pregnant women.

INTRODUCTION

Urinary tract infections (UTIs) are common during pregnancy due to physiological changes in the urinary tract, which increase susceptibility to bacterial invasion. These infections, marked by bacteriuria (bacteria in urine), pyuria (pus in urine), or hematuria (blood in urine), can be asymptomatic or symptomatic. Untreated UTIs can lead to serious maternal and fetal complications such as preterm labor, low birth weight, and systemic maternal infection [1]. In pregnant women, significant bacteriuria is defined as 10^5 CFU/mL or higher in a midstream urine sample, while symptomatic UTI is indicated by 10^2 CFU/mL along with symptoms and pyuria [2].

UTIs are the second most common ailment in pregnancy after anemia, significantly impacting maternal and fetal health [3]. According to the World Health Organization, one in five women will experience a UTI, and pregnant women are four times more likely to develop UTIs compared to non-pregnant women [4]. Prevalence rates among pregnant women are approximately 15.37% in Ethiopia, 3% to 24% in India, and 8.9% in Bangladesh [5-7].

Escherichia coli is the most common uropathogen in UTIs, responsible for 82.5% of pyelonephritis cases in pregnant patients [8]. Other bacteria include Klebsiella pneumoniae, Staphylococcus saprophyticus, Streptococcus, Proteus mirabilis, and

Enterococcus faecalis [9]. UTIs in pregnancy are classified into symptomatic and asymptomatic, with asymptomatic bacteriuria being more common and potentially progressing to symptomatic bacteriuria or acute pyelonephritis [3].

Physiological changes during pregnancy, such as urethral dilation starting at week 6 and peaking around weeks 22 to 24, increased bladder volume, and decreased bladder and urethral tone, increase susceptibility to UTIs [10]. The shorter urethra in women also facilitates bacterial invasion from the perianal area, vagina, and rectum [17].

Vitamin D, a prohormone crucial for immune function, is obtained from dietary sources and synthesized in the skin through UVB exposure [12]. Activated vitamin D (1,25-(OH)2D) plays a role in calcium-phosphorus homeostasis and immune regulation [13]. Vitamin D deficiency during pregnancy is linked to adverse fetal outcomes and maternal complications like preeclampsia and gestational diabetes [14]. It enhances the immune system by inducing antimicrobial peptides and modulating cytokine secretion [15]. Deficiency can impair bladder defenses against infections [16].

Despite ample sunlight, Bangladesh has high vitamin D deficiency rates due to limited sun exposure, lack of food fortification, and inconsistent prenatal vitamin intake [17]. This study aims to investigate the association between maternal serum vitamin D levels and symptomatic UTIs in pregnant women at a tertiary hospital in Dhaka, potentially guiding obstetricians in managing and preventing UTIs through vitamin D supplementation or dietary adjustments.

METHODS

This case-control study was conducted over 12 months, from July 2022 to June 2023, at the Department of Obstetrics and Gynecology, Institute of Child and Mother Health (ICMH), Matuail, Dhaka. The study population comprised pregnant women aged 18 to 40 years in their first or second trimester, attending the outpatient and inpatient services of the department. Participants were divided into two groups: cases (pregnant women between 6 to 28 weeks of gestational age with symptomatic urinary tract infection) and controls (healthy pregnant women with the same gestational age range without urinary tract infection). Purposive sampling was used, and the sample size was calculated using a formula for comparing two means, resulting in a requirement of 47 participants per group. However, due to constraints, 80 patients were enrolled, with 40 in each group. Inclusion criteria for cases included symptomatic UTI confirmed by ≥5 pus cells/HPF in urine R/M/E and a positive urine culture with ≥10^5 CFU/mL of a uropathogen, while controls were normal pregnant women without UTI, confirmed by <5 pus cells/HPF and a negative urine culture. Exclusion criteria included asymptomatic bacteriuria, anemia, gestational or overt diabetes mellitus, urinary tract anomalies, kidney stones, urinary incontinence, neurogenic bladder, acute or chronic kidney disease, history of recurrent UTI, multiple pregnancies, recent antibiotic treatment, and vitamin D or multivitamin supplementation in the last three months. The independent variables included age, occupation, education, household income, BMI, gravida, gestational age, and serum vitamin D level, while the dependent variable was urinary tract infection. Vitamin D levels, measured as serum calciferol, were classified according to Holick *et al.*, (2011): deficient (≤20 ng/ml), insufficient (20-29 ng/ml), and adequate/normal (≥30 ng/ml).

Statistical Analysis: Statistical analyses were performed using SPSS software version 27.0 (SPSS Inc, Chicago, IL, USA). Comparisons between groups were made using the Chi-square test or Fisher's Exact test for qualitative variables and the Unpaired Student's t-test for quantitative variables, as appropriate. Serum vitamin D levels were categorized into normal (≥30 ng/mL) and low (<30 ng/mL) based on established cut-off values. The association between maternal serum vitamin D levels and urinary tract infection was assessed by calculating odds ratios (OR) with 95% confidence intervals (CI). A p-value ≤0.05 was considered statistically significant.

Ethical Aspects: Ethical clearance for the study was obtained from the Institutional Review Board and the concerned authority at the Institute of Child and Mother Health (ICMH), Matuail, Dhaka.

RESULTS

Table-1: Distribution of the respondents according to socio-demographic characteristics between two groups (n=80)

Socio-demographic characteristics	Case (n=40)	Control (n=40)	p-value
Age group (years)			
15 – 20 years	3 (7.9)	9 (22.5)	0.061
21 – 29 years	21 (55.3)	23 (57.5)	
≥30 years	16 (40.0)	8 (20.0)	
Mean ± SD	27.5 ± 5.26	25.4 ± 4.86	
Education			

Socio-demographic characteristics	Case (n=40)	Control (n=40)	p-value
Up to primary	14 (35.0)	10 (25.0)	0.311
SSC/equivalent	19 (47.5)	17 (42.5)	
HSC/equivalent	5 (12.5)	6 (15.0)	
Graduate/postgraduate	2 (5.0)	7 (17.5)	
Occupation			
Housewife	27 (67.5)	23 (57.4)	0.168
Student	1 (2.5)	6 (15.0)	
Service holder	10 (25.0)	7 (17.5)	
Business	2 (5.0)	4 (10.0)	
Monthly household income			
Lower class (≤7,378 Tk.)	6 (15.0)	3 (7.5)	0.729
Lower middle class (7,379-28,810 Tk.)	30 (75.0)	32 (80.0)	
Upper middle class (28,811-89280 Tk)	4 (10.0)	5 (12.5)	
BMI (kg/m^2)			
Underweight (< 18.5)	3 (7.5)	1 (2.5)	0.060
Normal (18.5 – 24.9)	28 (70.0)	35 (87.5)	
Overweight (25.0 - 29.9)	8 (20.0)	4 (10.0)	
Obese (≥30.0)	1 (2.5)	0 (0.0)	
Mean ± SD	23.0 ± 2.78	21.9 ±2.37	

Case = pregnant women diagnosed with urinary tract infection
Control = healthy pregnant women

Table 1 shows there was statistically no significant differences in between the case and Control respondents regarding their socio-demographic characteristics (p > 0.05). There was no significant difference in mean body mass index of both case and Control respondents (p=0.060), and majority of the patients belonged to normal weight group (Case 70.0% vs. Control 87.5%), p-value>0.05.

Table-2: Distribution of the study subjects according to their obstetrical characteristics between groups (n=80)

Obstetrical characteristics	Case (n=40)	Control (n=40)	p-value
Gravida			
Primigravida	12 (30.0)	15(37.5)	0.478
Multigravida	28 (70.0)	25 (62.5)	
Gestational age (in weeks)			
6 – 12	21 (52.5)	16 (40.0)	0.351
13 – 28	19 (47.5)	24 (60.0)	
Mean ± SD	12.3 ± 5.27	13.4 ± 4.45	

Case = pregnant women diagnosed with urinary tract infection
Control = healthy pregnant women

There was no statistically significant difference observed in the study subjects in respect of their obstetrical characteristics (p>0.05). Majority of the participants in both the groups were multigravida (Case: 70.0% and Control: 62.5%). The mean (±SD) gestational age of the Case women were 12.3±5.27 weeks compared to Control respondents 13.4±4.45 weeks (p>0.05).

Table-3: Distribution of the symptoms in pregnant women with urinary tract infection (n=40)

Symptoms	Frequency (n)	Percentage (%)
Urgency/frequency	13	32.5
Dysuria	11	27.5
Loin pain	5	12.5
Burning micturition	20	50.0

Table-3 showing burning sensation during micturition was present in 50.0% of the respondents with UTI, urgency/frequency was complained by 32.5%, dysuria 27.5% and loin pain in 12.5%.

Table-4: Distribution of mean (±SD) serum vitamin D levels between groups (n=80)

Parameters	Case (n=40)	Control (n=40)	p-value
Serum vitamin D level (ng/ml)	21.1 ± 11.25	27.9 ± 9.58	0.004
Range (min-max)	7.8 – 40.6	8.0 – 54.2	

Table-4 demonstrated the overall distribution of maternal vitamin D level by group, where the mean (±SD) vitamin D levels among the Case were 21.1±11.25 ng/ml (range: 7.8 – 40.6 ng/ml) and in Control were 27.9±9.58 ng/ml (range: 8.0 – 54.2), which was statistically significant (p=0.004).

Table-5: Categorization of the respondents according to vitamin D level between groups (n=80)

Serum vitamin D level (ng/ml)	Case (n=40)	Control (n=40)	p-value
Deficient (≤ 20)	18 (45.0)	9 (22.5)	0.035
Insufficient (21-29)	10 (25.0)	8 (20.0)	
Sufficient (≥ 30)	12 (30.0)	23 (57.5)	

Table-5 shows the categorization of the levels of vitamin D among Case and Control respondents. Nearly three-fifths (57.5%) of the Control group of participants serum vitamin D level were sufficient/normal compared to 30.0% of the Case patients. Deficient levels of vitamin D were more common among the Case respondents 45.0%) than the Control (22.5%). Also, insufficient level of vitamin D was more obvious among the Case study subjects (25.0%) than the Control (20.0%). These differences in distribution of serum vitamin D levels were statistically significant (p=0.035).

Table-6: Odds ratios (OR) and 95% confidence intervals (CI) for urinary tract infection according to serum vitamin D level in pregnancy (Case = 40, Control = 40)

Serum vitamin D level (ng/ml)	Case (n=40)	Control (n=40)	p-value	OR (95% CI)
Low (deficient/insufficient, <30)	28 (70.0)	17 (42.5)	0.013	3.157 (1.255-7.938)
Normal (sufficient, ≥30)	12 (30.0)	23 (57.5)		

There was significant difference in regards of deficient vitamin D level in between Case and Control groups (p=0.013) and the respondents with insufficient/deficient level <30 ng/ml had 3.2 times more chance to develop urinary tract infections compared to that of the respondent with normal/sufficient vitamin D level (≥30 ng/ml) (OR=3.157; 95% CI = 1.255-7.938).

DISCUSSION

This case-control study was conducted to compare the serum vitamin D level in women with urinary tract infection and normal pregnant women without urinary tract infection, as a biochemical marker for risk estimation and evaluate any association between serum vitamin D level and urinary tract infection.

Eighty women between 18-40 years of age in their 6 to 28 weeks of gestation attending the inpatient and outpatient department of Obstetrics and Gynaecology, Institute of Child and Mother Health (ICMH) were included in this study. Among them, 40 diagnosed women with urinary tract infections were considered as the cases, and the rest of the 40 normal pregnant women without urinary tract infections were selected as the controls.

On evaluating the respondents' socio-demographic characteristics in the present study, ages were matched (±3years) according to selection criteria where the mean (±SD) distribution among the case and control groups was found 27.5±5.26 and 25.4±4.86 years respectively, p=0.061. 47.5% of the cases and 42.5% of the control group participants were educated up to the secondary or equivalent level. Most of the participants were housewives (case: 67.5% and control: 57.4%), followed by service holder (case: 25.0% and control: 17.5%). Most of the study participants belonged to lower middle class social status with an average monthly family income of 7,379- 28,810 Tk. only (case: 75.0%, vs. control: 80.0%). None of these socio-demographic characteristics in the study was found statistically significant (p>0.05). These findings were similar to Haghdoost *et al.*, (2019), where the mean maternal age of the cases was 26.4±4.49 and among controls was 27.5±4.69 years (p=0.106) and majority of the respondents passed their high school (cases 32.4% vs. controls 39%; p-value 0.355) (Haghdoost *et al.*, 2019) [18].

On evaluating the body mass index of the respondents, most of the women (79.7%) was found in normal weight group, and the average BMI was 23.0±2.78 kg/m2 among the cases which was slightly higher compared to control group women (21.9±2.37 kg/m2), but this difference in distribution was statistically not significant (p=0.060). Similar findings were observed by Nassaji *et al.*, (2015) who showed that the mean BMI of the UTI patients were 25.2±4.0 kg/m2 and for control was 25.1 ± 3.6 kg/m2. There was no significant correlation between BMI and UTI (p = 0.757). They also observed that the mean BMI of the patients with upper UTI was 25.6±4.1 kg/m2 and for lower UTI was 24.9 ± 4.0 kg/m2 (p = 0.573) (Nassaji *et al.*, 2015) [19].

In this study, among the cases, E. coli was found the most prevalent (60.0%) pathogen causing UTI in pregnancy. Among the other isolated organism in urine culture Klebsiella pneumoniae constituted 12.5%,

Enterobacteriaceae sp. 12.5%, Pseudomonas aeruginosa 10.0% and Staphylococcus saprophyticus (5.0%). The most prevalent symptom of the cases was burning sensation during micturition (50.0%) followed by urinary frequency (32.5%). Over a quarter of the respondents (27.5%) presented with dysuria, while 12.5% complained of loin pain. El-Kashif (2019) in their study showed that E. coli (37%) followed by Klebsiella pneumonia (27%) had the highest percentage of the isolated pathogens [20]. The clinical symptoms such as frequency of micturition, dysuria, lower abdominal pain, urine color change, painful burning sensation, incomplete bladder evacuation were the most common among infected women (El-Kashif, 2019) [20]. These findings were similar to the present study.

Serum vitamin D levels were significantly lower among the cases in comparison to the controls (21.1±11.25 vs. 27.9±9.58 ng/ml; p=0.004). Vitamin D level was found deficient in 45.0% of the case group, whereas in control group women in nearly 57.5% had sufficient (≥30 ng/ml) level. This difference in the distribution was found statistically significant (p=0.035). On the Odd's ratio calculation, it was observed that respondents with vitamin D deficiency (<30 ng/ml) had 3.2 times more chance to develop urinary tract infections compared to that of the respondent with sufficient vitamin D level (≥30 ng/ml) (OR=3.157; 95% CI = 1.255-7.938). There were no significant differences in distribution of serum vitamin D levels among the cases in regard to the isolated organism type, gram positive vs. gram negative; p=0.847 and also aerobic vs. anaerobic organisms (p=0.289).

Sadeghzadeh *et al.,* (2021) in their study documented that in females, serum levels of vitamin D in cases were significantly lower than for controls [OR (95%CI) = (5.417 (1.685–17.417), P-value = 0.005)] (Sadeghzadeh *et al.,* 2021) [21]. Ali *et al.,* (2020) also in their study conferred that woman of reproductive age with low vitamin D levels were more at risk of contracting UTI than the healthy ones [22]. They showed a significant association of vitamin D deficiency and urinary tract infections especially in moderate and severe infections (Ali *et al.,* 2020) [22].

On evaluating the post-menopausal women, Nseir *et al.,* (2013) observed that the mean serum levels of 25(OH) vitamin D among women with UTIs were significantly lower than those of controls (9.8 ng/ml±4 vs. 23 ng/ml±6; p < 0.001) (Nseir *et al.,* 2013) [23].

Haghdoost *et al.,* (2019) on evaluating vitamin D status diagnosed deficiency in 85.7% of case group and 52.2% of control group. They also found that the serum vitamin D levels were significantly lower in pregnant women in the case group compared to the control group (12.7±5.9 ng/ml vs. 26.05±10.37; p <0.001). Pregnant women in case group with acute pyelonephritis had significantly lower serum vitamin D levels than those with cystitis (p < 0.05) (Haghdoost *et al.,* 2019) [18].

Therefore, in the current study, all the findings showed the association of low vitamin D levels with urinary tract infection in pregnant women. So, screening for serum vitamin D level in preconceptions and early pregnancy might be considered as a part of the routine antenatal check-up.

CONCLUSIONS

The findings of this study suggest that low maternal serum vitamin D level is significantly associated with an elevated risk for urinary tract infection. Therefore, this study concludes that low levels of serum vitamin D can be considered an important risk factor responsible for the development of urinary tract infection.

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