Available online at https://www.sjomr.org

SCIENTIFIC JOURNAL
OF MEDICAL RESEARCH

Vol. 6, Issue 23, pp 1-6 , 2022

ISSN: 2520-5234

RESEARCH ARTICLE

Effect of Bacterial Infection on Few Hormones in Urinary Tract Infections Patients

Alaa A. H. Al- Daamy*, Aia H. Qahtan, Noor Al-Huda K. Mohammed, Teeba M. Khuthair, Thraa A. Mohammed

Department of Clinical Laboratories, Applied Medical Sciences College, University of Kerbala, Karbala, Iraq.

ARTICLE INFORMATIONS

Article history:

Received: 04 July 2022

Revised: 02 August 2022

Accepted: 05 August 2022

Published: 24 September 2022

Keywords:

Cortisol, Estrogen, FSH, Progesterone, UTI, Vitamin D.

Corresponding author:

Alaa A. H. Al- Daamy

Email: alaa.aldaamy@uokerbala.edu.iq

Department of Clinical Laboratories, Applied Medical Sciences College, University of Kerbala, Karbala, Iraq.

ABSTRACT

Objective: The current study aims to isolate and diagnose the bacteria from urinary tract infection patients and study its relationship to few hormones such as Progesterone, Estrogen, Cortisol and FSH, in addition to Vitamin D.

Methods: Collection samples were carried out in Al-Housani hospital and Zain Al-Aabdin hospital during the period from December 2021 to March 2022. Forty-two patients had blood and urine samples taken, while 42 people who weren't hospitalized served as the control group. The urine sample was centrifuged and examined microscopically to determine the urinary tract infection (UTI). Then the blood sample was cultured to obtain the bacteria and diagnose it with a VITEK device, hormones levels of progesterone, estrogen, cortisol and follicle-stimulating hormone (FSH), in addition to vitamin D in the serum, were measured.

Results: UTI females were more than (76.19%) of males (23.18%). Twelve bacterial isolates were obtained from only female patients belonging to four bacteria genus, these bacteria: Enterococcus sp. (4 isolates), Staphylococcus saprophyticus (4 isolates), Klebsiella pneumonia (2 isolates), and E. coli (2 isolates).

The concentration of vitamin D decreased in male and female patients (12.178 and 16.766) ng/mL, respectively, compared to the healthy controls. The presence of bacteria in female UTI patients led to an increase in the levels of both progesterone and estrogen (17.608 ng/mL and 1651.743 pg/mL), respectively. Also, the concentration of FSH in female UTI patients increased from its concentration in the healthy ones, which was (20.560 and 8.723) mIU/mL, respectively. The concentration of cortisol was not affected in patients.

Conclusions: Females are more infected with UTIs than males, and all bacterial species were isolated from females, Enterococcus sp. (4 isolates), Staphylococcus saprophyticus are the most common. Bacterial infection is related to a concentration of vitamin D in male and female patients, and have a relationship with a concentration of estrogen, progesterone and FSH in females.

CITATION: Al- Daamy AAH, Qahtan AH, Mohammed NAK, Khuthair TM, Mohammed TA. "The Effect of Bacterial Infection on Few Hormones in Urinary Tract Infections Patients". Sci. J. Med. Res. 2022;6(23):1-6. DOI: 10.37623/sjomr.v06i23.01

INTRODUCTION

Urinary tract infections (UTIs) include infections of the lower and higher urinary tracts as well as microbial colonization of urine. One of the most typical bacterial illnesses in adults is a UTI. Due to the growing occurrence of bacterial resistance to a variety of antibiotics, they pose a serious threat to public health.[1] Bacteria are the most frequent cause of these infections. *Escherichia coli*, which is present in 80% of cases, is the most significant member of the Enterobacteriaceae family and is responsible for more than 70% of UTIs.[2] The family is widespread in the environment and among its animal hosts, and it is relatively simple to pick up and spread the genetic determinants that confer resistance to the majority of antibiotic classes. One of the Gram-negative bacteria with the most thorough studies is *E. coli*.

UTIs have a 12% incidence in the female population across all age groups, and their frequency rises with age and peaks in adolescence.[3] More than half of the females have experienced a UTI at least once in their lives, although only 11% of females reported having one within a year. The most likely reason is a mix of risk factors, which include age, an active sex life, physiological and anatomical changes, and the proximity of the urethra, vagina, and rectum in women.[4]

A urine sample acquired by peeing is not regarded as a primary sterile sample since the urinary system represents a sterile space with the exception of the distal urethra, which is colonized by the saprophyte microbiota of the surrounding region. As soon as a bladder becomes infected, bacteria can readily multiply and reach significant quantities in the urine, which stimulates their growth. The rise of germs from the urethra is the most prevalent mechanism that leads to UTI, especially bacteria of intestinal origin, according to a wealth of clinical and experimental evidence. Microorganisms can enter the urinary system through blood circulation or lymphatic expansion (*E. coli* and other Enterobacteriaceae).[5] A few bacteria, including *Staphylococcus aureus*, *Candida* spp., *Salmonella* spp., and *Mycobacterium* TB, which cause initial infection elsewhere in the body, are only known to induce haematogenous UTI. According to the idea of bacterial virulence in the urinary system, not all bacterial species can result in infection. Lower levels of bacterial virulence are required to promote infection in defensive mechanisms that are more vulnerable (obstruction or bladder catheterization). The etiology of UTI is complicated; it is impacted by a variety of biological, behavioral, and uropathogen-related aspects of the host. Bacteria are the most frequent cause of UTI, though rarely fungi and viruses may also be found. *Staphylococcus saprophyticus* is the next most prevalent isolate, found in 5–15% of urine samples from patients with simple UTIs (cystitis), while *Klebsiella*, *Enterobacter*, and *Proteus* are uncommon sources of infection outside of hospitals (5–10%).[6] *E. coli* strains are the most common isolate, found in 80% of urine samples from patients with simple UTIs. These species and *Candida* spp. are typically responsible for UTIs acquired in hospitals, with *E. coli* accounting for only 35–50% of cases.[7]

Aim of the Study

The current study aims to isolate and diagnose the bacteria that cause urinary tract infection and study its relationship to some hormones such as Progesterone, Estrogen, Cortisol and FSH in addition to Vitamin D.

MATERIALS AND METHODS

Samples Collection

Collection samples carried out in Al-Housani hospital and Zain Al-Aabdin Hospital from December 2021 to March 2022. 42 patients had blood and urine samples taken, as well as 42 control subjects who weren't hospitalized. They were between the ages of 18 and 54.

Urine Sample

To participate in the current experiment, patients with symptomatic UTIs and controls were provided 10 mL clean-catch mid-stream collected in sterile containers. Every urine sample was divided in half in the medical lab and the second half was directly inoculated on standard culture media (MacConkey and Blood agar) and incubated aerobically at 37°C for 24–48 hours using conventional methods. The first half was centrifuged and stored at -80°C. To prepare urine debris for direct microscopic examination for pus cells, RBCs, epithelial cell count, cast, crystals, and parasite infection, if present, the remaining urine was centrifuged (1500 rpm for 5 minutes). RBC counts, pus cells, and epithelial cell counts may occasionally be present in normal urine sediment.

Bacterial Diagnosis

The bacterial species was determined using a fully automated VITEK-2 compact system. Gram-positive and Gram-negative cards were used for bacterial identification, and the system was used per the manufacturer's instructions. If the test organisms were isolated as pure isolates from MacConkey or blood agar, 3 mL of 0.45% sterile saline was added to the polystyrene tube, and the organism was then homogeneously suspended in the saline. Gram-negative and Gram-positive bacteria had bacterial suspension densities between 0.5 and 0.63.

Microorganism suspensions are inoculated onto the identity cards. The transfer tube is inserted into the matching suspension tube while a test tube with the microorganism suspension is put in the next slot.

Blood Samples

Each participant's three mL of blood were drawn into a gel tube, and the sera were separated by centrifuging the blood for five minutes at 1000 rpm. The serum was then tested for progesterone, estrogen, vitamin D3, cortisol, and FSH by MEGLUMI and VITEK immuno diagnostic assay system (VIDAS), respectively.

Table 1: Comparison of parameters concentration between healthy and UTI male patients.

Parameter	*Healthy persons (N=10)*	*UTI patients (N=10)*	*p-value*
Progesterone (ng/mL)	0.371 ± 0.021	0.164 ± 0.057	0.0001**
Estrogen (pg/mL)	30.785 ± 4.036	29.554 ± 2.740	0.4353
Vitamin D3 (ng/mL)	23.723 ± 5.813	12.178 ± 6.101	0.0004**
Cortisol (ng/mL)	101.526 ± 12.339	87.6 ± 27.923	0.1663
FSH (mIU/mL)	4.602 ± 1.142	3.852 ± 2.716	0.4313

*means significance differences (p <0.05) ** means high significances differences (p <0.001)

Table 2: Progesterone concentration (ng/mL)of UTI female patients with/without bacterial infection

Patients of UTI		*Control*	*p-value*
Infection	*Mean ± SD*	*Mean ± SD*	
Without bacterial infection	11.535 ± 1.548	10.307 ± 2.405	0.0475*
With bacterial infection	17.608 ± 1.588		0.0001**
Total	13.812 ± 1.566	10.307 ± 2.405	0.0001**
p-value	0.0001**		

*means significance differences (p <0.05) ** means high significances differences (p <0.001)

Statistical Analysis

The statistical analysis included determination of the significant differences between the factors studied in this study by use of the chi-square test and T test (One tail) at α = 0.05 (the probability level) by using SPSS program version 20.

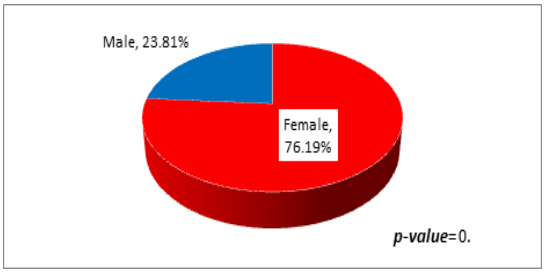

Figure 1: Patients with UTIs by gender distribution.

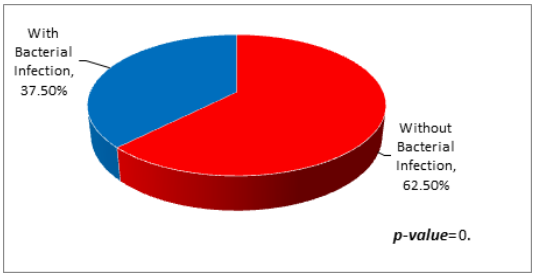

Figure 2: Distribution of UTI female patients according to bacterial infections.

RESULTS

Among the 42 UTI patients, 32 of them were females (76.19%) and 10 males (23.18%), and the results show in Figure 1 that the most infections were in females with a significant difference (p = 0.00069) from males in the current study.

The results of the urine culture for 32 females with urinary tract infection were a positive culture results in 12 samples (37.5%) while the results of culture were negative in 20 samples (62.5%) and no significant differences (p = 0.1573), Figure 2.

Four types of bacteria were diagnosis of 12 samples positive for culture, these species are *Enterococcus* sp. were 4 isolates (33.33%), *Staphylococcus saprophyticus* were 4 isolates (33.33%), *Klebsiella pneumonia* were 2 isolates (16.67%),

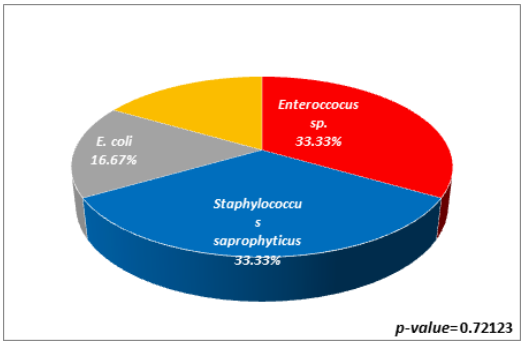

Figure 3: Bacterial types isolated from UTI Female patients.

Table 3: Estrogen concentration (pg/mL) of UTI female patients with/without bacterial infection.

Patients of UTI		*Control*	*p-value*
Infection	*Mean ± SD*	*Mean ± SD*	
Without bacterial infection	726.471 ± 133.33	293.77 ± 57.28	0.0001**
With bacterial infection	1651.743 ± 232.53		0.0001**
Total	1073.19±179.31	293.77 ± 57.28	0.0001**
p-value	0.0001**		

*means significance differences (p <0.05) ** means high significances differences (p <0.001)

Table 4: Vitamin D3 concentration(ng/mL) of UTI female patients with/without bacterial infection

Patients of UTI		*Control*	*p-value*
Infection	*Mean ± SD*	*Mean ± SD*	
Without bacterial infection	19.848 ± 12.081	28.117 ± 4.921	0.0011*
With bacterial infection	11.631 ± 7.886		0.0001**
Total	16.766 ± 11.307	28.117 ± 4.921	0.0001**
p-value	0.0446*		

* means significance differences ($p < 0.05$) ** means high significances differences ($p < 0.001$)

Table 5: Cortisol concentration(µg/dL) of UTI female patients with/without bacterial infection.

Patients of UTI		*Control*	*p-value*
Infection	*Mean ± SD*	*Mean ± SD*	
Without bacterial infection	119.632 ± 106.848	115.781 ± 3.022	0.8384
With bacterial infection	109.856 ± 55.419		0.5421
Total	115.966 ± 90.05	115.781 ± 3.022	0.9908
p-value	0.7716		

* means significance differences ($p < 0.05$) ** means high significances differences ($p < 0.001$)

Table 6 : FSH concentration (mIU/mL) of UTI female patients with/without bacterial infection

Patients of UTI		*Control*	*p-value*
Infection	*Mean ± SD*	*Mean ± SD*	
Without bacterial infection	25.424 ± 4.082	8.723 ± 2.071	0.0001**
With bacterial infection	12.481 ± 2.380		0.0001**
Total	20.560 ± 3.553	8.723 ± 2.071	0.0001**
p-value	0.0001**		

* means significance differences ($p < 0.05$) ** means high significances differences ($p < 0.001$)

and *E. coli* were 2 isolates (16.67%), according to the results of statistical analysis in Figure 3, it there are no significant differences ($p = 0.72123$) between the bacterial species isolated in this study.

The results in Table 1 show that the concentration of progesterone in UTI male patients decreased significantly ($p = 0.0001$) from its concentration in healthy males but within the normal value of the hormone. While the concentration of vitamin D was significantly lower ($p=0.0004$) than its concentration in healthy males, its concentration reached (12.178 and 23.723) ng/mL, respectively. As for the hormones estrogen, cortisol and FSH, there was no significant differences ($p > 0.05$) between males with UTI and healthy males.

The results of the statistical analysis in Table 2 show that there is a significant increase ($p=0.0001$) in the concentration of progesterone hormone of women with urinary tract infection compared to healthy women, as the concentration of the hormone reached (13.812 and 10.307) ng/mL, respectively. On the other hand, there is a significant increase ($p=0.0001$) in the progesterone concentration of women who have a bacterial infection compared to women patients who do not have a bacterial infection, as the progesterone concentration reached (17.608 and 11.535) ng/mL, respectively.

The results of the statistical analysis of Table 3 indicate that there is a very high significant increase ($p=0.0001$) in the estrogen concentration for women with urinary tract infection compared to healthy women, as the estrogen concentration reached (1073.19 and 293.77) pg/mL, respectively. There was also a significant increase ($p=0.0001$) in the estrogen concentration for UTI female patients with bacterial infection compared to female patients without bacterial infection. Its concentration reached (1651,753 and 726,471) pg/mL, respectively.

Through the results of the current study, the concentration of vitamin D3 decreased significantly ($p=0.0001$) for females with UTI compared to healthy females, as its concentration reached (16.766 and 28.117) ng/mL, respectively. Also, its concentration decreased significantly ($p= 0.0446$) in patients with bacterial infection compared to the absence of bacteria, as its concentration was (11.631 and 19.848) ng/mL, respectively, as shown in Table 4.

The results of the statistical analysis of Table 5 showed that the concentration of cortisol did not differ significantly when comparing patients with healthy subjects, not even when comparing patients with the presence and absence of bacteria, as the *p*-value s were (0.9908 and 0.7716), respectively.

The concentration of FSH hormone was significantly increased ($p=0.0001$) for UTI female patients compared to healthy females, as its concentrations were (20.560 and 8.723) mIU/mL, respectively. Also, the presence of bacteria in female patients with UTI significantly reduced ($p=0.0001$) the concentration of FSH hormone compared to its concentration of female patients with UTI when no bacteria were present, as its concentration reached (12.481 and 25.424) mIU/mL, respectively, as in Table 6.

DISCUSSION

In general, women are more likely than males to have urinary tract infections (UTIs).[8-10] Men and women experience UTIs differently in terms of incidence, presentation, and progression. Numerous reasons, including (pelvic) anatomical variations, voiding difficulties, and vaginal mucosa colonization, are to blame for this.[11-15] Additionally, men and women have different uropathogens that cause disease.[16]

UTIs are more prevalent in older men and women than in younger people, but women are more likely than males to get them.[17]

The UF-1000i bacterial count was greater in women compared to males at the same urine culture density. In comparison to men, women had a definite higher presence of aerobe gram-positive mix flora. This raises the possibility that at least some of the women's vaginal flora may have been contaminated, which would explain why women had a higher bacterial count.

Gram-negative bacteria are the main causative agents of UTIs; however, Gram-positive bacteria may also contribute to UT infections.[18,19] *E. coli, S. saprophyticus, K. pneumoniae, Proteus mirabilis, Enterococcus species, Pseudomonas aeruginosa*, and group B *streptococcus* are the main uropathogens.[20-24]

Different organisms respond differently to sex hormones, and studies have shown that progesterone, the most common hormone in adult females during the follicular stage, causes an increase in bladder oscillation in contrast to the luteal stage, which is distinguished by a decrease in bladder expansion.[25]

Numerous research in experimental animals and people have looked at how estrogen affects women's risk of UTI. These studies frequently yield results that appear to be in conflict: some claim that estrogens increase risk, while others claim that estrogens may act as a prophylactic. The physiological effects of estrogen on various anatomical regions of the urinary system vary depending on the specific effect and the outcome measured, contributing to some confusion. For instance, the periurethral and vaginal microflora, which is typically dominated by lactobacilli that produce hydrogen peroxide and few *E. coli*, changes rapidly in the absence of estrogen to a flora with few or no lactobacilli but many *E. coli*.[26]

Reduced estrogen levels alter the vaginal flora and promote bacterial colonization. While, elevated progesterone levels counteract the effects of estrogen and relax the ureters' muscle tone. This lessens the flow of urine that causes the infection during urination. Ureteral dilatation begins in the first trimester of pregnancy and ultimately progresses to hydronephrosis. Hormonal changes, especially caused by progesterone, are to blame. Mechanical compression of the urinary tract develops as the uterus grows, increasing the likelihood of infections.[27]

Micronutrients, natural products, and vitamins are increasingly used to treat a variety of pediatric illnesses.[28,29] There have been reports of the use of vitamin D as a supplement in the prevention and treatment of UTI and its consequences.[30] Furthermore, the relationship between vitamin D and a number of viral disorders has been researched extensively.[31] However, there is growing proof that a vitamin D deficiency plays a significant role in UTI susceptibility and that supplementing with vitamin D can help avoid infection. It was suggested that vitamin D intake could shield against UTIs.[30] Additionally, multiple studies showed that having a low 25(OH)D may increase your chance of getting a urinary tract infection.[32-36] No study has systematically assessed the relationship between blood vitamin D level and risk of UTI, despite the expanding body of evidence supporting the prevention and treatment of UTI in children with vitamin D supplementation. Low serum vitamin D levels have been linked to an increased risk of urinary tract infections, according to a systematic review and meta-analysis.[37]

As demonstrated in animal models, the etiology of vaginal dysbiosis and the consequent emergence of infection and inflammation depend on cortisol's ability to thwart this process. This phenomenon may be especially significant during pregnancy when a healthy vaginal microbiota dominated by Lactobacillus is required and more corticotropin-releasing hormone (CRH) is produced locally in the decidua, fetal membranes, and placenta. The potential involvement of cortisol in the maintenance of vaginal health is investigated in order to emphasize the connection between the stress hormone cortisol and the vaginal microbiomial architecture and function.[38]

There are no previous studies on the effect of UTI and FSH hormone.

CONCLUSIONS

We conclude that most UTI infections were in females compared with males in the current study. The common bacteria were diagnosed through 12 female samples positive for culture were *Enterococcus* sp. and *S. saprophyticus*. Vitamin D was decreased in UTI male patients. In females, there was an increase in progesterone concentration, especially in the presence of bacterial infections and in the case of estrogen and FSH. On the contrary, vitamin D was decreased in patients, especially with the presence of bacterial infection.

RECOMMENDATIONS

First: Conduct an extensive study to include a greater sample than the current study sample.

Second: Study of other parameters related to kidney function in patients with urinary tract infections.

Third: Study of Vasopressin and Adrenocorticotropin Hormones in these patients because of its high importance and relationship to the disease.

REFERENCES

1. Grabe M, Bartoletti R, Bjerklund Johansen TE, Cai T, Çek M, Köves B, et al. European Association of Urology: Guidelines on Urological Infections [Online] 2015. [[cited 2015 Feb]]. Available from: http://

uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf .
2. Uzunović-Kamberović S. Medicinska mikrobiologija. I izd ed. Zenica: Štamparija Fojnica; 2009. pp. 367–75. [Google Scholar].
3. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Dis Mon. 2003;49(2):53–70. [PubMed] [Google Scholar].
4. Zdravstveno stanje stanovništva i zdravstvena zaštita u Federaciji Bosne i Hercegovine 2013. godina Sarajevo. 2014:51–3. [Google Scholar].
5. Tambic-Andrašević A. Etiologija urogenitalnih infekcija. Medicus: Urogenitalne infekcije - izabrana poglavlja. 2012;21(1):15–21. [Google Scholar].
6. Hooton TM. Uncomplicated Urinary Tract Infection. N Engl J Med. 2012;366(11):1028–37. [PubMed] [Google Scholar].
7. Mahmutovic Vranic S, Uzunovic A. Antimicrobial resistance of Escherichia coli strains isolated from urine at outpatient population: a single laboratory experience. Mater Sociomed. 2016;28(2):84–7. [PMC free article] [PubMed] [Google Scholar].
8. LE. Nicolle. Urinary tract infection. Crit Care Clin, 29 (3) (2013), pp. 699-715.
9. SS Takhar, GJ. Moran. Diagnosis and management of urinary tract infection in the emergency department and outpatient settings Infect Dis Clin North Am, 28 (1) (2014), pp. 33-48.
10. B. Foxman. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Dis Mon, 49 (2) (2003), pp. 53-70.
11. G Finer, D. Landau. Pathogenesis of urinary tract infections with normal female anatomy. The Lancet infectious diseases, 4 (10) (2004), pp. 631-635.
12. A Schaeffer, N Rajan, Q Cao, B Anderson, DL Pruden, J Sensibar, et al. Host pathogenesis in urinary tract infections. Int J Antimicrob Agents, 17 (4) (2001), pp. 245-251.
13. AJ Schaeffer, LE. Nicolle. Urinary tract infections in older men. N Engl J Med, 2016 (374) (2016), pp. 562-571.
14. TM. Hooton. Pathogenesis of urinary tract infections: an update. J Antimicrob Chemother, 46 (2000), pp. 1-7.
15. TL. Griebling. Urologic diseases in America project: trends in resource use for urinary tract infections in men. J Urol, 173 (4) (2005), pp. 1288-1294.
16. E Magliano, V Grazioli, L Deflorio, AI Leuci, R Mattina, P Romano, et al. Gender and age-dependent etiology of community-acquired urinary tract infections. The Scientific World Journal (2012).
17. Harrington RD, Hooton TM. Urinary tract infection risk factors and gender. J Gend Specif Med. 2000 Nov-Dec;3(8):27-34. PMID: 11253265.
18. Fauci AS. Harrison's Principles of Internal Medicine. Vol. 2. McGraw-Hill, Medical Publishing Division New York; 2008.
19. Cheesbrough M. District Laboratory Practice in Tropical Countries, Part 2. Cambridge University Press; 2006:464.
20. Vasudevan R. Urinary tract infection: an overview of the infection and the associated risk factors. J Microbiol Exp. 2014;1(2):00008.
21. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13(5):269–284. doi:10.1038/nrmicro3432.
22. Moura A, Nicolau A, Hooton T, Azeredo J. Antibiotherapy and pathogenesis of uncomplicated UTI: difficult relationships. J Appl Microbiol. 2009;106(6):1779–1791. doi:10.1111/j.1365-2672.2008.04115.x.
23. Jatileni NJV, Maposa I, Mavenyengwa RT. A Retrospective Study of the variability in etiological agents of urinary tract infections among patients in Windhoek-Namibia. Open J Med Microbiol. 2015;05(04):184. doi:10.4236/ojmm.2015.54023.
24. Odoki M, Bazira J, Agwu E. Health-point survey of bacteria urinary tract infections among suspected diabetic patients attending clinics in Bushenyi district of Uganda. Spec Bacterial Pathog J. 2015;1(1):1–5.
25. AL Lateef BA, Al Hawani IAA, Jebar MS, Aljeburi NR. Effects of Progesterone Hormone on the Urinary Tract Infection in Pregnant Women. Medico-legal Update, October-December 2020; 20(4): 813-821.
26. Walter E. Stamm, Estrogens and Urinary-Tract Infection, The Journal of Infectious Diseases, Volume 195, Issue 5, 1 March 2007, Pages 623–624, https://doi.org/10.1086/511526.
27. Konapala LA, Vesalapu V, Kolakota RK et.al. pregnancy and hormonaleffects on urinary tract infections in women: A scoping review. International Journal of Researchand Review. 2018; 5(10):407-420.
28. Sharifi H, Minaie MB, Qasemzadeh MJ, Ataei N, Gharehbeglou M, Heydari M. Topical use of Matricaria recutita L (Chamomile) oil in the treatment of monosymptomatic enuresis in children: a double-blind randomized controlled trial. J Evid Based Complementary Altern Med. (2017) 22:12–7. doi: 10.1177/2156587215608989.
29. Mosavat SH, Heydari M, Hashempur MH, Dehghani SM. Use of complementary and alternative medicine among paediatric patients with hepatogastrointestinal diseases Utilisation des médicaments complémentaires et alternatifs chez les patients pédiatriques atteints de maladies hépato-gastro-intestinales. East Mediterr Health J. (2018) 24:1018–25. doi: 10.26719/2018.24.10.1018.
30. Jorde R, Sollid ST, Svartberg J, Joakimsen RM, Grimnes G, Hutchinson MY. Prevention of urinary tract infections with vitamin D supplementation 20,000 IU per week for five years. Results from an RCT including 511 subjects. Infect Dis. (2016) 48:823–8. doi: 10.1080/23744235.2016.1201853.
31. Mahyar A, Ayazi P, Rad MS, Dalirani R, Javadi A, Esmaeily S. The correlation between vitamin D and bacterial diarrhea in children. Arch Pediatr Infect Dis. (2019) 7:e84382. doi: 10.5812/pedinfect.84382.
32. Mahyar A, Ayazi P, Safari S, Dalirani R, Javadi A, Esmaeily S. Association between vitamin D and urinary tract infection in children. Korean J Pediatr. (2018) 61:90. doi: 10.3345/kjp.2018.61.3.90.
33. Tekin M, Konca C, Celik V, Almis H, Kahramaner Z, Erdemir A, et al. The association between vitamin D levels and urinary tract infection in children. Hormone Res Paediatr. (2015) 83:198–203. doi: 10.1159/000370046.
34. Javadi Nia S, Faramarzi M, Noorbakhsh S, Izadi A, Soheyli pour F, Tabatabaei A, et al. Comparison of serum vitamin A, D and zinc levels between children with urinary tract infection and control group in two University Hospitals. Iran J Pediatr. (2013) 23:S40. English.
35. Tekin M, Konca C, Celik V, Almis H, Kahramaner Z, Erdemir A, et al. Is vitamin D deficiency a risk factor for urinary tract infection in children? Arch Dis Childhood. (2014) 99:A201. English. doi: 10.1136/archdischild-2014-307384.543.
36. Shalaby SA, Handoka NM, Amin RE. Vitamin D deficiency is associated with urinary tract infection in children. Arch Med Sci. (2016) 14:115. doi: 10.5114/aoms.2016.63262.
37. Li X, Yu Q, Qin F, Zhang B and Lu Y (2021) Serum Vitamin D Level and the Risk of Urinary Tract Infection in Children: A Systematic Review and Meta-Analysis. Front. Public Health 9:637529. doi: 10.3389/fpubh.2021.637529.
38. Amabebe E and Anumba DOC (2018) Psychosocial Stress, Cortisol Levels, and Maintenance of Vaginal Health. Front. Endocrinol. 9:568. doi: 10.3389/fendo.2018.00568.