

Correlation of Bacterial Urinary Tract Infection with Prostate Specific Antigen Level in Patients Serum

علاقة التهاب المجاري البولية البكتيري مع مستوى مُسْتَضِد البروستات الخاص في مصل المرضى

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الخلاصة:

الهدف: لمعرفة تأثير التهاب المجاري البولية البكتيري على مستويات مُسْتَضِد البروستات الخاص في مصل المرضى الرجال المفرز من قبل غدة البروستات.

المنهجية: نفذت الدراسة على (113) مريض يعانون من الإصابة بالتهاب المجاري البولية راجعوا مستشفى الصدر الطبية ومستشفى الحكيم العام في مدينة النجف الاشرف و(40) شخص أصحاء، وكانت أعمار الجميع تتراوح بين 36-55 سنة للفترة (تشرين الاول 2012 – حزيران 2013) حيث تم فحص الإدرار مجهرياً وزراعة على الأوساط الزرعية وقياس مستوى مُسْتَضِد البروستات الخاص في المصل. الوسائل الإحصائية التي استخدمت في الدراسة كانت SPSS لغرض تحليل البيانات بواسطة اختبار الانوفا لاستخراج قيمة LSD

النتائج: أظهرت النتائج ارتفاع مستوى مُسْتَضِد البروستات الخاص في مصل المرضى المصابين بالتهاب المجاري البولية لنتيجة الزرع الموجب بنسبة (28.9%) وعدم وجود ارتفاع في المستوى في الأشخاص الأصحاء والمرضى ذو نتيجة الزرع السالب، وكانت المستويات الطبيعية لمُسْتَضِد البروستات الخاص تزداد طبيعياً مع زيادة العمر. أظهرت الدراسة ان بكتريا E. coli البكتريا الأكثر شيوعاً المسببة للالتهاب المجاري البولية.

الاستنتاجات: التهاب المجاري البولية البكتيري في الرجال يُؤثر على مستوى مُسْتَضِد البروستات الخاص، المفرز من غدة البروستات. ومستوى مُسْتَضِد البروستات الخاص يزداد مع زيادة العمر.

التوصيات: توصي الدراسة بالمعالجة السريعة للالتهاب المجاري البولية لتفادي التعقيد والتأثير على غدة البروستات وقياس مستوى مُسْتَضِد البروستات الخاص قبل وبعد العلاج.

Abstract:

Objectives: To find out the effect of bacterial urinary tract infection on prostate specific antigen levels in patients serum the secreted by the prostate gland.

Methodology: the present study was carried out on (113) patients suffering from urinary tract infection attending to Al-Sader Medical City and Al-Hakeem General Hospital in in Al Najaf governorate and Forty apparently healthy control males. Their ages ranged between (36-55) years the period of study from October 2012 to June 2013. With a examined urine analysis, urine culture on media and measure prostate specific antigen levels in patients serum. Data was analyzed using SPSS 17 for the analysis purpose of the data ANOVA test was used with the extraction of value LSD.

Results: Our findings were revealed high level of total prostate specific antigen in patients serum of urinary tract infection with positive culture (28.9%) and the absence of a rise in the level of total prostate specific antigen in patients serum with negative culture and apparently healthy control group, increasing in the normal levels of prostate-specific antigen in serum is associated with to increasing in age. The study showed that E. coli is the most common bacteria which is responsible for UTIs

Conclusion: bacterial urinary tract infection in men effect on total prostate specific antigen level, secreted by the prostate gland. The level of total prostate specific antigen increases with increasing age.

Recommendations: The study recommends the rapid diagnosis and treatment of urinary tract infection to avoid the complexity and the effect on the prostate gland, measuring the prostate specific antigen level before and after treatment.

Keywords: patients of UTI, urine, serum, t PSA, ELISA.

INTRODUCTION :

Urinary tract infection (UTI) can be defined as the persistent presence within the urinary tract of actively multiplying microorganisms. The UTI implies both microbial colonization of the urine and invasion of the lower or upper urinary tract by microorganisms⁽¹⁾. When the infection affects the lower urinary tract it is known as a simple cystitis (a bladder infection) and when it affects the upper urinary tract it is known as pyelonephritis (a kidney infection)⁽²⁾. Urinary tract infections are one of the most common bacterial infection in humans both in community and hospital setting⁽³⁾. Rarely they may be due to viral or fungal infections⁽⁴⁾. *E. coli* is the most common bacterial cause of urinary tract infections⁽⁵⁾. Other bacterial causes urinary tract infections include: *Klebsiella*, *Enterococci*, *Pseudomonas*, *Enterobacter* and *Staphylococcus spp.*^(5,6). Urinary tract infection can cause increase of prostate specific antigen level (PSA), because of the close proximity of the urinary tract with the prostate, the infection can irritate and inflame prostate cells and cause PSA to go up⁽⁷⁾. The increase in serum prostate specific antigen (PSA) in patients with urinary tract infection, this occur as a result of incidental or reflects an innate defense mechanism of the prostate⁽⁸⁾. Prostate specific antigen (PSA) is a glycoprotein that is mainly produced from prostatic epithelial cells. It liquefies semen and allows sperm to swim freely⁽⁹⁾. In healthy men, PSA can be found at high concentration 0.5 to 2 mg/ml in seminal fluid⁽¹⁰⁾ and low concentration in serum less than 4 ng/ml⁽¹¹⁾. The serum prostate specific antigen concentration (level) increases significantly correlated with advanced age^(12,13).

The aim of the study is to find out the effect of bacterial urinary tract infection on prostate specific antigen levels in patients serum the secreted by the prostate gland.

METHODOLOGY :

This study included 113 patients (men) complained from UTIs disease, attending to Al-Sader Medical City and Al-Hakeem General Hospital in Al Najaf governorate for medical care to check up were examined. Their ages ranged between (36-55) years Mean $\pm$ SD (44.6 $\pm$ 6.1). Forty apparently healthy males were included in this study. Their age ranged between (36-55) years, Mean $\pm$ SD (45.33 $\pm$ 5.903). Specimens were collected from healthy subjects only if were not receiving any medications. They have no previous history of any complaint of urinary tract infections or prostate diseases. The period of case control study was carried out from October 2012 to June 2013. The specimens taken from patients and apparently healthy control were midstream urine and serum. Urine specimens were diagnostic by microscopic examination and urine culture (identification of types bacterial isolates in urine culture) the isolated bacteria in urine culture were identified based on Morphological, Biochemical test, and API tests. The serum specimens examination by ELISA to measuring total prostate specific antigen level (PSA). Data was analyzed using SPSS 17 for the analysis purpose of the data ANOVA test was used with the extraction of value LSD and Z- test was also used.

RESULTS :

Table (1): Number and percentage of microscopical urine examination(Pus cells, RBCs, bacteruria) in patients and apparently healthy control.

Groups of study	Results of urine examination(Urine analysis)		
	Pus cells N0.(%)	RBC N0.(%)	Bacteruria N0.(%)
Patients (n=113)	81 (71.6%)	23(20.3%)	41(36.3%)
apparently healthy control (n=40)	0 (0%)	2 (5 %)	0
TOTAL (n=153)	81(52.9%)	25 (15.03%)	41(26.7%)

Table(1) showed that the microscopic examination of urine specimens collected from patients in study groups were found that pus cells were (81 ,71.6%), Bacteruria were (41, 36.3%) and RBCs were (23, 20.3%) compared with apparently healthy control. Urine analysis for (40) specimens of apparently healthy control, did not find pus cell and Bacteruria, but found RBC(2, 5%).

Table (2): Number and percentage of bacterial in patients with urinary tract infection using ordinary culture.

Type of Growth	Types of bacterial isolates	No. of isolates	%
Pure G+ve	<i>Enterococcus feacalis</i>	13	17.1%
	<i>Staphylococcus aureus</i>	5	6.57%
	<i>Staphylococcus saprophyticus</i>	3	3.9%
Pure G-ve	<i>E. coli</i>	30	39.4%
	<i>Klebsiellapneumoniae</i>	8	10.5%
	<i>Pseudomonas aeroginosa</i>	4	5.26%
	<i>Enterobacter</i>	1	1.3%
	<i>Neisseria gonorrhoeae</i>	2	2.6%
	Total	66	86.8%
Mix Growth	<i>E. coli</i> and <i>Enterococcus feacalis</i>	1	1.3%
	<i>E. coli</i> and <i>Staphylococcus aureus</i>	4	5.26%
	<i>Staphylococcus aureus</i> and <i>Enterococcus feacalis</i>	4	5.26%
	<i>Staphylococcus aureus</i> and <i>Klebsiellapneumoniae</i> .	1	1.3%
	Total	10	13.2%
Total		76	100%

No.=number, %=percentage, G+ve=Gram positive stain,G-ve=Gram negative stain

Regarding the results of urine cultures in patients with urinary tract infection , 76 patients (67.2%) had positive culture for bacteria. But result of urine culture for control group (apparently healthy control) were negative culture. Complete diagnosis of bacterial in bacterial laboratories

using Biochemical materials, and API tests (API Staph, API 20 Strep., API 20 E, API NH). Table (2) showed that the number and percentage of patients infected with bacteria were (66 , 86.8%) as pure culture , mixed culture were (10 ,13.2%),showed that *E. coli* is the most common bacteria than any other bacteria which is responsible for urinary tract infections.

Results prostate specific antigen (PSA) in serum

Table (3): Result of total PSA level in patients with urinary tract infection for positive culture, negative culture and apparently healthy control.

Serum total PSA	Groups of study			Total	P value
	Patients positive culture	Negative culture	apparently healthy control		
Normal N0.(%) PSA below 4.0 ng/ml	54 (71.1%)	37 (100%)	40 (100%)	131 (85.6%)	0.00002
High N0.(%)	22(28.9%)	0(0%)	0(0%)	22(14.4%0)	
Total	76 (100%)	37(100%)	40(100%)	153(100%)	

PSA=prostate specific antigen, P value=0.00002

Table (3) showed that the number and percentage of total prostate specific antigen(PSA) level in patients of urinary tract infections with positive culture for bacteria was 22 (28.9%) of patients had high tPSA level in serum the values more than 4.0 ng/ml ⁽¹⁴⁾, but 54 (71.1%) of patients had normal tPSA level in serum. The values were below 4.0 ng/ml . The results of total prostate specific antigen(PSA) level in the patients serum with negative culture for bacteria, have normal PSA level were 37 (100%). The results of total Prostate specific Antigen (PSA) level in the serum of apparently healthy control, have normal PSA level were 40 (100%).Showed that the statistical analysis of total prostate specific antigen (PSA) level demonstrated highly significant differences among patients with positive culture group having high tPSA and normal tPSA in comparison with patients had negative culture and apparently healthy control group(P =0.00002).

Mean of tPSA

Table (4) : Comparison mean of prostate specific antigen level in patients groups and apparently healthy control group.

Groups	Number	%	M±SD	LSD
APP. Healthy control	40	26%	1.5±0.7	2.8 sign. patients of positive culture with high PSA P=0.012
Patients negative culture	37	24%	2.1±0.8	
Patients positive culture with normal PSA	54	35%	1.5±0.8	
Patients positive culture with high PSA	22	15%	11.5±4.4	
Total	153	100%		

M=Mean, SD= standard deviation, LSD= Least Significant Differences

Table (4) the patients group were distributed into three groups according to the results of urine culture and the levels of total prostate specific antigen as follows: patients of UTI positive culture had normal tPSA group, patients of UTI positive culture had high tPSA group, and patients with negative culture group had normal tPSA level. Table (4) showed that a significant differences between the mean of tPSA in patients of UTI had positive culture with high tPSA group compared with other groups $P=0.012$. While no significant differences between apparently healthy control group, patients of UTI positive culture had normal tPSA group, and patients of negative culture ($P>0.05$).

Ages and PSA

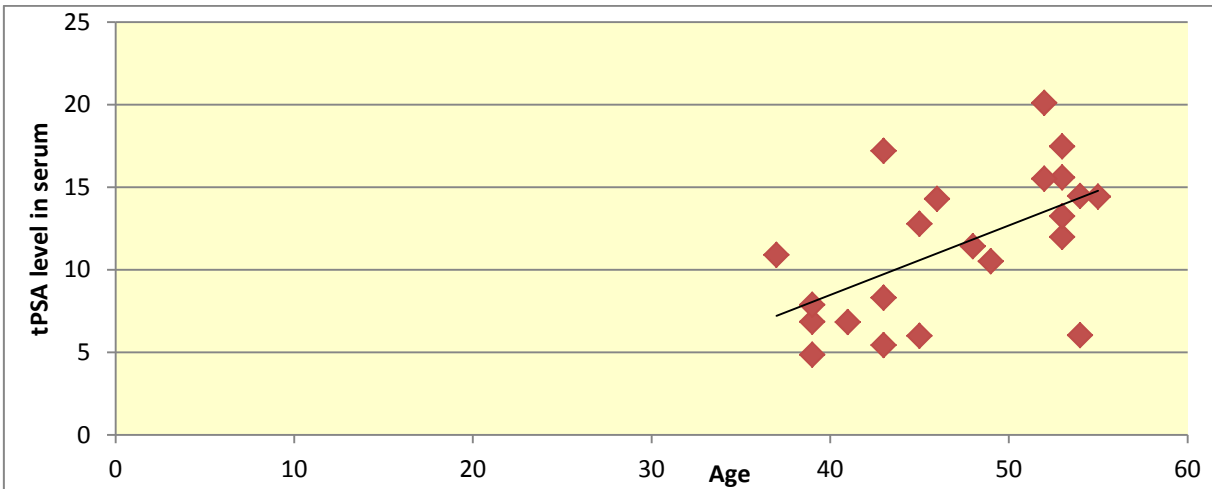


Fig.(1):The correlation between the patient's age of UTI positive culture with high PSA level and PSA level in serum. $r=0.56$

Fig.(1) showed that there was a direct correlation between the age of a patient of urinary tract infection with positive culture who had a high tPSA and the levels of prostate specific antigen in the patient serum. Increasing the levels of prostate specific antigen in the serum is associated with the increasing in the patient's age of UTI ($r=0.56$).

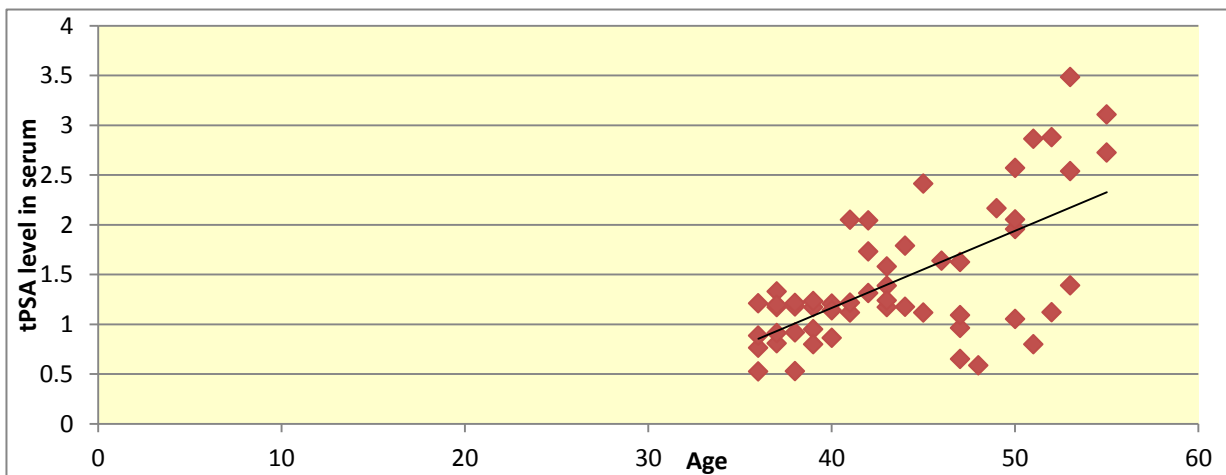


Fig. (2):The correlation between the patient's age of UTI positive culture with normal PSA level and PSA level in serum. $r = 0.56$

Fig.(2) showed that there was adirectcorrelation between patients age of UTI positive culture with normal PSA group (54patient) and PSA level in serum ($r=0.56$).

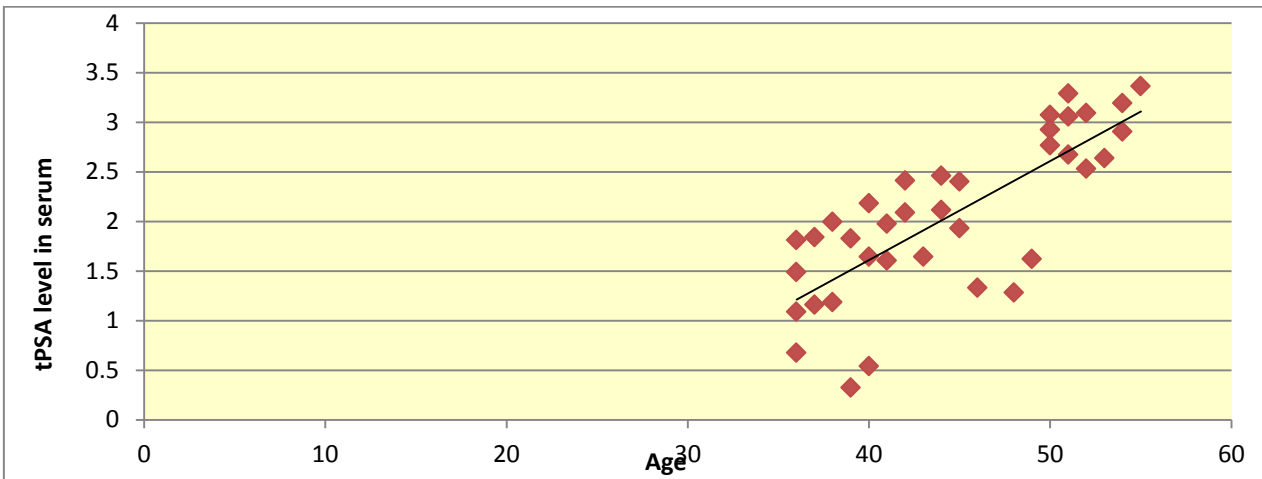


Fig. (3):The correlation between the patient's age of negative culture and PSA level in serum. $r= 0.61$

Fig.(3) showed that there was a direct correlation between patients age of negative culture group (37patient) and PSA level in serum ($r=0.61$).

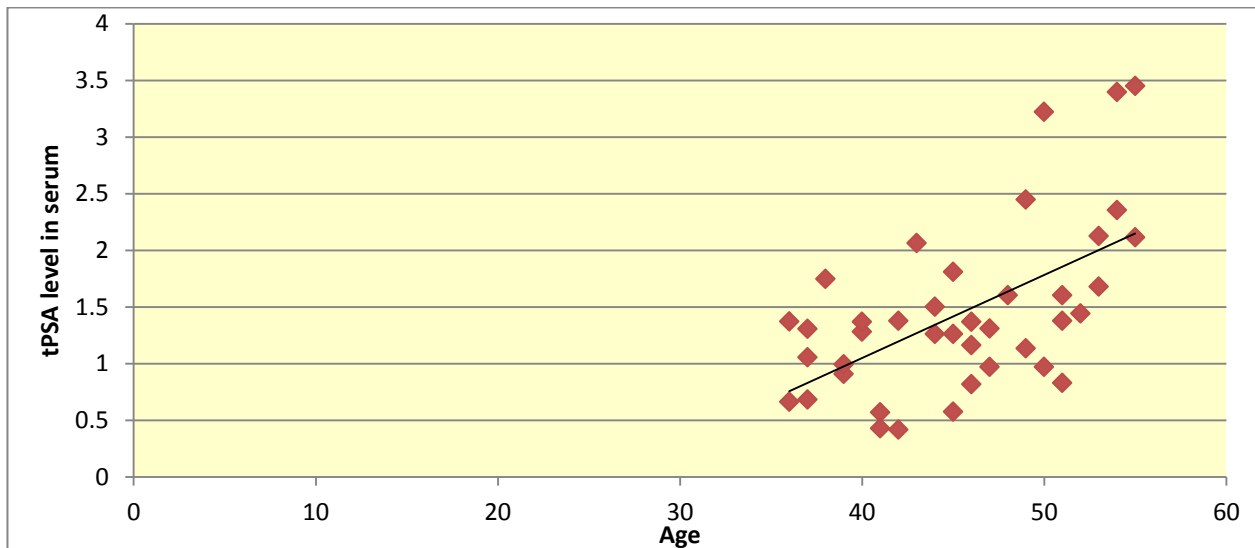


Fig. (4): The correlation between the man age of apparently healthy control and PSA level in serum. $r= 0.54$

Fig.(4) showed that there was a direct correlationbetween men age of apparently healthy control group (40 person) and PSA level in serum ($r=0.54$). Concluded that the normal levels of prostate specific antigen reach to 2.5 ng / ml in the age < 50 years and reach to 3.5 ng / ml in the

age ≥ 50 years in this study. Increasing in the level of prostate-specific antigen in serum is associated with to increasing in age.

Table (5): Number and percentage of bacteria of urinary tract infection leading to increase the level of total prostate specific antigen.

Types of bacterial	No. of bacteria high PSA	%
<i>E. coli</i>	10	45.45%
<i>Enterococcus faecalis</i>	5	22.7%
<i>Klebsiellapneumoniae</i>	3	13.6%
<i>Staphylococcus aureus</i>	1	4.54%
<i>Pseudomonas aeruginosa</i>	1	4.54%
<i>Mix E. coli and Enterococcus faecalis</i>	1	4.54%
<i>Mix E. coli and Staph. aureus</i>	1	4.54%
Total	22	100%

Table(5) showed that the high levels of total PSA were found in 22 patients of bacterial urinary tract infection, the most common bacteria of urinary tract infection leading to increase the level of Prostate specific antigen (PSA) in patients.

DISCUSSION :

The results of general urine examination in the study patients group, found that pus cells were present in 71.6%. These results are close to the results of Kadhum, (2006) who found the prevalence of Pus cell (54%) in General urine examination of patients⁽¹⁵⁾. Pyuria in males refers to the leukocyte excretion and is considered the standard for the determination of significant pyuria which is usually sufficient for a diagnosis of UTI in hospitalized and non-hospitalized patients. Also it is associated with inflammation of urinary tract⁽¹⁶⁾. RBC in this study represented (20.3 %). These results agree with results of Kadhum, (2006) who found the prevalence of RBCs (20.7%) in General urine examination of patients⁽¹⁵⁾. RBCs in urine may be associated with severe infection of urinary tract⁽¹⁷⁾. In this study, bacteruria was presented in 36.3% of specimens, but these data appeared because bacteria are normally present in digestive system and on the skin around the rectum. These results disagree with results of Kadhum, (2006) who found the prevalence of Bacteruria (8%) in General urine examination of patients⁽¹⁵⁾. Clinically, urinalysis that reveals both bacteruria and pyuria is diagnostic of urinary tract infection⁽¹⁸⁾.

In this study of (113) urine culture, it is revealed that (76) specimens had resulted in positive culture for bacteria 67.2%. These results are close to the results of Al-Yassery, (2011) who found that positive culture of urinary tract infection was (57.1%)⁽¹⁹⁾.

On the other hand, the most common bacteria isolated from growth in this study Table(2). These results agree with results of Al-Yassery, (2011) who found that most common bacteria in UTI patients was *E.coli* (40.8%), then *Enterococcus spp.* represented (16.7%), *Klebsiellaspp* (22.5%), and *Staphylococcus spp* were (2.5%)⁽¹⁹⁾. Moreover, These results agree with results of Al-Amedi, (2003) which confirmed that *E. coli* was the commonest uropathogen (35.6%) in the UTI⁽²⁰⁾. Also, Al-Hamadani et al.(2011) showed the majority of bacterial species isolated from patients of UTIs were *E.coli* (35.9%), followed by *Pseudomonas aeruginosa* (29.2%), *Staphylococcus aureus* (12.6%) and *Klebsiella pneumonia* (7.8%)⁽²¹⁾. This high percentage for this bacteria have also been observed by another searcher who reported that *E. coli* the most common bacteria isolated from the urinary tract, it was responsible for urinary tract infection in both male and female which comprise (55.7%), followed by *Klebsiellaspp* (16.8%), *Proteus spp.* (14.8%), *Staphylococcus aureus* (6.95%), *Pseudomonas spp.* (4.9%) and isolated were *Streptococcus spp.* (0.9%)⁽²²⁾. *E. coli* is the most common bacteria than any other bacteria which is responsible for UTIs. The study approach with Al-Dulaymi, (2005) who found *E. coli* pilli, capsule and some specific surface protein may give bacteria the adherence characteristics which confer the ability to adhere to epithelial cells and mucoid membranes lining the urinary tract⁽²³⁾.

The current study demonstrated that the number and percentage of patients with positive culture had high total prostate specific antigen (PSA) level were 22 (28.9%) patient. Table (3) indicates that there is a significant correlation between prostate specific antigen and urinary tract infection with positive culture for bacteria in comparison with patients who had negative culture and apparently healthy control group ($P=0.00002$).

A similar finding was observed by Alex et al. (2012); Hara et al. (2004); Ulleryd et al. (1999) who found high total prostate specific antigen levels in men of urinary tract infection^(24,25 and 26). In a study included 48 men with UTI, Alex et al. (2012) who found that the PSA levels were higher than 4 ng/ml in 26 patients with urinary tract infection⁽²⁴⁾. Also, Ulleryd et al. (1999) pointed out that 58 of 70 men had a raised Prostate Specific Antigen during a urinary tract infection, after treatment of UTI the PSA level returned to normal in 57%, 58%, 68% and 76% at 1, 3, 6 and 12 months, respectively⁽²⁵⁾. Furthermore, Hara et al. (2004) who found that Six of nine cases, initially diagnosed as pyelonephritis, presented with elevated PSA levels⁽²⁶⁾.

Urinary tract infection can cause an increase of prostate specific antigen level (PSA), because of the close proximity of the urinary tract with the prostate, the infection can irritate and inflame prostate cells and cause PSA to go up⁽⁷⁾. Also, the increasing PSA in patients of UTI is reflects an innate defense mechanism of the prostate⁽⁸⁾.

Table (4), showed that there were significant differences centralized in patients of UTI positive culture who had high tPSA group $P=0.012$ compared with other groups. These results were in agreement with many investigators (Zackrisson et al., 2003; Lorent et al., 2002; Ulleryd et al., 1999) who observed urinary tract infections resulting in an increase in mean of high serum PSA values^(25,27 and 28). There were no significant differences between patients of negative culture group ($P>0.05$) in comparison with apparently healthy control group. Because of that all persons in these groups (patients of positive culture had normal tPSA, patients with negative culture, and apparently healthy control group) have normal prostate specific antigen level, and thus there is no difference in the mean levels in groups. These results agree with results of Abdrabo et

al.(2011) who found the mean PSA level 1.48 ng/ml in healthy Sudanese men ⁽²⁹⁾. Also, Andreas *et al.*(2003) found that the mean PSA level 2.9 ng/ml in persons without infection⁽³⁰⁾.

Fig.(1),there were direct correlations between elevated prostate specific antigen level and patients age of positive culture with high tPSA level ($r= 0.56$) .These results agree with results of Vesely *et al.* (2003) who found a correlation between high prostate specific antigen level of PSA and patients age of UTI ($r = 0.28$)⁽¹³⁾.

On the other hand, there were direct correlation between tPSA level in patients' serum and the patients' age of positive culture with normal PSA levels ($r=0.56$),patients' age of negative culture ($r=0.61$), age of apparently healthy control ($r=0.54$)Fig.(2), (3), (4). These results agree with results of Kuo-Jen Lin *et al.* (2010) who found that the serum PSA values were correlated with age in Taiwanese men ($r = 0.31$)⁽¹²⁾. Also, these results agree with results of Oesterling *et al.* (1993) who found that serum PSA concentration is correlated with patient age ($r=0.43$),the serum PSA concentration increases by approximately 3.2% per year (0.04 ng/mL per year)⁽³¹⁾. Abdrabo *et al.*(2011), pointed out that the total serum PSA ranges in the age groups in Sudanese men was 0-3 ng/ml for 40-49 years, 0-3.02 ng/ml for 50-59 years, 0-3.8 ng/ml for 60-69 years and 0-8.7 ng/ml for 70-90 years.⁽²⁹⁾. Also, Andreas *et al.*(2003) showed that a total of 10,267 PSA tests were available for study performed at Innsbruck University, Austria, between 2001 and 2002. PSA levels correlated linearly and positively with age. PSA showed a significant increase with age , which may be attributed to the increase in prostate volume with advancing age⁽³⁰⁾. The serum total prostate specific antigen level is directly correlated with age and prostatic volume, the latter of which also is directly related to age^(30,31).

The presence of bacteria, Table (5) elevated serum tPSA levels in most patients with urinary tract infection, because *E. coli*, *Enterococcus faecalis* and *Klebsiella pneumonia* were the most common bacterial infection of urinary tract in pure and mix growth in this study . In the study by Townes *et al.* (2013) observed that the increase in serum prostate specific antigen (PSA) during patients of urinary tract infection (UTI) is reflects an innate defense mechanism of the prostatic epithelium against *Escherichia coli* infection⁽⁸⁾.

CONCLUSIONS :

Increasing total prostate specific antigen (PSA) levels in patients with symptoms of urinary tract infection (positive culture group), indicates that bacteruria in men affect the prostate gland leading to increasing the total prostate specific antigen (PSA) levels of secretion in patient serum. There are significantly correlations between levels of total prostate specific antigen and men age.

RECOMMENDATIONS :

The study recommends the rapid diagnosis and treatment of urinary tract infection to avoid the complexity and the effect on the prostate gland , measuring the prostate specific antigen level before and during interval several times after a proper treatment to urinary tract infection, making sure that there are no other infections influential on the prostate gland. Understanding the high number of *E. coli* in patients of UTI with high total prostate specific antigen level.

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