


**Research Article**
**Evaluation of Serum Metalloproteinase-9 (MMP-9) in Iraqi men with urinary tract infection**
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**Abstract: Objective:** The inflammation of the urinary tract and its various causes is one of the important diseases, which neglect and non-treatment lead to many complications, therefore, many countries including the United States of America has given urinary tract infection "UTI" a great interest. Since the disease is sometimes without obvious symptoms and because of research lacking that are using MMP-9. The aim of this work is to study the alterations in the Metalloproteinase-9 (MMP-9), and its role in pathogenicity of urinary tract infections "UTI" in serum of men who are initially diagnosed with this disease.

**Methods:** This study was applied in educational Alsader hospital in Najaf city by using Enzyme Linked Immuno Sorbent Assay (ELISA) on serum taken from 42 men infected with UTI, and other 38 healthy considered as a control group to detect MMP-9.

**Data analysis:** SPSS computerizing system has been used for statistical analysis of data.

**Results:** The results revealed a highly significant ( $P < 0.05$ ) level of "MMP-9" in serum of patients in comparison with the control group. The result also demonstrated the strong relation between MMP-9 and other parameters such as age and smoking.

**Conclusion:** It was concluded from the results of the present study that Metalloproteinase-9 "MMP-9" was good prognostic biomarker for "UTI" in men, and these results significantly correlate with the early stages of disease.

**Recommendation:** 1-It may be recommended that using MMP-9 to predict and diagnosis the urinary tract infection. 2-It may be also recommended to measure MMP-9 in women to establish its role in this disease

**Keywords:** MMP-9, UTI, Iraqi men, Serum, ELISA.

**Introduction**

"Matrix metalloproteinases" which are engaged with extracellular matrix partition "ECM" are a huge group of calcium-subordinate zinc-containing endopeptidases, they have multiple function that are affect the biological activities of cells, MMP-9 has a focal part in increasing of cells number, maturation, relocation, angiogenesis, immunity system alterations and apoptosis [1]. It was demonstrated the strong relation between deregulation of "MMPs" and many diseases such as severe ulcers, encephalomyelitis, joint inflammation and tumor [2], it discharges as an inert star protein at that point experiences enactment by various sorts of extracellular proteases [3]. Action of MMP-9 directed by various biochemical stimulators as growth factor and several types of cytokines such as interleukin eight "IL-8" in which the pathways of intracellular flagging adjusted because of their expression [4].

"MMPs" are an extensive family, there are no less than 26 human MMPs of calcium-subordinate zinc-containing endopeptidases, which are in charge of the tissue redesigning and partitioning of proteins of the extracellular matrix "ECM", and these proteins have the crucial role on metalloproteinases classification including collagens, elastins, gelatin, glycoproteins, and proteoglycans. Another subclass of "MMPs" is spoken to by the layer sort MMPs

"MT-MMPs", which contain a trans membrane and an intracellular area served as an attachment space [5].

The principle capacity of "MMPs" is to corrupt basic segments of the ECM. In any case, MMP proteolysis can make space for cell movement, deliver particular substrate-cleavage sections with autonomous natural action, manage tissue engineering through consequences for the ECM and intercellular connections, and adjust the action of signaling molecules, both straight forwardly and by implication [6].

"MMPs" could doubly affect in "angiogenesis". Apoptosis, (programmed cell death) is an exceptionally very much requested process by which undesirable, imperfect, or expired cells are quickly and specifically dispensed with from the body. "MMPs" assume a fascinating part in programmed cell death [7]. "MMPs" influence cell survival and division by managing (survival signals); these specific impacts of "MMPs" act as mirror to explain the variations in MMP substrates associated with every reaction [8-9].

A urinary tract infection "UTI" is a contamination that influences some portion of the urinary tract. When it influences the lower urinary tract it is

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known as a bladder contamination "cystitis" and when it influences the upper urinary tract it is known as kidney infection "pyelonephritis" [5]. Symptoms from a lower urinary tract incorporate agony with pee, and wanting to urinate in spite of having a discharge bladder. Kidney infection symptom are fever and flank torment more often than notwithstanding the indications of a lower "UTI" (5). The appearances of blood in the urine is rarely [6] in the exceptionally old and the extremely youthful, manifestations might be obscure or non-specific [7].

There are many causes for "UTI" and the most widely recognized reason for contamination is *Escherichia coli*, however other microorganisms may seldom be the cause [8]. The, sex, diabetes, increase body mass, and family history are constituting the well-known risk factors for this disease [8]. The upper urinary infection, in the event that it happens, generally takes after a lower urinary infection yet may likewise come about because of a bloody infection [9].

Diagnosis can be troublesome in light of the fact that microbes might be available without there being an infection [10]. In confused cases or in the case of treatment failure, a urine specific examination might be useful [11].

Urinary tract infections are the most widely recognized reason for healing facility obtained diseases which result in if be neglected many muddled infections, for example, urethritis, interstitial cystitis and prostatitis [12].

In the United States, urinary tract infections represent about 7,000,000 office visits, a 1,000,000 crisis division visits, in addition to 100,000 hospitalizations each year [6]. The cost of these diseases is critical both as far as lost time at work and expenses of restorative care. In the United States the immediate cost of treatment is evaluated at one and half billion USD yearly [13].

The aim of current study is to detect the alterations in the MMP-9 level in serum of men who are initially diagnosed with urinary tract infections in urinalysis laboratory after doing general urine examination "GUE" without special urine examination. Also in trying to measure the MMP-9 in future diagnosis for urinary tract infections.

## Patients and Methods

The current study included 42 patients of Iraqi males with urinary tract infections and 38 other healthy groups adjusted as control group. The blood was drawn to get the serum from the patients when coming to urinalysis laboratory for checking and treating at AL-Sader medical city hospital in AL-governorate Najaf. The patients

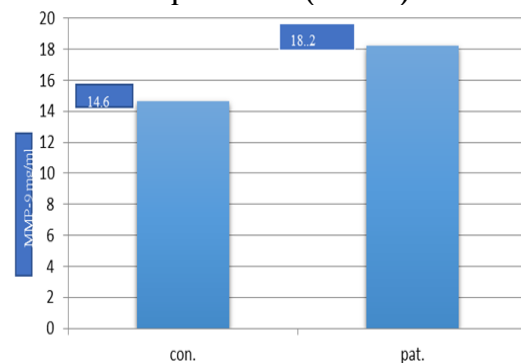
group were classified into subgroups according to ages (40. 49Y), (50. 59Y), (60. 69Y), (70. 80Y), and two other subgroups smokers and nonsmokers.

## The Metalloproteinase-9 (MMP-9) ELISA Assay

This assay is based on the formation of colored product in proportion to the amount of human MMP-9 present in the sample. The reaction is terminated by addition of acid and absorbance is measured at 450nm. The specific Kit for this test is supplied by (eBioscience Company, Inc. Campus Vienna Biocenter 21030 Vienna, Austria. human MMP-9platinum ELISA. BMS277/2/BMS277/2TEN).

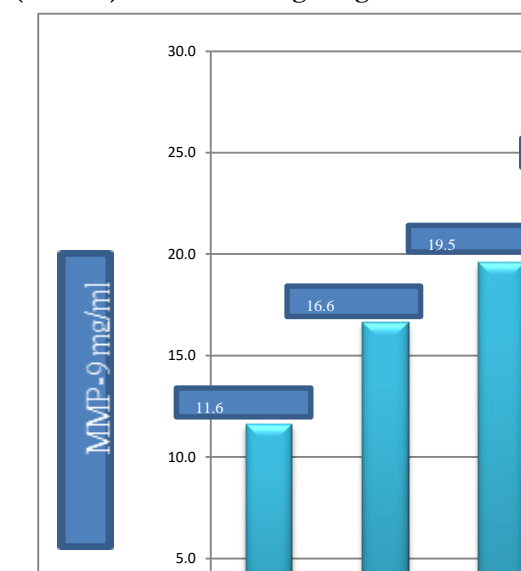
## Results

### 1-The Metalloproteinase-9 (MMP-9) level.



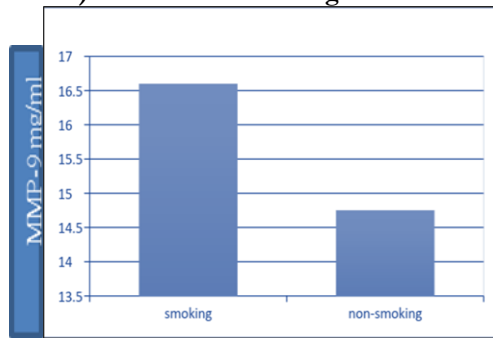
**Figure 1.** Comparison between MMP-9 level and control. Serum analysis of MMP-9 levels revealed there was statistically significant increase ( $p < 0.05$ ) in patients ( $18.2 \pm 1.3$ ) in comparison with the control group ( $14.6 \pm 1.3$ ) as in (Figure1).

### 2-Comparison between Metalloproteinase-9 (MMP-9) levels according to ages.



**Figure 2.** Comparison between MMP-9 level and ages. This result revealed the significant increased ( $p < 0.05$ ) in the levels of MMP-9at all ages, highly significant increase ( $p < 0.05$ ) of (70-79Y) ( $23.8 \pm 1.1$ ).

### 3-Comparison between Metalloproteinase-9 (MMP-9) levels and to smoking:



**Figure 3.** Comparison between MMP-9 level and smoking. The mean values and the standard errors of smokers and non-smokers groups of patients are shown in figure (3), this result demonstrate statistically significant increased ( $p < 0.05$ ) in serum MMP-9 level ( $p < 0.05$ ) in smokers ( $16.6 \pm 0.8$ ) compared with the non-smokers ( $14.7 \pm 0.6$ ).

### Discussion

The present study in Figure (1) revealed a significant increase ( $p < 0.05$ ) in serum MMP-9 of urinary tract infection patients in comparison with control. The studies on inflammation proved a significant increasing of matrix metalloproteinase-9 [14-15]. Expression of MMP-9 is watched principally in leukocytes including monocytes, macrophages and neutrophils [16]. It is profoundly initiated in response to chemokines and cytokines, and improved articulation has been related to an assortment of incendiary pathologies including autoimmunity, joint pain, ischemia/reperfusion injury, transplant dismissal and inflammatory diseases [17].

Metalloproteinases are proteolytic chemicals that corrupt principle segments of the cellular layer and extracellular network [18]. These matrix metalloproteinases related with the cell surface [19]. Additionally, they have a part in angiogenesis particularly matrix metalloproteinase-9 "MMP-9" [20]. The result of current study is in agreement with the study of Huda [21] which demonstrated the high level of MMP-9 in urine of patients with cystitis (urinary bladder infection) in correlation with the control. This outcome was in concurrence with past report of [22]. Also some data revealed high level of MMP-9 in urine in correlation with cell tumor conduct [23]. Such result have been shown in study of Carlo *et al.*, [24] which is utilize zymography to examine MMP-2 and MMP-9 in urine of patient with bladder tumor and watched that the urinary estimations of these two biomarkers corresponded with the expansion in MMP-9 lytic action in advanced stage and grade of this disease.

Figure (2) in the current study demonstrated high level ( $p < 0.05$ ) in serum MMP-9 in (60-69 Y) age group in comparison with other age group, this

result disagree with study of [25] which explained the decreasing in the level of MMP-9 in serum with advancing in age in men particularly up to 50 years old.

The present study revealed a highly significant increase ( $p < 0.05$ ) in the level of MMP-9 in serum of smokers patient with urinary tract infections in comparison with non-smokers. This result agree with conclusion of Inga S. *et al.*, [26] which proved increasing MMP-9 levels in smokers group and being most minimal in non-smokers group.

### Conclusions:

The current study proved the medical importance of MMP-9 measurement in the detection of urinary tract infection in men, especially at the onset of the disease, also demonstrated the strong relation between MMP-9 levels and ages, further more to the highly increasing of MMP-9 levels in smokers patients.

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