Evaluation of C-Reactive Protein in Urinary Tract Infected Patients Attending Madonna University Teaching Hospital

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Abstract

This study was carried out to determine the level of C-reactive protein (CRP) in Urinary Tract infection Patients attending Madonna University Teaching Hospital. C- reactive protein was measured using the ELISA (Enzyme-Linked Immunosorbent Assay) method. The statistical software for social sciences (SPSS) version 26 was used to statistically analyze the data acquired from this study. C- reactive protein values in the UTI group (20.75±8.35 mg/L) were significantly higher than those in the control group (3.08±1.28 mg/L), demonstrating a strong inflammatory response to UTIs. Additionally, age-related study showed that children and adolescents had greater CRP levels than adults. Patients with *Escherichia coli* showed considerably higher CRP levels than *Klebsiella pneumoniae* and *Proteus mirabilis* in the bacterial growth categories, however no significant difference was seen between *Klebsiella pneumoniae* and *Proteus mirabilis*. Differences in immune response dynamics, pathogen pathogenicity, and host-pathogen interactions can be used to explain these variances in CRP levels. The results show how useful CRP is as an inflammatory marker in UTIs.

Keywords

C-Reactive Protein, Urinary Tract, Infected Patients

1. Introduction

C-reactive protein (CRP) is a substance that produced by the liver in reaction to inflammation. It can be measured in blood tests to assess inflammation levels and is a crucial part of the body's innate immune system. Typically, CRP is made up of five identical subunits that were organized around a central pore in a cyclic pentamer. Nonetheless, there are two isoforms of the protein: monomeric (mCRP) and pentameric (pCRP). PCRP, which possesses anti-inflammatory qualities, is the circulating form under normal circumstances. In the meantime, mCRP has pro-inflammatory qualities and is generated during inflammation.

pCRP alternates between these two forms when it separated into monomers, which typically reacts to some stimuli such as tissue damage or response to any inflammatory which happen frequently towards human’s body. . Because mCRP possesses pro-inflammatory properties including platelet activation, leukocyte recruitment, and endothelial dysfunction where all related to the aetiology of numerous disorders, including cardiovascular disease—this structural change is noteworthy. The dual role of CRP in inflammation is highlighted by these structural and functional differences: it mediates anti-inflammatory responses while simultaneously inducing inflammatory processes under pathological conditions.

This protein recognises and facilitates the removal of invading infections and those damaged or broken cells by binding to phosphocholine, phospholipids, histones, chromatin, and fibronectin (see Image. C-Reactive Protein Isoforms and Their Phosphocholine Complexes). CRP activates the classical complement cascade and engages phagocytic cells via Fc receptors, speeding up the clearance of apoptotic cells, necrotic debris, and pathogens.

Pathologic activation can be caused by CRP when it binds to autoantibodies that expose in phosphocholine residues as in these autoimmune processes to human body. CRP can cause pathologic activation in autoimmune processes when it binds to autoantibodies that expose phosphocholine residues. This pathway leads to diseases like idiopathic thrombocytopenic purpura. In some cases, CRP-mediated complement activation might aggravate tissue injury by releasing inflammatory cytokines.

Unlike erythrocyte sedimentation rate, which indirectly represents inflammation, CRP levels respond quickly to inflammatory stimuli. CRP levels rise sharply and then fall quickly after the underlying cause is resolved. Infections such as rheumatoid arthritis may be continued where causing inflammation that increased chronically. CRP levels can be elevated by a variety of diseases, both acute and chronic, infectious or non-infectious. It is significantly raised for the CRP concentrations where most typically associated with infection, demonstrating pathogen-associated molecular pattern (PAMP) recognition. Besides that, another serious issue such as Trauma could also having a large increase in CRP through the alarmin response. More modest CRP rises are frequently caused by a larger range of triggers, such as sleep difficulties, periodontal disease, or mild systemic inflammation. Higher CRP levels are associated with less mild

or moderate-to-vigorous physical activity and more sedentary time. The blood plasma contains an annular (ring-shaped) pentameric protein called C-reactive protein (CRP), the content of which increases in response to inflammation. It is an acute-phase protein with hepatic origin that rises when macrophages and T cells secrete interleukin-6. In order to activate the complement system via C1q, its physiological function is to bind to lysophosphatidylcholine expressed on the surface of dead or dying cells (and some other types of bacteria) [1]

In reaction to substances secreted by macrophages and fat cells (adipocytes), the liver produces CRP. It belongs to the family of proteins called pentraxins. It has nothing to do with protein C (blood coagulation) or C-peptide (insulin). The first pattern recognition receptor (PRR) discovered was C-reactive protein [2]

Acute phase reactants, such as CRP, are proteins produced by the liver and released into the blood within hours of tissue damage, the start of an infection, or another inflammatory trigger. Significantly elevated values are seen, for instance, following injury or a heart attack, when autoimmune illnesses are active or uncontrolled, and when people have serious bacterial infections like sepsis. In reaction to inflammation, CRP levels can rise up to a thousand-fold, and their rise in the blood can occur before pain, fever, or other clinical signs. The test gauges CRP levels in the blood and can be useful in spotting acute inflammation or keeping track of disease activity in chronic inflammation [3]

Infections, in particular, can enter the urinary system through the urethra while also allowing urine to escape Infections, particularly urinary tract infections (UTIs), can enter the urinary system via the urethra, the tube that drains urine from the body. While the urinary system is intended to prevent infections, germs can occasionally escape these defences and migrate up the urethra, potentially resulting in bladder infections (cystitis) or even kidney infections. Women are more prone to UTIs because their urethra is shorter and closer to the anus. Furthermore, some illnesses and behaviours may raise the chance of infection.

Bacteria, particularly E. coli from the digestive system, can enter the urethra and rise into the bladder. This can occur as a result of sexual intercourse or simply due to bacteria near the anus in women. Sexually transmitted infections or other microorganisms can cause urethra infection, often known as urethritis. Bladder infection is the most prevalent kind of UTI. E. coli is the most common cause, however other bacteria may also be involved. Women are more susceptible to UTIs because of their anatomy. Other risk factors include diabetes, diseases that obstruct urine flow, impaired immune systems, and the use of urinary catheters. A UTI can cause a burning sensation when urinating, frequent and urgent urination, murky or strong-smelling urine, and pain in the lower abdomen or back.. Both in men and in women, bacteria live in the urethra and close to the urethral entry, but they are flushed out after micturition [4]. Women have a closer proximity to the bladder, which allows germs to colonize the bladder more quickly before being eliminated through micturition. Additionally, it was found that the urethral entrance in females lies near the rectum and vaginal cavity, both of which are home to sizable bacterial communities [5]. Lower UTIs (limited to the bladder) and higher UTIs (pyelonephritis) are separated into uncomplicated and complicated categories, respectively. A normal host with no anatomical or functional abnormalities, who is not pregnant, and who has not been instrumented (for example, with a catheter) is considered to have an uncomplicated UTI. Complexity is applied to all other UTIs [6]

The movement of bacteria from the vaginal cavity, rectal opening, and periurethal area into the urethra is facilitated by urogenital manipulations associated with daily activities and medical interventions; however, even if bacteria reach the bladder and multiply to significant numbers, bacterial colonization rarely results in symptoms. While germs frequently travel from the vaginal, rectal, and periurethral sites into the urethra, it does not necessarily result in symptomatic urinary tract infections (UTIs). Though these bacteria can enter the bladder and multiply, the body's defences frequently prevent them from creating a full-blown infection and its associated symptoms. Sexual intercourse, catheterisation, and even routine hygiene habits can introduce bacteria into the urethra. The presence of bacteria in the urinary tract does not automatically indicate a UTI. The body has mechanisms in place to eradicate or control microorganisms that could cause infection. These mechanisms include the flushing action of urination, urine's acidic environment, and the body's immunological response. When these defence mechanisms fail, germs multiply, causing inflammation and symptoms such as discomfort or burning during urinating, frequent urine, and urgency. [7]. Given the structure of the human body, urinary tract infections (UTIs) are among the most prevalent bacterial illnesses. In fact, given the ongoing microbial attack on our urinary system, we should be astonished that UTIs are not more common. The likelihood that asymptomatic colonization goes away on its own or develops into a symptomatic infection depends on both host and bacterial characteristics. Host variables include anatomical or functional defects, a genetic predisposition, and behaviours (such as sexual activity) that enhance exposure to uropathogens or transfer germs into the bladder. Numerous virulence traits exhibited by bacteria allow the infection to enter and populate the bladder while eluding the human immune system [8]

Urinary symptoms and urine cultures showing numbers of a known uropathogen above a specified threshold (typically defined as >1,000 cfu/ml of urine, though thresholds as low as 100 cfu/ml and as high as 100,000 cfu/ml are also used) are used to diagnose UTIs [9]. However, urinary symptoms and bacteriuria frequently occur separately from one another: Approximately 20% of women who arrive with 'classic' UTI symptoms have negative urine cultures. The urine of apparently healthy, asymptomatic people frequently contains high concentrations of germs [10]. With increasing age and after sexual activity, the likelihood of asymptomatic bacteriuria rises [11]

Among of all the bacterial illnesses, uninary tract infections (UTIs) are the illness that people keep got into hospital that comparing in the community [12]. Millions of patients worldwide continue to be significantly impacted by UTI, the majority of whom are otherwise healthy women. Recurrences, which affect up to one-fourth of women after a first UTI, are not prevented by antibiotic treatment for acute cystitis [13]. Increasing uropathogenic bacterial antibiotic resistance complicates therapy choices further, requiring novel strategies based on fundamental biology research. The growing antibiotic resistance in uropathogenic bacteria is a severe issue, limiting treatment options and necessitating novel remedies. Bacteria evolve strategies to circumvent antibiotic effects, such as pumping them out, lowering membrane permeability, and altering or destroying the medications. To address this, researchers are focussing on fundamentally understanding these mechanisms in order to create novel techniques such as efflux pump inhibitors and phage therapy. When bacteria develop resistant, many standard antibiotics become ineffective, resulting in longer illnesses and an increased risk of consequences. While antibiotic resistance is a natural process, human activities such as abuse and misuse of antibiotics in human, animal, and plant health hasten its development and dissemination. Bacteria use a variety of methods to fight antibiotics, including: Efflux pumps actively remove antibiotics from the bacterial cell. Membrane permeability: Changes in bacterial cell membranes can prevent antibiotics from entering. Enzymatic inactivation: Bacteria can create enzymes that breakdown or change antibiotic molecules [4].

A number of Studies have been carried out on the evaluation of C- reactive protein in UTI patients in various parts of the world. There is however, limited or no documented expository literature on the evaluation of lipid profile in UTI patients in Madonna University Teaching Hospital (MUTH) in recent time.

2. Materials and Methods

2.1 Study Area

This study was carried out in Madonna University Teaching Hospital Elele, Rivers state. A community situated in Ikwerre local government Area of Rivers State. at 50402 N and 64909 E South-south Nigeria.

The laboratory investigations was carried out in chemical pathology Laboratory of Madonna University Teaching Hospital (MUTH) Elele, Rivers State.

2.2 Research Design

This research is an experimental study, where conducting a cross sectional study designed to estimate C reactive protein in UTI patients in Madonna University Teaching Hospital, Elele, Rivers state.

2.3 Ethical Approval/Consideration

It was approved by the ethical committee of Madonna University, Elele, to proceed this research and this study was carried out according to the good clinical practice guidelines of the modified Helsinki declaration. Individual consent was sought for and obtained from the subjects prior to sample collection. Subjects' names and medical details are treated as confidential.

2.4 Inclusion and Exclusion Criteria

Inclusion

Samples were obtained from subjects with fungal or bacteria growth on the urine culture media in Madonna University Teaching Hospital.

Exclusion

Subjects with no fungal or bacterial growth in the urine culture plates in Madonna University Teaching Hospital.

Sample Collection

5mls of whole blood was collected from each subject via venupuncture, introduced into plain container and labelled according to their respective age and laboratory number. The sample was allowed to clot and retract, after which it was dislodged and spun at 12000 rpm for five minutes. The serum (supernatant) was transferred to an Ependolf tube with a micropipette and labelled accordingly. All collected samples were stored at a temperature of -20°C.

Laboratory Assay

Determination of C Reactive protein was carried out using ELISA Method

3. Statistical Analysis

SPSS version 26 was used in this study by analyse the data obtained from the research that conducted. The results were expressed as mean ± (Standard deviation) SD and comparisons of different means done using independence students T-test and one way analysis of variance (ANOVA). Values were considered significant at $p<0.05$ and not-significant at $p>0.05$.

4. Results

According to the Table 1, the mean CRP level in the control group was 3.08 ± 1.28 mg/L, while in the UTI group, it was 20.75 ± 8.35 mg/L. A comparison of the CRP levels between the two groups revealed a statistically significant difference (p = 0.000). The analysis of variance (ANOVA) test yielded an F-value of 231.812, indicating a substantial difference in CRP levels between the control and UTI groups.

Table 1. C reactive protein of control and patients with UTI

Parameter	Groups	Mean±SD (mg/l)	F	P-value
C-reactive protein (mg/l)	Control (53)	3.08 ±1.28	231.812	0.000*
	UTI infection (52)	20.75±8.35		

P<0.05 equal to Significant

p>0.05 equal to Not significant

In table 2, the mean CRP level for the 1-12 years age group was 20.68 ± 8.87 mg/L, for the 13-18 years age group was 21.75 ± 8.17 mg/L, and for the 19-65 years age group was 9.75 ± 10.03 mg/L.

Statistical analysis using analysis of variance (ANOVA) indicated a significant difference in CRP levels among the three age groups (p = 0.000). The F-value of 10.74 further supported this finding, indicating substantial variation in CRP levels between the age groups.

Table 2. C reactive protein in different age groups among patients with UTI

Age	CRP (mg/l)	F	P-value
1-12 years	20.68±8.87		
13-18 years	21.75±8.17	10.74	0.000
19-65 years	9.75 ±10.03		

P<0.05…… Significant

p>0.05……..... Not significant

In table 3, the mean CRP level for the No Growth group (A) was 3.08 ± 1.28 mg/L, for *Escherichia coli* (B) was 27.93 ± 5.10 mg/L, for *Klebsiella pneumoniae* (C) was 12.99 ± 4.08 mg/L, and for *Proteus mirabilis* (D) was 15.51 ± 4.05 mg/L. Post hoc analysis results showed the following pairwise comparisons. The comparison between the No Growth group and *Escherichia coli* group revealed a significant difference in CRP levels (p = 0.000). The comparison between *Klebsiella pneumoniae* and *Proteus mirabilis* showed no statistically significant difference in CRP levels (p = 0.054). The comparison between *Escherichia coli* and *Proteus mirabilis* indicated a significant difference in CRP levels (p = 0.000). The comparison of Klebsiella pneumoniae and Proteus mirabilis revealed no statistically significant difference in CRP levels (p = 0.054), indicating that their influence on CRP is likely similar. In contrast, the comparison of Escherichia coli and Proteus mirabilis revealed a statistically significant difference (p = 0.000), indicating that these two bacteria likely had different impacts on CRP levels.

Table 3. C reactive protein among different bacteria

Bacterial Growth	Mean ±SD mg/l
No Growth (A)	3.08±1.28
Escherichia coli (B)	27.93±5.10
Klebsiella pneumonia (C)	12.99± 4.08
Proteus mirabilis (D)	15.51±4.05
Post Hoc	
A vs B	0.000
C vs D	0.054
B vs D	0.000

P<0.05…… Significant

p>0.05…….. Not significant

5. Discussion

According to the study's findings, there were notable disparities in the levels of C-reactive protein (CRP) between the control and urinary tract infection (UTI) groups, as well as across various age groups and bacterial growth categories. These findings offer insightful information on the physiological mechanisms behind differences in CRP levels across

settings and populations [14]. CRP binds to phosphocholine found in microorganisms. It is hypothesised to help complement bind to foreign and injured cells and improve phagocytosis by macrophages (opsonin-mediated phagocytosis), which have a CRP receptor. It contributes to innate immunity by acting as an early defence system against pathogens.

The discernible difference in CRP levels between the UTI and control groups lends evidence to the long-standing link between inflammation and UTIs. The greater mean CRP level in the UTI group (20.75±8.35 mg/L) in comparison to the control group (3.08±1.28 mg/L) implies that those with UTIs have a significant systemic inflammatory response. The immune system's reaction to the presence of infectious pathogens and the resulting tissue damage is what causes the high CRP levels [15]. In UTIs, bacterial infections start an inflammatory cascade that releases several pro-inflammatory mediators, including CRP, and activates immune cells [16]. Bacterial infections in UTIs generate an inflammatory response, including the release of pro-inflammatory mediators including CRP (C-reactive protein) and immune cell activation. This cascade begins when bacteria, such as uropathogenic E. coli, adhere to and infiltrate the urinary tract lining, triggering the immune system to respond.

Uropathogenic bacteria, which often originate in the gut, can colonise the urethra and bladder by sticking to uroepithelial cells.

This attachment triggers the creation of signalling chemicals, such as chemokines, which attract immune cells like neutrophils to the infection site.

The immune response generates and releases pro-inflammatory mediators include cytokines (IL-1β and IL-18), chemokines, and acute-phase proteins (CRP).

Various immune cells, such as neutrophils, macrophages, and dendritic cells, are activated and drawn to the infection site, amplifying the inflammatory response. The inflammatory response is meant to get rid of the infection, but it can cause pain, fever, and tissue damage. In some cases, if the infection spreads to the kidneys, it can produce pyelonephritis, a more serious infection. CRP, an acute-phase protein, is an indication of inflammation that is commonly elevated during UTIs, indicating the body's response to the infection. Uroepithelial cells in UTIs can activate TLR4, a toll-like receptor that promotes inflammation. Significant differences were seen in the CRP levels between the age groups, according to the investigation. The mean CRP levels were higher in the age groups of 1 to 12 years (20.68±8.87 mg/L) and 13 to 18 years (21.75±8.17 mg/L) than in the age group of 18 to 65 years (9.75±10.03 mg/L). These results imply that compared to adults, children and adolescents may show a more significant inflammatory response. This age-related discrepancy is caused by a number of variables, including the maturing immune system, puberty-related hormonal changes, and a younger person's higher susceptibility to infections [17,18].

Different bacterial growth categories' CRP levels were compared in order to get insight into the distinctive inflammatory reactions brought on by various bacterial infections. CRP levels were significantly greater in the *Escherichia coli* group (27.93±5.10 mg/L) than in the No Growth group (3.08±1.28 mg/L), demonstrating the pathogen's strong ability to cause an inflammatory response. While *Klebsiella pneumoniae* (12.99±4.08 mg/L) had somewhat lower CRP levels than *Proteus mirabilis* (15.51±4.05 mg/L), the difference was not statistically significant. The changes in virulence factors, pathogen-host interactions, and immunological reactions induced by particular bacterial species may be responsible for these variances in CRP levels between bacterial growth categories [19].

According to [20], CRP is an inflammatory cytokine, specifically interleukin-6 (IL-6), induced acute-phase reactant that is largely made in the liver. Immune cell activation during infections results in the release of IL-6, which triggers the production of CRP and its release into the bloodstream. C-reactive protein (CRP) is an inflammatory marker, specifically an acute-phase reactant, produced largely in the liver. It is induced by the cytokine interleukin-6 (IL-6), which immune cells produce during infections. Increased IL-6 causes the liver to generate and release CRP into the circulation. CRP is one of several proteins whose levels in the blood fluctuate in reaction to inflammation or illness. Interleukin-6 (IL-6) is a cytokine, or signalling molecule, that plays an important part in the inflammatory response.

When the body experiences an infection or injury, immune cells become activated and release IL-6. IL-6 travels to the liver and increases the formation of CRP. The freshly synthesised CRP is subsequently released into the bloodstream, where its concentration can be tested to determine the presence and severity of inflammation.Therefore, the degree of tissue injury, the pathogenicity of the bacterial species involved, and the observed fluctuations in CRP levels can all be attributed.

6. Conclusion

This study's findings showed that CRP levels between the control and UTI groups, as well as between various age ranges and bacterial growth categories, differed significantly. The systemic inflammatory response brought on by bacterial infection and tissue damage is reflected in the higher CRP levels in UTIs. CRP levels that vary with age show that immunological responses fluctuate at various developmental stages. Additionally, changes in pathogen virulence and host immune responses are reflected in CRP levels across different categories of bacterial growth. These results help us understand the physiological processes behind the inflammatory response in UTIs and offer important new information for UTI clinical therapy and further research

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