# The Role of Procalcitonin and C-Reactive Protein as An Indicator of Bacterial Infection in Chronic Kidney Disease Undergoing Hemodialysis

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**Abstract**
Background: This is a cross- sectional study that included a bacteriology and biochemical markers comparative between Procalcitonin (PCT), and C-reactive protein in chronic hemodialysis patients Aim of the study: The purpose of this study was to clarify the diagnostic accuracy of the use of Procalcitonin ( PCT) level and C-reactive protein,and to prove the value of these markers in the diagnosis of infections in patients with Infections-CKD and Non-infections CKD.To establish a new cut-off value for PCT to eliminate confusion in the diagnosis and treatment of bacterial infections in hemodialysis (HD) patients. Methodology: Blood samples were collected, approximately 10 ml with complete information achronic kidney disease n the blood was divided into three parts, one part for culture, second part to separate by the centrifuge and the serum was used to measurement the levels of Procalcitonin, and C-reactive protein (CRP), and the Third part was used to performed Complete blood count (CBC). Results: Through comparing the results statistically, this study showed that the older people were more likely to have chronic renal failure than young; moreover, the present study showed that the rate of chronic renal failure was higher in females by 63% versus 37% for males, as the study showed the most common cause of chronic kidney failure is hypertension, and the least it is diabetes. In our current study, there were 46 patients who had a positive culture result with a percentage of 34%, and 35% of them were caused by Gram-positive bacteria which is the highest and an average of 28 isolates and a percentage of 60.9%) and 9 isolates of Gram-negative bacteria with a percentage (19.6% )and 9 isolates (19.6%) is unknown,the system was not able to diagnose it, the isolates were diagnosed with the VITEK 2 compact system, and a sensitivity test for the bacteria that was diagnosed using the same system.While the percentage of negative culture was 66% of the total samples. The study proved that the level of the PCT is not useful in distinguishing bacterial infection and may be indicate the presence of impaired kidney function, while CRP was more sensitive and accurate in diagnosing bacterial infection in those patients. Conclusion: that PCT does not superior to CRP as an infection marker.
Keywords: Procalcitonin, C-reactive protein, chronic kidney disease.

## 1. Introduction

The term renal failure denotes inability of the kidneys to perform excretory function leading to retention of nitrogenous waste products from the blood, function of kidney is electrolyte regulation, excretion of nitrogenous waste, elimination of exogenous molecules (ex, drugs), synthesis of a variety of hormones (ex, erythropoietin), metabolism of low molecular weight protein (ex, insulin). (Pallos et al, 2015).

Acute and chronic renal failure are the two kinds of kidney failure.

Acute kidney disease (AKD) is a heterogeneous disorder that is common in hospitalized patients and associated with short and long-term morbidity and mortality, that AKD is not a self- limited process, but is strongly linked to increased risk for chronic kidney disease (CKD), and future mortality (Moore et al, 2018).

Chronic kidney failure (CKF) also known as Chronic kidney disease (CKD) defined as a persistent abnormality in kidney structure or function ( eg, glomerular filtration rate (GFR) < 60ml/min/1.73m or albuminurea ≥30 mg per 24 hours) for more than 3 months, CDK affects 8% to 16% of the population worldwide.(Chen et al, 2021). CKD is slowly progressive and leads to irreversible loss of nephrons, end stage renal disease and / or early death. Therefore. CKF represent a worldwide major concern and its prevalence continues to rise, also it is one of the most common diseases. (Ruiz-Ortegn et al, 2020)

One of the major complications of hemodialysis catheter use is bloodstream infection, which is associated with an increased risk of systemic infection complication, hospitalization, and death (Opine et al, 2019.

A bloodstream infection (BSI) is the present of one or more viable pathogens in systemic circulation confirmed by positive microbiogical blood culture. BSI elicite a lifethreatening systemic inflammatory response characterized by fever, chills and / or hypotension. (Viscomi, 2016; and Santoro et al, 2014)

Procalcitonin (PCT), a protein that consists of 116 amino acids, is the peptide precursor of calcitonin, a

doi.org/10.31838/hiv22.02.509 Received: 29.05.22, Revised: 12.07.22, Accepted: 17.08.22

hormone that is synthesized by the parafollicular C cells of the thyroid and involved in calcium homeostasis. Procalcitonin arises from endopeptidase-cleaved preprocalcitonin. The reference value of PCT in adults and children older than 72 hours is 0. 15 ng/mL or less. ( Giannetta et al , 2020)

C- reactive protein (CRP), an acute phase protein secreted by liver when acute and chronic inflammation, is widely applied in clinical setting as an inflammation biomarker, and elevated level of CRP is associated with prognosis of various diseases related to inflammation (Tong et al,2017).CRP is also involved in diseases associated with sepsis and transplantation as CRP level is increased not only in serum, but also in infarcted tissue of multiple organs such as kidney during sepsis(Bielas et al,2018).

## 2. Material and Method

### Isolation and Identification of Bacterial Isolates

4-5 ml of blood were incubated in BacT/ALERT 3D Blood Culture System for 5-7 days, then identification and antibiotics sensitivity test performed using Vitek 2 compact system. As shown below:

### Principle of the test

BacT/ALERT Microbial Detection Systems and culture bottles provide both a microbial detection system and a culture media with suitable nutritional and environmental conditions for organisms which might be present in the test sample. Inoculated bottles are placed into the instrument.

Where they are incubated and continuously monitored for the presence of microorganisms that will grow in the BacT/ALERT bottles, (BacT/ALERT (green lable) for adult which is intended for culture of aerobes, put 5 ml of blood, and BacT/ALERT (yellow label) for Infants and Children collect a maximum of 4 ml of blood). BacT/ALERT Microbial Detection Systems utilize a colorimetric sensor and reflected light to monitor the presence and production of carbon dioxide (CO2) that is dissolved in the culture medium, if microorganisms are present in the test sample, carbon dioxide is produced as the organisms metabolize the substrates in the culture medium, when growth of the microorganisms produces CO2, the color of the gas-permeable sensor installed in the bottom of each culture bottle changes to yellow.

### Identification and Antibiotics Sensitivity test

#### VITEK 2 compact

This format focuses on the industrial microbiology-testing environment while also having application for low to middle volume clinical laboratories. Features specifically developed for industrial microbiology and a colorimetric reagent card (BCL) used to identify the spore-forming Gram-positive bacilli (i.e, *Bacillus* and related genera), the other colorimetric reagent cards (GN, GP, YST) apply to all system formats for both industrial and clinical laboratories.

### Reagent Cards

The reagent cards have 64 wells that can each contain an individual test substrate, substrates measure various metabolic activities such as acidification, alkalinization, enzyme hydrolysis, and growth in the presence of inhibitory substances. An optically clear film present on both sides of the card allows for the appropriate level of oxygen transmission while maintaining a sealed vessel, that prevents contact with the organism-substrate admixtures. There are currently four reagent cards available for the identification of different organism classes as follows:

1. GN Gram-negative fermenting and non-fermenting bacilli
2. GP Gram- positive cocci and non –spore forming bacilli
3. YST- yeast and yeast –like organisms.
4. BCL- Gram positive spore-forming bacilli.

### Determination of Procalcitonin (PCT)

#### 1. Intended use

The fluorecare PCT is application to the quantitative detection of the concentration of PCT in human serum and plasma.

#### 2. Principle

The fluorecare PCT, based on the principle of the immunochromatographic assay, is used to detect the concentration of PCT in human serum or plasma by double antibody sandwich method. 3. Requirements of Specimens

1- The serum and plasma are obtained from the whole blood collected by the conventional method; the hemolysis and severe jaundice sample should not be used during the whole process. All specimens should be treated as infection factors. The serum or plasma specimens cannot be placed over 1 day under room temperature (20-25 oC), sample cannot be stored over 3 days within 2-8 oC, or no more than 3 times, after being thawed, the specimens should be fully mixed. Before being tested, the sample must be recovered to room temperature. Frozen preserved specimens that are to be detected need to be completely malted, rewarmed and mixed well.

#### 3. Test Setup

1. Take out the test card from refrigerator and leave it at room temperature (20-25oC), turn on the instrument according to the instructions.
2. Check the consistence of the ID chip and the lot number or the diagnostic kits.
3. Place the test card on the flat operation table, the test card should be used within 1 hour.
4. Holding the pipette vertically, add 20μL serum and plasma sample or the reference product without air bubbles to the 180 μL diluents solution (the diluents is along with the kit box) tube and mix,and then apply 70 μL mixture to

the specimen well on the test card.

5. Being placed at the room temperature for 15 minutes, and then insert it into test card holder of analyzer and start to test, few seconds later, the result will be automatically displayed on the screen.

NOTE: The experiment should be done at 20-25 oC, humidity 35%-85%.

Determination of CRP

1. Samples

-Fresh serum, stable 7 days at 2-8 °C and 6 months at -20 °C.
- The samples with presence of fibrin should be centrifuged before testing
-Do not use highly hemolized or lipemic samples.

2. Principle

CRP- Q is a quantitative turbidimetric test for the measurement of C- reactive protein (CRP) in human serum or plasma.
Latex particles coated with specific anti-human CRP are agglutination causes an absorbance change,dependent upon the CRP contents of the patient sample that can be quantified by comparison from a calibrator of know CRP concentration.

3. Procedure

| Procedure | |
|---|---|
| Wavelength: | 540nm (530-550) |
| Lighpath: | 1cm |
| Termperature: | 37oC |

3.1. Use as monoreagent: Mix gently latex 4-5 times before use, prepare the necessary amount as follows: 1ml Reagent B (Latex) + 9 ml Reagent A (Diluent). The workin solution (A+B) is stable 30 days at 2-8 °C. Adjust the instrument to zero with distilled water:

| Pipette | Sample | Calibrator |
|---|---|---|
| **Working solution (A+B)** | **1000µl** | **1000µl** |
| Sample | 5µl | |
| Calibrator | | 5µl |

Mix, read the absorbance of the sample and the calibrator immediately (A1) and after 2 minutes (A2).

## 3. Results calculation

In the bireagent procedure is obtained a nonlinear curve, obtain manually absorbance values to report on diagram.
CRP (mg/l) = (A2-A1) Samples/ (A2-A1) calibrator × Calibrator Value.

## Results and Discussions

### Distribution of the study groups

In the present study, groups were distributed according to the type of group, number of persons,age, and gender, as shown in the table (1).

**Table (1): Distribution of the current study groups.**

| Type of group | Number | Age (Years) | Gender | |
|---|---|---|---|---|
| | | | Male | Female |
| Chronic kidney disease (CKD) patients' groups | 128 | 15-84 | 80 | 48 |

In the present study, the highest percentage of the patients was in the age group (more than 60 years) in the percentage of (47%), followed by (40-60 years) (41%), (20-40 years) (25%) and (less than 20 years) (15%) as shown figure (1).

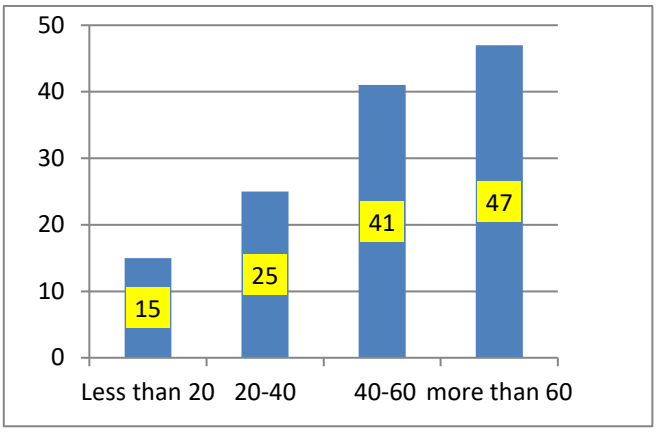



*Figure (1): Distribution of total chronic renal failure patient (n= 128) according to age.*

The current study demonstrated that the highest percentage of CRF patients was among the older age groups, these results were in agreement with the results of (Sabti, 2021) who showed that patients who more than 60 years of age, recorded a highest range for incidence with CRF with growing in age. Many subjects show a gradual decrease in the rate of glomerular filtration and renal blood flow, with significant variation among individuals (Delanaye et al, 2019). The decrease in glomerular filtration rate was due to the decrease in the flow rate of glomerular capillary plasma and glomerular capillary ultrafiltration coefficient (Weinstein and Anderson,2010).

### Sex distribution of total Chronic Renal Failure patients.

Distribution by sex for the total CRF patients showed a difference in the incidence rate of chronic renal failure diseases among both genders.
The current study showed that the highest rate of patients with chronic renal failure were males (63%) while the females recorded incidence rate (37%), as shown in figure (2)

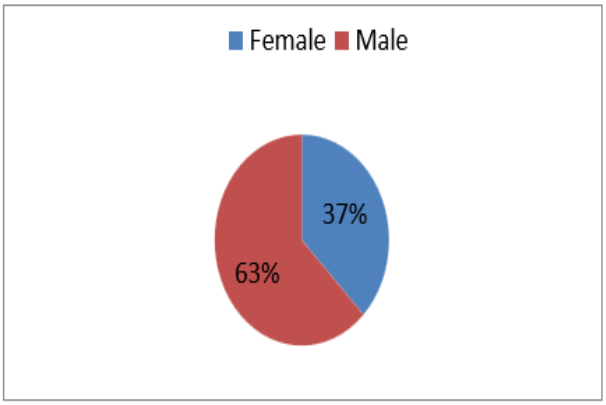



*Figure (2): Distribution of total chronic renal failure patients (n=128) according to gender.*

This result was approach to result (Hameed, 2020; Sabti, 2021) who reported that male's percentage

were (62%) and females were (38%), and with (Neugarten and Golestaneh, 2019) were suggest that the development of kidney disease is slower in females than in males and this sexual form is primarily due to the direct actions of sex hormones on the cellular metabolism. In another hand, finding of this study disagree from results of (Inker et al,2015; Abed, 2018) were reported that the percentage was almost similar of both genders.

## Risk factor

This study showed that hypertention was the most common risk factor of CKD which accounts for (38.15% ). The second most common,the other causes such as, renal stones, chronic glomerulonephritis, congenital single or small kidney, duplex kidney, Lupus erythematosus, drugs and toxins, infection (UTI) and unknown etiology, that totally account for (32.89% ), then hypertention and diabetes mellitus together (19.73%), and finally diabetes mellitus (9.21%).Figure (3).

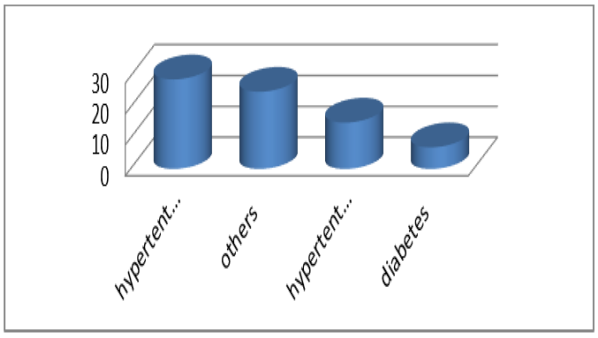



*Figure (3) Distribution of risk factor of CKD*

The effect of sex on the development of kidney disease has been reported, in patients with chronic kidney disease.

Sex hormones have direct effects on the cellular processes that involved in the response to the renal injury, sex hormones influence upon the synthesis and the activity of various cytokines and vasoactive agents, synthesis and degradation of the matrix components, and the generation of reactive oxygen species (Neugarten and Golestaneh, 2019)

## Distribution of results for blood culture of chronic renal failure patients according to positive and negative culture.

During this study, the results of blood culture samples for hemodialysis patients group showed that the positive culture was (34%) whereas the negative culture was (66%) as shown in figure (4).

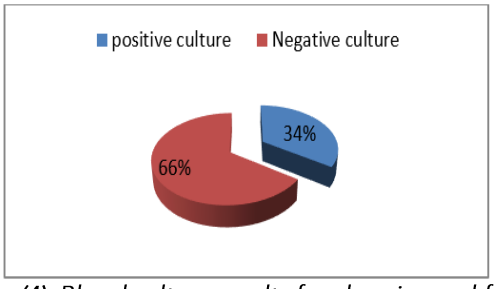



*Figure (4): Blood culture results for chronic renal failure patients (n= 128).*

This study agrees with agree with (Weiss and Qureshi, 2021), they found that positive culture (38.8%) less than negative culture (61.1%), and disagree with Ahmed *et al,* 2021, they showed that the percentages of positive blood culture (77%) less than of negative culture (23%).

Distribution and constitution of isolated pathogens

In the present study, there were 46 patients with positive blood culture, and the positive rate of culture was 35.9%. Pathogen distribution was dominated by Gram-positive bacteria (28) isolates of Gram-positive bacteria, (9) isolates of Gram-negative bacteria, and (9) Unknown organism, shown in Table (2). They were identified by VITEK 2 compact system, this system were performed to identification the bacteria isolated and antibiotics sensitivity test.

**Table (2) Causative organisms isolated from blood stream among hemodialysis patients**

| Isolates (N= 46) | N (%) |
|---|---|
| Gram-positive organism | 28(60.9) |
| Staph epidermidis | 11(23.9) |
| Staph hominis | 4(8.7) |
| Kocuria kristinae | 3(6.5) |
| Staph aureus | 3(6.5) |
| Staph capitis | 2(4.3) |
| Staph pseudintermedius | 1(2.2) |
| Staph lentus | 1(2.2) |
| Staph haemolyticus | 1(2.2) |
| Enterococcus faecalis | 1(2.2) |
| Leuconostoc meseteroides | 1(2.2) |
| Gram-negative organism | 9(19.6%) |
| Escherichia coli | 3(6.5) |
| Pseudomonas luteola | 1(2.2) |
| Pseudomonas aeruginosa | 1(2.2) |
| Sphingomonas paucimobilis | 1(2.2) |
| Moraxella lacunata | 1(2.2) |
| Methylobacterium spp | 1(2.2) |
| Pasteurella pneumotropica | 1(2.2) |
| Unknown organism | 9(19.6) |

## Gram positive isolates

This study showed that Gram-positive bacterial infection were the most common isolated bacteria from hemodialysis patients compared with Gram-negative bacteria, the percentage of Gram- positive (60.9%, n= 28), the principle isolates Staph epidermidis is (23.9%, n=11), Staph hominis (8.7, n=4), Staph aureus (6.5, n=3), Kocuria kristinae (6.5%, n=3) and Staph capitis (4.3, n=2), the other isolates were Staph pseudintermedius, Staph lentus, Staph haemolyticus, Enterococcus faecalis, Leuconostoc meseteroides, the percentage of each isolate was (2.2, n=1).

This study agrees with (Yen et al, 2016), who were reported that Gram-positive bacterial infection was the most common with hemodialysis patients. and result disagree with Çalık et al, 2022, they found the Gram- negative bacilli were the most frequently isolated pathogens in blood culture (71%), and the

majority of them (81%) were belonging to the Enterobacteriaceae family.

Our study which was consistent (Del Polo et al,2012), there found, Staphylococcus epidermidis, Staphylococcus hominis, Staphylococcus haemolyticus, Enterococcus faecalis and two polymicrobial (S.epidermidis . and S. hominis ), the most common bloodstream infections,

## Gram negative isolates

Of 46 organisms cultured, the percentage of Gram-negative organism (19.6 %, n=9), the principal isolates were Escherichia coli (6.5, n= 3), other isolates were Pseudomonas luteola, Pseudomonas aeruginosa, Sphingomonas paucimobilis, Moraxella lacunata, Methylobacterium spp, Pasteurella pneumotropica, percentage of isolates (2.2%, n=1).

E. coli is one of the most common organisms that cause gram-negative in dialysis patients and is associated with high probability of mortality and technique failure (Zurowska et al, 2008). Moreover, the virulence of E. coli was reported to get more severe than previously found, which had led to even worse outcomes in dialysis patients with E. coli (Feng et al, 2014). Zeng et al, 2021 reached E. coli was the most common pathogen of the Gram-negative organisms.

## Antibiotics susceptibility test results

The Vitek automatic microbiological analyzer (BioMerieux, France) were used in the antibiotic sensitivity test and the result were determined according to the National Committee for Clinical Laboratory Standards (NCCLS). For Gram -positive bacteria,the Drug susceptibility to, Cefoxitin, Benzylpenicillin, Ampicillin, Oxacillin, Gentamicin, Linezolid, Ciprofloxacin, Clindamycin, Erythromycin, Daptomycin, Teicoplanin, Vancomycin, Tetracycline, Tigecycline, Fusidic Acid, Trimethoprim, as shown in table(4.3 A,B,C,D). For Gram-negative bacteria,the Drug susceptibility to,Ticarcillin, Clavulanic Acid, Piperacillin Ceftazidime, Aztreonam, Imipenem, Meropenem, Amikacin, Gentamicin, Tobramycin, Ciprofloxacin, Minocycline, Colistin, Refampicin, Trimethoprim had been tested, as shown in table(3&4).

## Antibiotics susceptibility of Gram-positive bacterial

In present study, the gram-positive bacterial isolates were showed more sensitivity to Linezolid (92.9%), Trimethoprim (85.7), Ciprofloxacin (78.6%), Tigecycline (71.4), Vancomycin (64.3), and Gentamicin (60.7). Erythromycin was the least effective antibiotics towards gram positive isolates, where these isolates recorded resistant to this antibiotics with (85.7%), followed Fusidic Acid (82.1), Tetracycline (78.6), Daptomycin (71.4), Cefoxitin(64.3), Teicoplanin (57.1), and Oxacillin(53.6), as shown table (3)

**Table (3): Antibiotics susceptibility pattern of gram-positive bacterial isolates.**

| Antibiotics susceptibility pattern | | | Total N |
|---|---|---|---|
| Antibiotics used | Sensitive n (%) | Resistant n (%) | |
| Cefoxitin | 10 (35.7) | 18(64.3) | 28 |
| Benzylepenicillin | 13(46.4) | 15(53.6) | |
| Ampicillin | 15(53.6) | 13(46.4) | |
| Oxacillin | 13(46.4) | 15(53.6) | |
| Gentamicin | 17(60.7) | 11(39.3) | |
| Ciprofloxacin | 22(78.6) | 6(21.4) | |
| Clidamycin | 16(57.1) | 12(42.9) | |
| Erythromycin | 4(14.3) | 24(85.7) | |
| Linezolid | 26(92.9) | 2(7.1) | |
| Daptomycin | 8(28.6) | 20(71.4) | |
| Teicoplanin | 12(42.9) | 16(57.1) | |
| Vancomycin | 18(64.3) | 10(35.7) | |
| Tetracycline | 6(21.4) | 22(78.6) | |
| Tigecycline | 20(71.4) | 8(28.6) | |
| Trimethoprim | 24(85.7) | 4(14.3) | |
| Fusidic Acid | 5(17.9) | 23(82.1) | |

The mechanisms of resistance remain far from clear. The remarkable ability of these bacteria to acquire useful genes from various organisms may explain why some strains are capable of infecting humans of diverse genetic backgrounds, eliciting severe immune reactions (Hiramatsu, 2001). It is possible that resistant strains may develop a thickened cell wall and/or an increase in glutaminenon- amidated muropeptides in the peptidoglycan, the thicker cell walls may sequester the antibiotic so that the antibiotic cannot reach the cell wall precursors (Cui et al, 2000).

## Antibiotics susceptibility of Gram-negative bacterial

In present study, the gram negative bacterial isolates were showed more sensitivity to Imipenem, Meropenem, Amikacin, Ciprofloxacin, Minocycline, were (100%), Pipracillin(88.9%), Gentamicin and Tobramicin (66.7), and Clavulanic Acid (55.6). Aztreonam, Refampicin, and Colistin were the least effective antibiotics towards gram negative isolates, where these isolates recorded resistant to this antibiotic with 100%. Followed Ceftazidime, and Trimethoprim (22.2), and Ticarcillin (44.4), as shown in table (4).

**Table (4): Antibiotics susceptibility pattern of gram-negative bacterial isolates.**

| Antibiotics susceptibility pattern | | | Total N. |
|---|---|---|---|
| Antibiotics used | Sensitive n (%) | Resistant n (%) | |
| Ticarcillin | 4(44.4) | 5(55.6) | 9 |
| Clavulanic Acid | 5(55.6) | 4(44.4) | |
| Pipracillin | 8(88.9) | 1(11.1) | |
| Ceftazidime | 2(22.2) | 7(77.8) | |
| Aztreonam | 0 | 9(100) | |
| Imipenem | 9(100) | 0 | |
| Meropenem | 9(100) | 0 | |
| Amikacin | 9(100) | 0 | |
| Gentamicin | 6(66.7) | 3(33.3) | |
| Tobramicin | 6(66.7) | 3(33.3) | |
| Ciprofloxacin | 9(100) | 0 | |
| Minocycline | 9(100) | 0 | |
| Refampicin | 0 | 9(100) | |
| Trimethoprim | 2(22.2) | 7(77.8) | |
| Colistin | 0 | 9(100) | |

Infections that caused via the multidrug- resistant (MDR) strains, frequently lead to death. MDR isolates showed resistance to more than 2 groups of antibiotics, in both gram negative and positive groups (Johnson et al, 2004).

The present of MDR isolates may be due to continual treatment with broad spectrum antibiotics, During CRF the patient is exposed to many types of complications and to control them, various antibiotics are used which can increase the microorganism's resistance to the different antibiotics (Richa et al, 2016).

In another hand, the resistant to antibiotics may be due to the occurrence of mutations in the germ cell chromosome, or the germs may be carried plasmids that have antibiotic resistance, or when the germs are of the one type that produce the B-lactamase enzyme (Manikandan et al, 2011).

## Procalcitonin (PCT) level in chronic kidney disease (CKD) patients

Mean serum PCT levels showed non significantly difference (ns) in the patient's infection compared with Non- infections CKD patients (1.73 ng/ml and 1.82 ng/ml), respectively. P. value= 0.915. (Table 5 & Figure 5).

**Table (5): - Level of Procalcitonin (PCT ng/ml), in patients with Infection- CKD and non-infection – CKD.**

| Parameter Groups | | PCT ng/ml |
|---|---|---|
| Infection- CKD | Mean ± SD | 1.73 ± 4.11 |
| Non infection CKD - | Mean ± SD | 1.82 ± 5.17 |
| P. value | | 0.915 |

This study showed that serum PCT level is an independent predictor of infection among CKD patients. PCT reflects chronic inflammation, is related chronic HD, and can be useful as a stratifying tool for detecting patients at high risk for longterm infections.

The results, regarding the diagnostic accuracy of Procalcitonin (PCT) showed lower reliability for bacterial infections in patients with renal impairment, because PCT levels, cannot usefully identify chronic hemodialysis patients with bacterial blood stream infections, Thus, the use of a PCT for differentiating patients with CKD- infections and CKD -non infections are impractical, and higher cut-off values should be applied to patients with impaired renal function.

Several studies have evaluated the potential of the infection biomarker procalcitonin (PCT) to improve the diagnosis work-up of patients with bacterial infections and its influence on decisions regarding antibiotic therapy, among these researches are, Lai et al , 2020; Sager et al , 2017 and Cabral et al , 2016 it is from studies that reached the effectiveness of PCT protocols in early diagnosis of bacterial infection and further in assisting in the initiation and termination of antibiotics treatment, most research has focused on lower respiratory tract infections,burn, critically ill sepsis patients,, UTI infections, postoperative infections, meningitis, pneumonia, acute heart failure, and recognizing Gram-negative bloodstream infection.

The existing knowledge shows that the elevated serum PCT levels in the infection or inflammatory status might be related to the impaired renal clearance of PCT in the chronic kidney disease (CKD) setting (Wu et al, 2020).

One of the studies on serum PCT in ESRD patients on dialysis obtained a mean value of 0.69 ± 0.81 ng/ml before dialysis, and a level higher than standard value of 0.5 ng/ml in 57% of patients (Level et al, 2001).

Dahaba et al, 2003 measured the PCT values of terminal renal failure patients that had not reached a state of septicemia, measurements were taken before dialysis, and PCT levels were also higher than those of normal healthy controls, the expected lowest value for serum PCT levels was 1.5 ng/ml.

This study disagree with Lee et al, 2015, were reached,serum PCT levels were significantly higher in dialysis patients with a bacterial infection, the mean serum PCT concentration of the infection end stage renal disease(2.95±3.67 ng/ml) vs. (0.50±0,49 ng/ml, p= 0.006) in the control end stage renal disease (cESRD) group, demonstrating the utility of serum PCT as an index of infection. And disagree with Tao et al, 2022, were showed that PCT had a high diagnostic accuracy for diagnosis of bacterial infections in patients undergoing hemodialysis at a cutoff value of 1.5 ng/ml, also compared the diagnostic accuracy of PCT and C- reactive protein (CRP), and their results were showed that the diagnostic accuracy parameters for PCT were significantly higher than those for CRP. Serum PCT levels below 0.1 ng/ml are commonly detected in healthy individual (Meisner et al, 2001). Cutoff values of > 0.25 ng/ml have been used for distinguishing between bacterial infection and non-infection in patients with normal renal function (Grace, & Turner, 2015).

In case of those receiving HD, PCT cutoff values are yet to be appropriately determined. Previous studies involving chronic HD patients indicated the appropriate cutoff of serum PCT levels to be 1.5 ng/ml accurately indicate chronic HD patients with severe infections and sepsis and discriminate well from patients without infection (Herget-Rosenthal et al 2001; Schmidt et al, 2000).

However, several recent studies determined the PCT cutoff levels to be 0.5 ng/ml, which can be used to rule-infection while levels of <0.5 ng/ml can be used to rule-out infection in patients undergoing HD (Mori et al, 2012; Grace, & Turner, 2014; Fadel et al ,2016).

## C-reactive protein (CRP) level in chronic kidney disease (CKD) patient with infection and non-infection

The mean serum CRP concentration showed significant difference between patients with

Infection-CKD group and Non infection –CKD group (23.7±26.3 mg/ml, 13.9±20.3 mg/ml, P. value=0.031). (Table 6 and Figure 5).

**Table 6: Level of C-reactive protein (CRP mg/L) in patients with Infection- CKD and non-infection – CKD.**

| Parameter Groups | | CRP |
|---|---|---|
| Infection- CKD | Mean ± SD | 23.7 ± 26.3 |
| Non infection CKD - | Mean ± SD | 13.9 ± 20.3 |
| *P. value* | | 0.031 |

Our results showed that CRP is more sensitive than PCT in the diagnostic of bacterial infections in patients undergoing chronic HD.

The study suggests that in spite of its higher cost, PCT is not superior to CRP as an infection marker in term of diagnostic value, and this study demonstrates that CRP is accurate for predicting infection in patients with impaired kidney function. CRP would be a more valuable marker of infection in those patients, and more effective option in diagnosing infection among CKD patients, and eventually avoid unnecessary damage to residual renal function.

This study agree with Park et al , 2014, were reached both CRP and PCT are useful to distinguish infectious conditions from non-infectious conditions, not only in patients with normal renal function, but also in patients with impaired renal function.

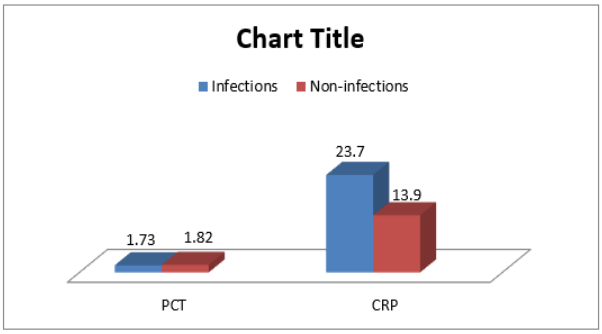
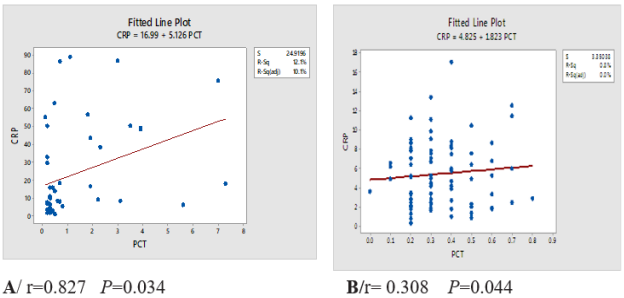



*Figure (5):- Levels of PCT (ng/ml ), CRP (mg/L), in Infection CKD group and Non -infection CKD group.*

## Correlation between PCT and CRP with infections and non-infections CKD.

Our study showed positive correlation between PCT and CRP with infection and non-infection (r=0.827, P=0.034 and r=0.308,




**A**/ r=0.827 *P*=0.034 **B**/r= 0.308 *P*=0.044

*Figure (6): Correlation between serum procalcitonin (PCT) and C-reactive protein, (A) with infections and (B) non-infections. Serum PCT had a positive correlation with CRP.*

The present study demonstrated that the combination of elevated PCT and CRP level can be used as a reliable marker of chronic inflammation in CKD patients and to increase the sensitivity and strengthening inflammation detection.

This study agrees with Opatrná et al, 2005 who were demonstrated a significant positive correlation between PCT and serum C-reactive protein (CRP) (r=0.59, P< 0.01). And agree with Lee et al, 2015 were showed positive correlation between serum PCT and CRP level (R2= 0.567, P < 0.01).

In spite of the impressive improvement in clinical and technology treatment of CKD patients, an insidious pitfall is an enhanced risk of complications, particularly chronic inflammatory diseases, the chronic inflammatory state of long-term CKD patients' dependents upon two factors: defective immune system function and continuous nonspecific immune cell stimulation by dialytic device.

## 4. Conclusions

PCT levels cannot usefully identify chronic hemodialysis patients with bacterial blood stream infections, Thus, the use of a PCT for differentiating patients with CKD-infections and CKD-non infections is impractical.

CRP is more sensitive than PCT in the diagnostic of bacterial infections in patients undergoing chronic HD.

### Recommendation

Higher cut-off values should be applied to patients with impaired renal function. This study suggests that serum PCT at a cutoff of ≥2 ng/ml is an appropriate indicator of infection in chronic HD patients.

Expand in the study of markers in chronic renal failure patients and find the correlation between inflammatory markers and PCT.

Meta-analysis studies are recommended to evaluate the use of PCT as a predictor for the need of kidney transplantation in end stage renal disease patients.

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