

Clinical research

Usefulness of serum procalcitonin as a diagnostic biomarker of infection in children with chronic kidney disease

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Abstract

Introduction: Serum procalcitonin (PCT) levels are known to be low in healthy individuals in healthy subjects but are increased in patients with a severe bacterial infection. It has not been extensively studied in children with chronic kidney disease (CKD), treated either with hemodialysis (HD) or with renal transplantation.

Material and methods: During a 6-month period, blood samples were taken from 102 (55 HD children and 47 renal transplant recipients) children with a strong clinical suspicion of infection. Procalcitonin levels were measured by ELISA.

Results: Thirty-four/102 cases had proven infections as defined previously. Children with proven infections had a significantly higher PCT (0.920 ± 0.24 ng/ml) than those without (0.456 ± 0.53 ng/ml), $p = 0.04$. The ideal cutoff value derived for serum PCT was 0.5 ng/ml. This threshold value established a sensitivity of 94.1% and a specificity of 87.9%.

Conclusions: This study indicates that significantly increased PCT concentration is a promising predictor of systemic bacterial infection in children with CKD, with good sensitivity and specificity. This study proposes that serum PCT is a convenient index of infection in CKD children at a cutoff value of 0.5 ng/ml.

Key words: chronic kidney disease, children, infection, procalcitonin, cutoff value, hemodialysis, transplantation.

Introduction

Chronic kidney disease (CKD) is a significant public health dilemma [1] with an advanced requirement for dialysis either hemodialysis (HD) or peritoneal dialysis every year. The increased risk of infection in CKD patients has been demonstrated [2, 3], especially in those treated with chronic HD [4]. Risk markers that possibly mark this susceptibility to infection are plentiful, including [5–8] coexisting illnesses such as immunosuppressive therapy for the underlying kidney disease, uremia-induced leukocyte dysfunction, vaccine hyporesponsiveness, malnutrition, bloodstream infections fundamentally concerning vascular (fistula or catheters) access

[8, 9] and hemodialysis with frequent disturbance of the skin barrier. For all these reasons, CKD may be considered as a condition of acquired immunodeficiency [6]. Moreover, it has been reported that at the moment infection, CKD patients had a much greater risk of mortality than healthy individuals [9, 10], due to which infection is the second main cause of mortality after cardiovascular diseases [4]. Furthermore, infectious disease is a leading reason for intensive care unit (ICU) admittance and accounts for 15% to 25% of overall ICU admittance in CKD patients [11–15].

Clinical and laboratory signs of systemic infection, including hypo/or hyperthermia, apnea or tachypnea, tachycardia and increased white blood cell counts, are critical. However, their application is restricted by inferior specificity and peculiarity for the diagnosis of sepsis, as seriously sick patients often have the systemic inflammatory response syndrome (SIRS) but no infection [16–18]. Some inflammatory parameters, such as leukocyte cell count, cytokines (TNF- α , IL-1 β , or IL-6) and C-reactive protein (CRP), have been applied for the diagnosis of infection and inflammation, but their deficiency of specificity has drawn attention to the need for more specific laboratory investigations [19, 20].

Procalcitonin (PCT), the precursor protein of calcitonin, is a polypeptide of 116 amino acids (MW 13 kDa) which has been reported to be able to accurately distinguish bacterial from nonbacterial infections and other inflammation conditions [21, 22].

In contrast to C-reactive protein, PCT secretion is inhibited by interferon γ (IFN- γ), a cytokine which is manufactured during viral infections. It has been confirmed as helpful in distinguishing complications due to bacterial infections [22–24]. Serum PCT level is rising at 3 to 6 h following bacterial infection, but is not in autoimmune disease, non-infectious inflammatory responses, local infection, viral infection or sepsis. So, it might seem that PCT measurement has the ability to raise the certainty of the diagnosis of a bacterial infection greater than measuring other infection parameters, such as leukocyte counts or CRP [25].

Procalcitonin has not been widely studied in children with ESRD or renal transplant (RTx). The scarce presently obtainable studies are either comparatively small in sample size or use unrepresentative individuals [26–29]. Therefore, the comparative advantage of PCT testing in children with chronic kidney disease is not certain.

The present study aimed to identify early biological predictors of infection by determining the diagnostic significance of PCT in comparison to other traditional inflammatory factors in a considerable CKD children group, applying principles for the definitions of systemic infections and to determine an appropriate cutoff level.

Material and methods

Inclusion criteria

One hundred and two consecutive children (with suspected infection detected initially by clinical symptoms) were included in this retrospective (case-control) study during a 6-month period. All patients were treated in the Center of Pediatric Nephrology and Transplantation (CPNT), Children Hospital, Cairo University, Cairo, Egypt. Informed consent was taken from the parents of each participant. The study protocol was approved by the Ethics Committee of the National Research Center (NRC) in Egypt.

Hemodialysis children

The patients were routinely hemodialyzed three times per week in sessions lasting 4 h using polysulfone dialyzer membrane. The dialysate flow rate was 500 ml/min, blood flow rates ranged from 80 to 200 ml/min, and the ultrafiltration rate was between 300 and 1,000 ml/h. Each patient was treated with heparin just prior to the start of HD. The water treatment system consisted of simple reverse osmosis, disinfected weekly. According to the guidelines of the American Association of Medical Instruments and the European Pharmacopoeia, appropriate laboratory methods were chosen to detect bacteria (upper limit for bacterial growth < 100 CFU/ml in the dialysate) and endotoxins (upper limit 0.25 EU/ml) and other bacteria-derived substances (whole-blood cytokine induction assay). Vascular access (VA) was via arteriovenous (AV) fistulas ($n = 44$) and a tunneled permanent catheter (TPC) ($n = 11$).

Transplant children

Transplantation was performed in 46.1% of cases from living donors. All children received intravenous methylprednisolone (12.5–30 mg/day) in the first month of transplantation, and then oral prednisolone was tapered down to 2.5–7.5 mg/day in the first year of transplantation. The renal transplant patients received an immuno-suppressive regimen including a calcineurin inhibitor, mycophenolic acid (MMF), and mammalian target of rapamycin (mTOR). In transplant cases with increased PCT, cytomegalovirus and polyoma BK virus infections were ruled out if the copy number by real-time polymerase chain reaction (RT-PCR) was less than 2,000 copies/ml or with tissue biopsy.

Healthy control subjects having no history or clinical signs of renal, cardiac, cerebrovascular disease or infectious disease were recruited from the Pediatric Clinic of NRC.

Infection definition

The definition of infection was standardized using criteria stated by the Centers for Disease Control and Prevention and included bloodstream, pulmonary or intra-abdominal infections detected by radiological findings, clinical symptoms, and proven by micro-biological tests. Clinical symptoms of infection included a combination of any of the following parameters: a temperature less than 36°C or greater than 38°C, chills, or purulent sputum or urine. Chest X-rays, ultrasound examinations, or computed tomography scans were recommended when a clinically based infection was suspected, and on the basis of these examinations, prompt therapy was started. Samples from the suspected site of infection (e.g. urine, blood, or catheter tips) were taken and cultured. According to the 2001 Society of Critical Care Medicine/European Society of Critical Care Medicine/American College of Chest Physicians/American Thoracic Society/Surgical Infection Society criteria, sepsis was defined by the occurrence of infection and SIRS [30].

Definition of infection as per principles

Community-acquired pneumonia (CAP) and urinary tract infection are acute illnesses as defined previously [31, 32]. Enterocolitis was detected through diarrheal syndrome [33]. Arterial-venous fistula infections were defined by clinical inflammatory presentation and/or positive blood culture.

Peripheral blood sampling

A peripheral blood sample was obtained pre-dialysis from the hemodialysis children, transplant recipients (after transplantation) and healthy controls. Immediate centrifugation was done for 10 min at 5000 rpm at 4°C. The centrifuged serum was transferred into sterile tubes. All samples were stored at -70°C until assay.

Investigated laboratory parameters

Procalcitonin was measured using the PCT ELISA assay (Bio Vendor R&D, Germany). The normal range was defined as 0–0.2 ng/ml. For the analysis, we used two different cutoff values: (1) 0.5 ng/ml, (2) 0.75 ng/ml. High-sensitivity CRP (hs-CRP) was determined by the solid phase chemiluminescent immunometric assay (Immulite/Immulite 1000) (supplied by SIEMENS Medical Solution Diagnostics). Biochemical laboratory parameters were measured by an automatic biochemistry analyzer.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) program version 16.0 was used for analysis of data. Data were summarized as mean \pm

SD, range or percentage. Histograms and normality plots were used for evaluating the normality of data. For those data with skewed distribution, log transformation was performed before a *t*-test. Data were evaluated between the experimental groups by an independent *t*-test or Pearson χ^2 test. Sensitivity, specificity, predictive values of PCT, CRP, and white blood cells (WBC) were calculated from data of the entire cohort and by subgroups. The diagnostic accuracy of the biomarkers for diagnosis of infection was expressed as the area under the corresponding receiver operating characteristic curve (AUROC), and the respective areas under the curves were calculated with 95% confidence intervals. The different AUROCs were compared using the method described by Hanley and McNeil [34]. We used the Youden index to find the optimal threshold point from the ROC curve. Pearson's analysis was performed to correlate between PCT and different variables. A *p*-value of < 0.05 was considered statistically significant.

Results

Patients

The study group consisted of 102 children (age 2–20 years, 48 females) divided into two subgroups: 34 patients with proven infection and 68 without proven infection.

Fifty-five were on HD and 47 were RTx recipients. General characteristics of the retrospective study groups are shown in Table I. Children with proven infection had a lower erythropoietin requirement and a lower percentage of patients on dialysis (Table II). The main comorbidities of the studied CKD children were cardiovascular disease (22.55%) and viral infections (20.59%).

Infectious state

During the study period, 34/102 children had proven infections according to infection definitions with the following breakdown: 15 children with vascular access infections (44.11%), 11 with pyelonephritis (32.35%), 4 with pneumonia (11.77%), and 4 with enterocolitis (11.77%). Six of the 34 children studied with proven infections were diagnosed with sepsis (2 children on HD, and 4 transplanted recipients) in the form of pneumonia (1), pyelonephritis (3), enterocolitis (1), and AV fistula infection (1).

Procalcitonin values

Procalcitonin levels were increased (> 0.5 ng/ml) in 64.71% of the patients (66/102), with a mean \pm SD of 0.814 \pm 0.46 ng/ml. These levels were significantly higher than in controls (0.145 \pm 0.09, *p* = 0.0001). Children with proven infections had

Table I. Baselines characteristics of studied groups

Parameter	All patients (n = 102)	Controls (n = 20)	P-value
Age [years]	10.86 ±3.81	10.00 ±8.80	0.66
Gender (M/F)	54 (52.94%)/48 (47.06%)	12 (60%)/8 (40%)	0.31
BMI [kg/m ²]	21.76 ±7.21	22.88 ±7.50	0.27
Renal replacement (dialysis, %)	55 (53.40%)		
Erythropoietin requirement [IU/W]	4214.30 ±1652.75		
SBP [mm Hg]	115.11 ±14.26	94.55 ±9.80	0.03
DBP [mm Hg]	73.98 ±9.68	60.59 ±10.11	0.62
Albumin [g/dl]	3.72 ±0.53	4.92 ±0.39	0.06
Hemoglobin [g/dl]	10.52 ±1.70	14.20 ±1.50	0.27
WBC [×10 ³ /mm ⁻³]	6.94 ±2.57	3.57 ±1.42	0.002
PCT [ng/ml]	0.814 ±0.46	0.145 ±0.09	0.0001

Values were presented as means ± SD or percentage as applicable, BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, WBC – white blood cells, PCT – procalcitonin. P < 0.5 was considered significant.

Table II. Baseline characteristics of patients with and without proven infection

Parameter	Confirmed infection (n = 34)	Without confirmed infection (n = 68)	P-value
Age [years]	10.41 ±4.21	11.09 ±3.59	0.40
Gender (M/F)	7/9	17/18	0.90
BMI [kg/m ²]	20.89 ±6.04	22.33 ±7.98	0.57
Renal replacement (dialysis, %)	16 (47.01%)	40 (57.97%)	0.04
Erythropoietin requirement [IU/W]	3695.7 ±1240.78	4512.5 ±1795.61	0.05
SBP [mmHg]	111.88 ±12.03	116.80 ±15.11	0.11
DBP [mm Hg]	73.44 ±9.02	74.26 ±10.08	0.69
Albumin [g/dl]	3.68 ±0.64	3.74 ±0.46	0.62
Hemoglobin [g/dl]	10.55 ±2.04	10.50 ±1.50	0.89
WBC [×10 ³ /mm ⁻³]	7.16 ±2.76	6.83 ±2.49	0.55
PCT [ng/ml]	0.920 ±0.24	0.456 ±0.53	0.04

Values are presented as means ± SD or percentage as applicable, BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure, WBC – white blood cells, PCT – procalcitonin. P < 0.5 was considered significant.

a higher concentration of PCT (0.920 ±0.24 ng/ml) than those without (0.456 ±0.53 ng/ml), p = 0.04.

The diagnostic achievement of PCT at various cutoff levels is shown in Figure 1 and Table III.

Overall, for a cutoff level of 0.5 ng/ml, the sensitivity of the trial was 94.1% and the specificity 87.9%, while using a cutoff level of 0.75 ng/ml, as expected, decreased its sensitivity by 11.7% and specific-

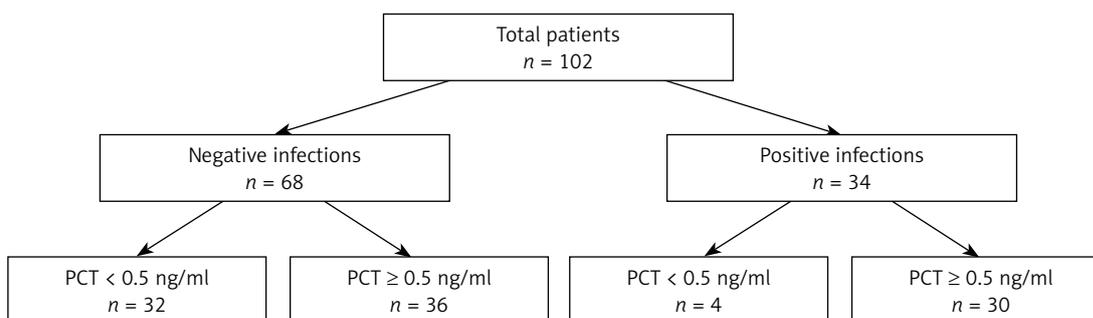


Figure 1. Diagram of diagnostic performance of serum PCT levels

Table III. Analysis of procalcitonin at various cutoff levels (*n* = 102)

PCT	Sensitivity (%)			Specificity (%)			Positive predictive value (%)			Negative predictive value (%)		
	All	D	RTx	All	D	RTx	All	D	RTx	All	D	RTx
> 0.5 ng/ml	94.1	80	94.1	87.9	14.3	96.8	52.8	86.1	50.3	47.8	14.9	50.2
> 0.75 pg/ml	82.4	73.3	76.5	66.7	2.9	74.2	56.4	97.5	51.9	44.3	0.04	48.8

D – dialysis, *RTx* – renal transplant, *PCT* – procalcitonin.

ity by 21.2%. The best thresholds for the diagnosis of infection by PCT (ROC analysis – Youden index) were 0.441 ng/ml (sensitivity 94.1%, specificity 93.9%). Also, when using the same method, we gained different cutoff levels in HD (0.381 ng/ml) and transplanted children (0.529 ng/ml).

High-sensitivity CRP values

High-sensitivity CRP was tested in only 50 children. Mean CRP serum concentration was 4.61 ±5.24 mg/l, with levels over the pre-specified cutoff (> 3 mg/l) detected in 36/50 children (72%). These levels were significantly higher than in controls (0.77 ±0.63, *p* = 0.04). Patients with proven infections had higher levels of CRP than those without proven infections (7.81 ±6.17 vs. 2.23 ±2.60, *p* = 0.0001).

For comparison of the overall performance of the infectious biomarkers independently of the pre-specified threshold levels, we tested the comprehensive degree of test performance using the AUROC. The ROC curves are shown in Figure 2 and Table IV. We found a significant difference in AUROC (*p* = 0.03, *z* statistic = 2.151, 95% CI: 0.022–0.472) for PCT (0.804, 95% CI: 0.691–0.918, *p* = 0.0001) compared to WBC (0.557, 95% CI: 0.411–0.704, *p* = 0.43), but no significant difference in AUROC (*p* = 0.85, *z* statistic = –0.1875, 95% CI: 0.2061–0.1701) for PCT (0.833, 95% CI: 0.736–0.931) in comparison to CRP (0.835, 95% CI: 0.730–0.940) – see Figure 2 and Table IV.

Sub-relationship between PCT and CRP

The sensitivity, specificity, and positive and negative predictive values for PCT and CRP in this subgroup of CKD children are shown in Table V. To compare the overall performance of the threshold

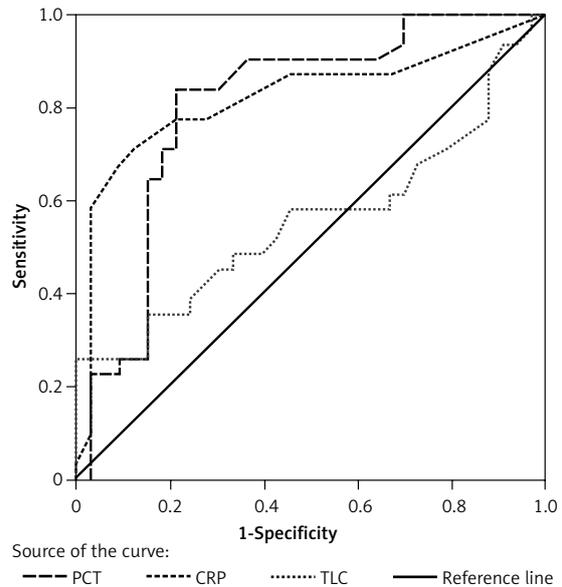


Figure 2. ROC curve for determining area under the curve for PCT, hs-CRP, and total leukocytic count

effects of the two biomarkers independently of the threshold effects, we calculated the global measure of test achievements, area under the ROC. We did not find a significant difference in AUROC (*p* = 0.97, *z* statistic = –0.0437, 95% CI: 0.1755–0.1835) for PCT (0.832, 95% CI: 0.733–0.931) in comparison to CRP (0.836, 95% CI: 0.731–0.940).

Correlation between PCT and both WBC and CRP

Of the markers that had a significant difference in the groups with and without proven infections, WBC and CRP had positive correlations with serum PCT (*r* = 0.30, *p* = 0.004 and *r* = 0.44, *p* = 0.000, respectively) (Figure 3).

Table IV. Values of area under the curve for PCT, hs-CRP, and WBC

Parameter	Area	SE	Asymptomatic sig.	Asymptomatic 95% CI	
				Lower bound	Upper bound
PCT	0.804	0.058	0.000	0.691	0.918
Hs-CRP	0.822	0.057	0.000	0.710	0.934
WBC	0.557	0.075	0.43	0.411	0.704

PCT – procalcitonin, *hs-CRP* – high-sensitivity C-reactive protein, *WBC* – white blood cells, *p* < 0.5 was considered significant.

Table V. Diagnostic performance of serum PCT levels versus hs-CRP (n = 102)

Parameter	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
PCT > 0.5 ng/ml	90.6	40	70.6	30.2
PCT > 0.75 pg/ml	81.2	17.5	83.5	17.5
Hs-CRP > 3 mg/l	78.1	25	77.1	23.9

PCT – procalcitonin, hs-CRP – high sensitivity C-reactive protein. P-value < 0.5 was considered significant.

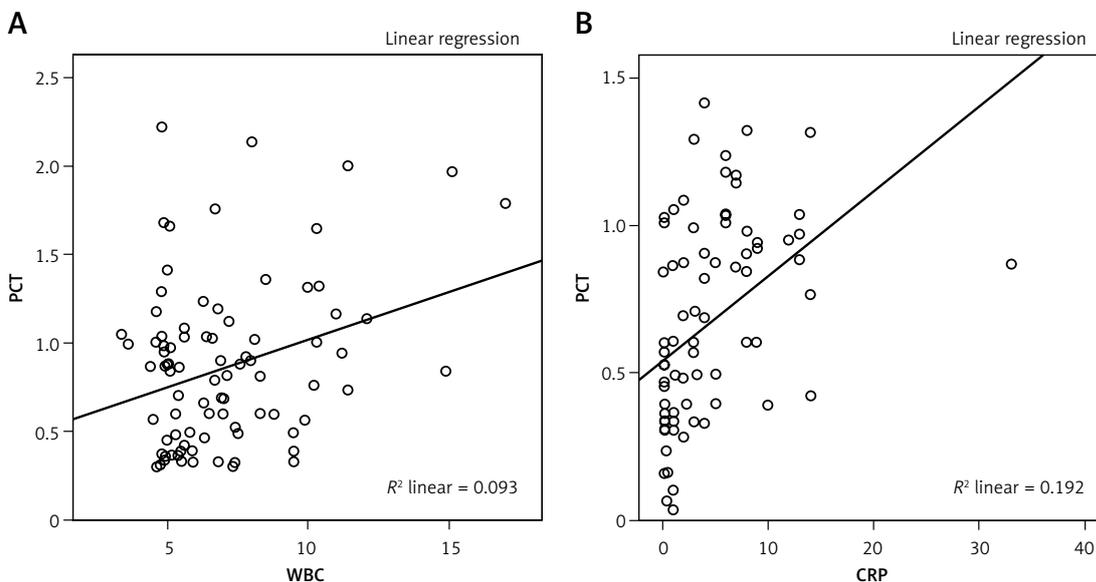


Figure 3. Correlations between procalcitonin (PCT) concentrations, with (A) white blood cells (WBC), and (B) C-reactive protein (CRP). The PCT concentration had a positive correlation with both WBC and CRP

Discussion

The inflammatory reaction manifests with redness, swelling, pain and fever because of a local reaction against infection or body tissue damage and is replenished with monocytes and neutrophils and inflammatory mediators within thirty to 60 min after the occurrence of inflammation [35, 36]. The degree of inflammation is managed by measuring acute phase reactant levels in the blood. C-reactive protein is mainly used as an index by clinical diagnosis, but it is not easy to differentiate between the symptoms and signs of infection and inflammation. Procalcitonin values elevate from 3 to 6 h following a bacterial infection or sepsis, but do not highly elevate in patients with non-infectious inflammation, viral infections, local infections or autoimmune diseases. Hence, PCT helps in the diagnosis of bacterial infections, and has greater sensitivity and specificity than CRP [37, 38].

Procalcitonin is a well-known index of bacterial infection, but in cases with multiple injuries, in severe burn cases, and in patients in the early stages of a critical surgery, PCT levels can be increased regardless of infection. Levels can also be elevated during an organ perfusion disorder or after a severe cardiogenic shock [39, 40]. Furthermore,

patients with chronic renal failure have increased PCT values that became lower after HD [41, 42]. Thus, the utility of PCT cutoff values for differentiating normal subjects from patients is impractical. In various studies, HD patients without infection had PCT levels slightly higher than normal subjects due to the occurrence of dialysis-related inflammation (e.g. an invasive procedure for HD or peritoneal dialysis (PD)), or an elevation in peripheral blood mononuclear cell counts [43].

A few studies have been done on children to detect the role of procalcitonin as a marker for inflammation and infection. Yavuz *et al.* [29] reported that CRP and PCT may not be good indicators of reflux nephropathy in vesicoureteral reflux children. Also, the study by Mahyar *et al.* [39] revealed that serum PCT and IL-1 β are not good biologic markers for differentiating acute pyelonephritis from lower urinary tract infection. Conventional inflammatory markers such as erythrocyte sedimentation rate (ESR) and CRP besides the clinical findings are more reliable for the diagnosis of acute pyelonephritis in children. According to Rahimzadeh *et al.* [26], serum procalcitonin concentration is a sensitive and promising predictor of high-grade vesicoureteral reflux (VUR). Also, Lorton *et al.* [27] concluded that increase of serum PCT in children with severe

bacterial infections is mostly massive (10-fold to 1,000-fold), indicating a low risk for false negative results in these patients. Lastly, the study by Decaluwe *et al.* [28] revealed that serum levels of PCT are associated with the severity of illness in children with diarrhea-associated hemolytic uremic syndrome.

The present study was performed on the largest group of CKD patients, in which rigorous definitions for a positive bacterial infection were applied, and provides up-to-date insight into PCT and bacterial infections in children on dialysis or with kidney transplantation and an appropriate threshold level. The results of this analysis confirmed comparable diagnostic accuracy for PCT testing in renal impaired children compared with those with normal renal function. Our data show that children with proven infections had higher values for PCT than those without, so it is a powerful biomarker for diagnosis of serious clinical bacterial infections in children with kidney transplantation or on dialysis.

As regards the reference level of serum PCT in normal subjects, at a cutoff of 0.5 ng/ml, PCT levels had a sensitivity and specificity of 94.1% and 87.9%, respectively, with an AUROC of 0.804. In renal transplant children PCT had a higher sensitivity and specificity, compared to dialysis children. The best cutoff level for the diagnosis of infection for PCT was 0.441 ng/ml in our study, which is approximately similar to the common level [44]. However, these results are different from those previously published [45].

Previous studies reported that the urine values of PCT were decreased significantly in patients with massive renal impairment. In spite of the decreased renal excretion, the clearance rate of plasma correlated exclusively weakly with renal deterioration, and clinical recommendations based on PCT may not be affected by the stage of renal impairment [46–48]. ROC curve analysis was used in this study to determine the ability of PCT to detect the occurrence of infection. At a cutoff of 0.75 ng/ml, its sensitivity and specificity were 82.4% and 66.7%, respectively, with an 11.7 % decrease in sensitivity, and was accompanied by a significant drop (of 21.2%) in specificity. Moreover, the ROC analysis supports the lower cutoff level. For these results, this study revealed that a serum PCT cutoff of 0.5 ng/ml is more suitable for the diagnosis of infection in CKD children populations. In a previous study, it was revealed that mean serum PCT decreased following the use of high-flux dialysis, but did not decrease significantly after low-flux dialysis [49]. When using high-flux membranes, serum PCT concentrations should be determined prior to the start of HD. Moreover, PCT levels varied according to the method of dialysis [50].

Other studies in the field of renal transplantation have used a range of cutoffs for PCT, for the diagnosis of infection. These values, from 0.512 to 5.9 mg/l [51, 52], are substantially similar to those detected in this study. This is possibly due to similar criteria used to diagnose infectious episodes, mainly happening in the early posttransplant phase. However, PCT checking for assessing infectious complications in renal transplant recipients must be explained carefully, during antibody therapy [53].

In our study, the number of blood leucocytes significantly increased in children with CKD compared to healthy subjects, and serum hs-CRP significantly increased in children with proven infection compared to the group without proven infection. We did not find a significant difference in AUROC for PCT compared to CRP when comparing the overall performance of the PCT and CRP markers. Though CRP is an extremely sensitive biomarker of inflammation, it cannot usually be applied to differentiate bacterial-related from other inflammations, because it acts likewise and unspecifically to acute phase reactants. We performed a previous study about the role of microinflammation as represented by CRP in VA dysfunction in maintenance pediatric hemodialysis patients, and we concluded that patients with VA dysfunction have significantly higher levels of serum IL-10 and hs-CRP. An altered immune response and microinflammation might contribute to vascular access failure [54]. The diagnostic precision of PCT and CRP is different from those found in intensive care regulation, in which thresholds of 0.6 mg/l and 7.9 mg/l for PCT and CRP, respectively, were accompanied with sensitivities of 67.6 and 71.8% and false positive rates of 39 and 33%, respectively [55]. Several factors differed significantly in the proven group, and among these factors we found positive correlations between each of WBC and CRP with serum PCT. The WBC and CRP are well-known markers of infection and were positively correlated with PCT [56]. Our data favor the idea of combining PCT and CRP in order to increase the sensitivity and specificity of the tests.

The present study has some limitations. The results represent a single-center experience of a racially homogeneous cohort and may not be generalizable to other populations, and a mixed one, including transplant recipients with immunosuppressive therapy, but it may be suitable as we are researching the Egyptian pediatric population. While screening and surveillance of CKD in adults, either population-based or targeted at-risk populations, have become important parts of CKD prevention strategies worldwide, the benefit of such programs in children is much more controversial. Tests used for CKD screening in children are usually limited to urinary dipstick protein instead of

urine albumin/creatinine ratio or creatinine-based calculation of estimated glomerular filtration rate (GFR), as recommended for adults. However, there is substantial variation in the methods used and approaches taken by different countries, and the findings have shown poor reproducibility. There is limited information on the epidemiology of the early stages of CKD in the pediatric population as it is often asymptomatic and therefore under-diagnosed and under-reported. Although some pediatric CKD registries using the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (K/DOQI) classification are beginning to emerge, only a few reports on the epidemiology of CKD stages 2 to 5 in children are available, and even less is known about low-income countries. For these countries, data are mostly obtained from reports of major tertiary care referral centers, but the validity of these data is variable.

Furthermore, though blood samples were collected during 24 h of the clinical diagnosis of infection, PCT samples might not be identical and similar, in spite of a lengthy half-life for circulating PCT (up to 25–30 h). Procalcitonin sensitivity and specificity were calculated using the first level detected and not established on a dynamic range. Notwithstanding, our study also has several strengths. There was a healthy normal control group, and rigorous definitions were used for infections (including localized) during a pertinent period of time.

In conclusion, this study has confirmed the previous findings that PCT seem to be activated in circulation of children with established chronic kidney disease. Serum PCT concentrations were significantly increased in CKD children with a bacterial infection, showing the usefulness of serum PCT as an index of infection. Furthermore, this study reveals that a serum PCT cutoff of 0.5 ng/ml is more appropriate, with good sensitivity and specificity for the diagnosis of infection in CKD children. Procalcitonin can be used as a sensitive biomarker to differentiate systemic bacterial infections from other comorbidities in transplantation of organs.

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Conflict of interest

The authors declare no conflict of interest.

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