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Role of procalcitonin in the fight against bacterial resistance. The case of the Cliniques Universitaires de Lubumbashi

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Abstract

Introduction. Procalcitonin, one of the precursors of calcitonin, is a peptide of 116 amino acids. Procalcitonin circulates in very low quantities (< 0.05 ng/ml) in the blood of healthy subjects, and is secreted mainly by the para-follicular cells of the thyroid gland. In the absence of high-performance diagnostics that can rapidly identify the etiology of fever, and given the high morbidity and mortality associated with delayed antimicrobial treatment of bacterial infection, it is necessary to diagnose with procalcitonin in order to institute preventive treatment before bacterial culture and antibiotic susceptibility testing.

Objective. The aim of our study was to contribute to the improvement of the health of the population through a better knowledge of the use of procalcitonin in the fight against bacterial resistance in the laboratory of the Cliniques Universitaires de Lubumbashi.

Methodology. This was a cross-sectional descriptive study, with prospective data collection over a one-year period. Our sample size was 49 patients selected on the basis of our inclusion and non-inclusion criteria.

Results. The maximum procalcitonin value was 16.88 ng/ml with a minimum value of 0.1 ng/ml, giving a range of over 16.78 ng/ml. *Escherichia coli* was the most isolated germ, with a percentage of over 30%. A high rate of resistance to aminopenicillins was recorded (amoxicillin 92% and ampicillin 80%).

Conclusion. Procalcitonin alone does not appear to be the absolute diagnostic marker of bacterial infection, and it is therefore necessary to combine it with other parameters to confirm the bacterial origin of an infection. PCT release is part of the host's response to aggression. Any situation generating inflammation with systemic repercussions appears to be a source of elevated PCT.

Keywords: PCT; Antibiotics; Diagnostic; Fight against; Bacterial Resistance; The Cliniques Universitaires de Lubumbashi.

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1. Introduction

Procalcitonin (PCT), one of the precursors of calcitonin (a hormone involved in calcium homeostasis), is a peptide of 116 amino acids. Procalcitonin circulates in very low quantities (< 0.05 ng/ml) in the blood of healthy subjects, and is secreted mainly by the para-follicular cells of the thyroid gland [1].

Bacterial infections can lead to elevated PCT levels. The mechanisms that trigger procalcitonin synthesis in the presence of infection, and its pathophysiological role, remain unclear. Many cells and tissues, particularly peripheral mononuclear cells and the liver, produce PCT in response to bacterial infection [2].

As traditional diagnostic tools often fail to exclude bacterial infection in a febrile state, all patients receive prolonged empirical antimicrobial therapy [3].

Various methods are available for measuring procalcitonin in blood. Among quantitative tests, the immunofluorescence procalcitonin assay is the one used in our study. This test reliably measures PCT levels quantitatively from 0.3 ng/ml upwards. The test is available from the Cliniques Universitaires de Lubumbashi for as little as ten US dollars.

In the absence of high-performance diagnostics that can rapidly identify the etiology of fever, and given the serious morbidity and high mortality associated with delayed antimicrobial treatment of bacterial infections, antibiotic treatment of certain life-threatening illnesses requires early, empirical antibiotic therapy before the results of the antibiogram are available. As a result, PCT may appear to be an early marker that can not only guide us towards an early diagnosis of a bacterial infection, but also, and above all, guide us in initiating antibiotic treatment [4].

Procalcitonin is not the only marker that can point to an early diagnosis. This is where the diagnosis needs to be combined or integrated with CRP. Often, the two go together to complete the early diagnosis.

On the other hand, as cultures and antibiotic susceptibility tests are not available in most hospitals in the Democratic Republic of Congo, PCT can be a biomarker that can help

Providers to make an early decision on initiating antibiotic treatment. This would also limit the phenomenon of persistent antibiotic resistance of certain bacterial strains in the community.

In certain diseases requiring multiple and prolonged anti-infectious therapies, PCT measurement is necessary to guide the clinician in stopping antibiotic therapy, with the aim of reducing the disadvantages of prolonged antibiotic treatment (side effects, emergence of resistance, costs).

Few studies have investigated the application of PCT in clinical practice to influence patient management and diagnosis of bacterial infections. Zeni F. et al. recently showed that in patients consulting an emergency department for lower respiratory infections, it was possible to forego antibiotic therapy without exposing them to the risk of severe infectious complications if PCT measured by KryptorPCT was below 0.1 ng/ml. This study illustrates the potential role of PCT in limiting the prescription of antibiotics when bacterial infection cannot be ruled out by conventional diagnostic means [5]. The usefulness of PCT in the diagnosis of serious infections in emergency departments and intensive care units was the subject of an article by Al-Nawas B. and Krammer I. [6].

Complementary tools to improve the initial diagnosis and follow-up of infection in patients would therefore be very useful. Various markers (IL-6, IL-8, TNF, soluble IL-2 receptors) could also be used for the same purpose. However, due to a lack of reagent availability in our environment, PCT and CRP were the only biomarkers used in this study. PCT seems to be the most promising, the other (CRP) having shown little sensitivity or even specificity. What's more, the response time to CRP infection is longer (24 - 48 hours) than that reported for PCT (< 24 hours). The other markers mentioned above (IL-6, IL-8, TNF, soluble IL-2 receptors) will be the subject of our next study.

In the DRC, and particularly in Lubumbashi, there is an obvious lack of studies in this field. Hence the need to invest in it, relying on existing advances made by other researchers.

1.1. Objectives

1.1.1. General objective

The general objective of our study was to contribute to the improvement of the health of the population through a better knowledge of the use of procalcitonin in the fight against bacterial resistance in the laboratory of the Cliniques Universitaires de Lubumbashi.

1.1.2. Specific objectives

To achieve our general objective, we set ourselves the following specific objectives:

- Determine CRP and PCT levels.
- Determine the most common germs and their antibiotic resistance.
- Correlate CRP, urea, creatinine, blood glucose, GPT and GOT levels.

2. Methodology

This is a descriptive cross-sectional study conducted over a one-year period from January 1 to December 31, 2023, on a sample of 49 selected patients, aged from 0 to over 60 years, without distinction of sex, while taking into account our inclusion criteria.

The study was carried out on patients attending the medical biology laboratory of the University Clinics of Lubumbashi, whose prescribing physician had at least requested PCT, CRP, liver and renal function tests and, above all, cultures for germ isolation and antibiotic susceptibility testing. All requisition forms for patients who did not have all the above tests were not included.

CRP and PCT were measured by immunofluorescence using a Finecare semi-automated system. The Finecare rapid quantitative test is based on fluorescence immunoassay technology. The Finecare quantitative test uses a sandwich immunodetection method.

2.1. Principle of PCT and CRP assay

When the sample is added to the well of the test cartridge, CRP or PCT antibodies from the fluorescently-labeled detector on the sample pad bind to the CRP or PCT antigen in the blood sample, forming immune complexes. As the complexes migrate onto the strip's nitrocellulose matrix by capillary action, the CRP or PCT detector antibody complexes are captured as immobilized CRP or PCT antibodies on the test strip.

So, the more CRP or PCT antigens there are in the blood sample, the more immune complexes accumulate on the test strip. The intensity of the fluorescence signal from the detector antibodies reflects the amount of PCT or CRP captured

2.2. Test procedure

2.2.1. Step 1 Preparation

Before testing, activate “Use” in the settings and save. Ensure that the lot number of the test cartridge corresponds to the ID chip and detection pad. Insert the ID chip into the Finecare FIA system.

2.2.2. Step 2 Sampling

For CRP: Sample 8.5 µl of whole blood or 5 µl of serum or plasma with a transfer pipette and add to the detection buffer tube.

For PCT: Remove 50 µl of serum or plasma with a transfer pipette and add to the detection buffer tube.

2.2.3. Step 3 Mixing

- Close the lid of the detection buffer tube and thoroughly mix the sample mixture by shaking 10 times.

2.2.4. Step 4 Loading

- Pipette 75 µl of sample mix into the sample well of the test cartridge.

2.2.5. Step 5 Testing

There are two test modes for the Finecare FIA system, Standard Test mode and Rapid Test mode.

- For Standard Test mode: Insert the test cartridge into the Finecare FIA system's test cartridge holder immediately after adding the sample mix to the single well. Press “Test” to start the test.
- For Rapid Test mode: Set the timer and countdown just after adding the sample mix to the sample well and leave at room temperature for 3 minutes for CRP and 15 minutes for PCT. Press “Test” to begin testing. The Finecare FIA system will immediately start analyzing the test cartridge loaded in the sample.
  - Results are displayed on the main screen or printed by pressing “Print”.
  - Dispose of the used test cartridge in accordance with local regulations and procedures after it has been removed from the Finecare FIA system.

Reference values for CRP and PCT.

For CRP, the normal value varies between 0 - 1 mg/dl

For PCT the normal value is between 0 - 0.5 ng/ml

Other analyses such as urea, creatinine, GOT, GPT and blood glucose were measured spectrophotometrically. Spectrometry measures the optical density or absorbance of the substance to be assayed.

Our study was authorized by the ethics committee of the University of Lubumbashi. Approval: UNILU/CEM/034/2014.

Data analysis was performed using IBM SPSS version 20.0 software.

3. Results

The results of our study are presented in the following tables and figures:

Table 1 Distribution of number of patients by quarter

Quarter	Frequency	Percentage	Cumulative Percentage
T1 2023	17	34.70%	34.70%
T2 2023	11	22.45%	57.15%
T3 2023	6	12.24%	69.39%
T4 2023	15	30.61%	100.0%
Total	49	100,0%	

The table shows that the first and fourth quarters recorded the highest number of patients.

Table 2 Distribution of patients by sex

Sex	Frequency	Percentage	Cumulative Percentage
F	31	63.27	63.27%
M	18	36.73	100.0%
Total	49	100,0%	

The results of this table show that 63% of patients were female, with a sex ratio of 1.7

Table 3 Distribution of patients by department of origin

Department	Frequency	Percentage	Cumulative Percentage
Pediatrics	15	30.61%	30.61%
Gynecology – Obstetrics	12	24.49%	55.10%
Internal Medicine	7	14.29%	69.39%
Surgery	5	10.20%	79.59%
Dermatology	4	8.16%	87.75%
Ophthalmology	4	8.16%	95.91%
ORL	2	4.08%	100.0%
Total	49	100,0%	

The results of this table show that the pediatrics department recorded the highest number of patients, 30.61%.

Table 4 Breakdown of patients by municipality of residence

Residence	Frequency	Percentage	Cumulative Percentage
Lubumbashi	16	32.65%	32.65%
Annexe	9	18.36%	51.01%
Katuba	8	16.33%	67.34%
Kenya	5	10.20%	77.54%
Kamalondo	4	8.16%	85.70%
Rwashi	4	8.16%	93.86%
Kapemba	3	6.12%	100.0%
Total	49	100,0%	

This table shows that over 30% of patients came from the Lubumbashi commune.

Table 5 Distribution of patient vouchers by category

Patient category	Frequency	Percentage	Cumulative Percentage
Subscribers.	25	51.02%	51.02%
Private	15	30.61%	81.63%
UNILU	9	18.37%	100.0%
Prodeo	0	0.00%	100.0%
Total	49	100,0%	

The results of this table show that over 50% of patients were subscribers.

Table 6 Age distribution of patients

Age group (in years)	Frequency	Percentage	Cumulative Percentage
0 – 10 years	14	25.57%	25.57%
11 – 20 years	5	10.20%	35.77%
21 – 30 years	3	6.12%	41.89%
31 – 40 years	5	10.20%	52.09%
41 – 50 years	2	4.08%	56.17%
51 – 60 years	8	16.33%	72.05%
> 60 years	12	24.49%	100.0%
Total	49	100,0%	

This table shows that the 0-10 age group was the most represented, with 14 patients out of 49, i.e. 25.57%

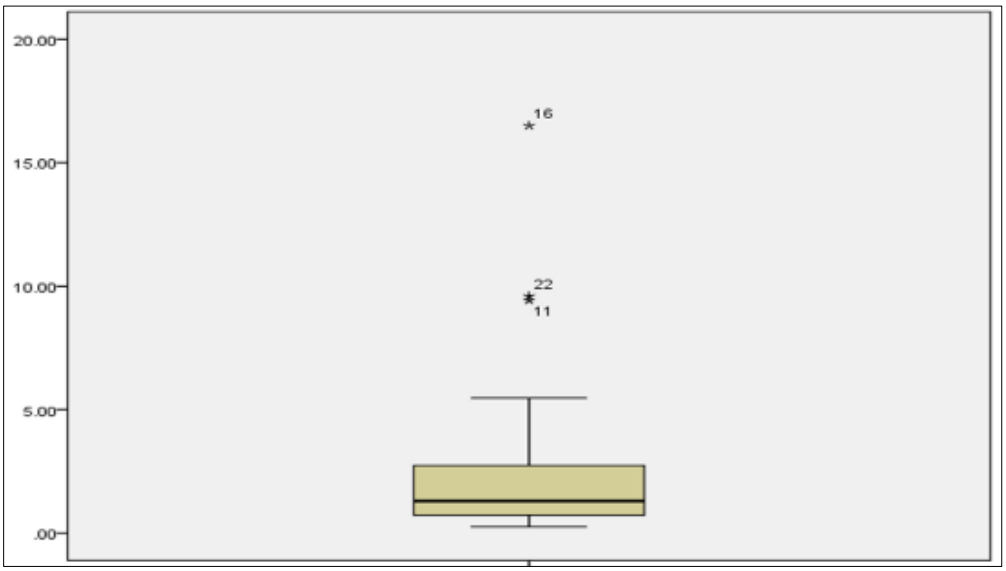

Figure 1 Moustache box of CRP level distribution.

Table 7 Percentiles of CRP level distribution in the box plot.

CRP level in mg/dl	Percentiles								
	Q5	**Q10**	**Q25**	**Q50**	**Q75**	**Q90**	**Q95**	**MIN**	**MAX**
	0.375	**0.5**	**0.71**	**1.30**	**2.73**	**5.15**	**9.51**	**0.25**	**16.50**
	RANGE: 16.25 INTERQUATILE DEVIATION: 2.02								

Comments: This whisker box (box plot) has allowed us to visualize key information about the distribution of CRP values in our series: The minimum CRP value is 0.25 mg/dl; The maximum value is 16.50 mg/dl.; The first quartile (Q1) is 0.75 mg/dl; The median (Q2) is 1.30 mg/dl.; The third quartile is 2.73 mg/dl.; The normal CRP value is 0 - 1 mg/dl.

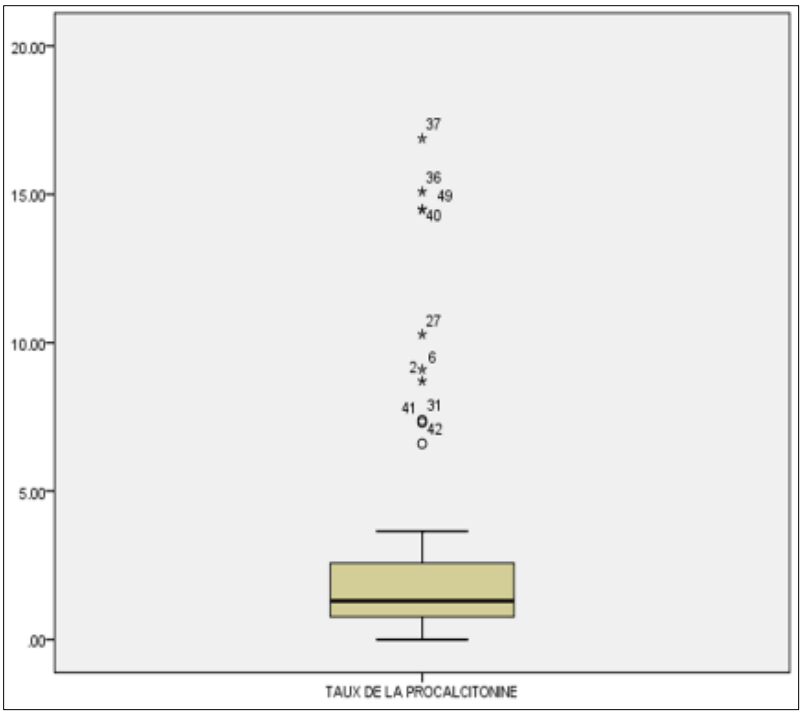

Figure 2 Box plot of PCT rate distribution

Table 8 Percentiles of PCT level distribution in box plot.

PCT levels in ng/ml	Percentiles								
	Q5	**Q10**	**Q25**	**Q50**	**Q75**	**Q90**	**Q95**	**MIN**	**MAX**
	0.1	**0.5**	**0.71**	**1.50**	**2.73**	**5.15**	**9.51**	**0.00**	**16.88**
	RANGE : 16.78 MEAN : 3.24								

Procalcitonin normal value: 0 – 0.5 ng/ml

Table 9 Distribution of cases according to germs isolated

Germs isolated	Frequency	Percentage	Cumulative Percentage
Escherichia coli	17	34.69%	34.69%
PGI	10	20.41%	55.10%
Staphylocoque spp	6	12.24%	67.34%
Klebsiella spp	5	10.20%	77.54%
Candida spp	2	4.08%	81.62%
Proteus spp	2	4.08%	85.70%
Citrobacter freundi	2	4.08%	89.78%
Enterobacter cloacae	2	4.08%	93.86%
PFPA	1	2.04%	95.90%
Proteus mirabilis	1	2.04%	97.94%
Hafnia alveï	1	2.04%	100.0%
Total	49	100,0%	

The results in this table show that Escherichia coli was the most isolated germ, with a percentage of over 30%.

Table 10 Strain resistance to standard antibiotics

Antibiotic discs tested	Sensitivity (%)	Resistance (%)
Ampicillin	10%	92%
Gentamycin	12%	76%
Amoxicillin	14%	80%
Amikacine	18%	78%
Cefixime	20%	65%
Cefotaxime	22%	82%
ciprofloxacin	23%	69%
Cefoxitin	24%	70%
Ceftazidine	24%	73%
Ceftriaxone	25%	74%
Cotrimoxazole	26%	68%
Doxycycline	26%	29%
Levofloxacin	33%	45%
Norflaxacin	53%	42%
Nitrofurantine	54%	42%
Amoxi + a. clavulanique	57%	40%
Imipenem	99,51%	0.49%
Total antibiotic discs tested	204	204

There was a high rate of resistance to aminopenicillins (amoxicillin 92% and ampicillin 80%), and an average of 204 antibiotic discs were tested for each antibiotic.

Table 11 Distribution of patients by leukocyte count

NEUTROPHIL		**LYMPHOCYTE**		**MONOCYTE**		**EOSINOPHIL**	
Class	Number	Class	Number	Class	Number	% Eosinophil	N
[30% -40%]	1	[1% -10%]	4	[1% - 5%]	5	E0%	11
[41% -50%]	4	[11% -20%]	20	[6% - 10%]	30	E1%	19
[51% -60%]	11	[21% -30%]	12	[11% -15%]	13	E2%	12
[61% -70%]	5	[31% -40%]	5	[16% -20%]	1	E3%	2
[71% -80%]	20	[41% -50%]	4	[20% -25%]	0	E4%	4
[81% - 90%]	8	[51% - 60%]	4	[25% - 30%]	0	E5%	1
TOTAL	49	TOTAL	49	TOTAL	49	TOTAL	49

This table shows that all patients had a predominantly neutrophilic WBC count

Table 12 Correlations between PCT, UREA, CREATININE, GOT, GPT AND GYCEMIA

		PCT rate	UREA	CREA	GOT	GPT	GLYCEMIA
PCT rate	Pearson correlation Meaning(bilateral) N	1 49	-0.19 0.895 49	-0.142 0.331 49	-0.126 0.331 49	-0.156 0.284 49	0.076 0.605 49
UREA	Pearson correlation Meaning(bilateral) N	-0.019 0.895 49	1 49	0.149 0.327 49	-0.057 0.697 49	0.037 0.802 49	0.019 0.897 49
CREATININE	Pearson correlation Meaning(bilateral) N	-0.142 0.331 49	0.143 0.327 49	1 49	0.097 0.509 49	-0.107 0.463 49	-0.043 0.771 49
GOT	Pearson correlation Meaning(bilateral) N	-0.126 0.389 49	-0.057 0.697 49	0.097 0.509 49	1 49	**0.765** **0.0001** **49**	-0.013 0.929 49
GPT	Pearson correlation Meaning(bilateral) N	-0.156 0.284 49	0.037 0.802 49	-0.107 0.463 49	**0.765** **0.0001** **49**	1 49	0.145 0.321 49
GLYCEMIA	Pearson correlation Meaning(bilateral) N	0.076 0.605 49	0.019 0.897 49	-0.043 0.771 49	-0.013 0.929 49	0.145 0.321 49	1 49

Comments: This table shows that there is no link between increases in PCT and increases in urea, creatinine, GOT, GPT and blood glucose. Increases in PCT have no impact on increases in the other parameters.

But there is a strong correlation between the increase in GOT and GPT, as the significance threshold is below 0.05 and the correlation coefficient is close to 1. Indeed, Pearson's correlation coefficient r varies between +1 and -1. If the correlation coefficient r is greater than 0.6, there is a high correlation, between 0 and 0.3, there is a low correlation, and between 0.3 and 0.6, there is a medium correlation. The correlation coefficient between GOT and GPT is equal to 0.765 and the p-value is equal to 0.0001, which means that the increase in GOT enzymatic activity has an impact on GPT enzymatic activity. Thus, there is a covariation between GOT and GPT enzymatic activity.

Table 13 Mean, Maximum and Minimum Values for PCT, UREA, CREATININE, GOT, GPT AND GLYCEMIA

Analyses	**Means**	**Max**	**Min**
PCT rate (in ng/ml)	3.2418	16.88	0.1
UREA (in mg/dl)	50.7347	147.00	21.00
CREA (in mg/dl)	1.8455	0.60	6.40
GOT (in IU/l)	62.5714	284.00	13.00
GPT (en IU/l)	57.7347	300.00	8.00
GLYCEMIA (en mg/dl)	127.0408	304.00	57.00

This table shows that

- The mean procalcitonin level is 3.2118 ng/ml, with a maximum value of 16.88 ng/ml. This value is well above the reference value for procalcitonin, which lies between 0 and 0.5 ng/ml.
- The mean urea value was around 50 mg/ml, with a standard deviation of 32.97 mg/dl. This mean value is higher than the normal urea value (15 - 45 mg/dl).

- The maximum creatinine value was 6.40 mg/dl, above the normal creatinine value of 0.6 - 1.3 mg/dl.
- The mean value for GOT enzyme activity was 62.5714 IU/l, above the normal value for Glutamo-oxaloacetic transaminase enzyme activity (reference values < 31 IU/l in women and < 38 IU/l in men).
- Finally, the mean blood glucose level in our patients was 127.040 mg/dl with a standard deviation of 72.91. This mean blood glucose level is close to the normal value for men, which is 60 - 110 mg/dl

4. Discussion

Due to the dry tropical climate of Lubumbashi, whose seasons are divided into rainy (September to March) and dry (April to August) semesters, the first and fourth quarters recorded the highest number of cases compared with the other quarters. This suggests that a high incidence of bacterial infections is linked to the influence of the environment on health.

Table 2 shows that over 63% of patients were female, with a sex ratio of 1.7. This trend may be linked to women's anatomy and pregnancy, which make them vulnerable to bacterial infections. On the one hand, the patency of the female urethra and the proximity of the vagina to the anal orifice favor the appearance of certain bacterial infections in women, and on the other, pregnancy diminishes a woman's immunity. This decrease in the immune system accentuates the incidence of bacterial infections in women. The same applies to children, whose immune systems are still immature, and to the elderly, whose immunity is diminished. In this category, the 0-10 and over-60 age groups accounted for the highest percentage of cases, at 25.57% and 24.49% respectively.

The maximum procalcitonin level was 16.88 ng/ml with a minimum level of 0.1 ng/dl, representing a range of 16.78 ng/ml. This value is well above the reference value for procalcitonin, which lies between 0 and 0.5 ng/dl, and Escherichia coli was the germ most frequently isolated from urine. Both endotoxin and bacteria are capable of inducing systemic PCT release [7]. One study showed that, in healthy volunteers, there is a clear rise in PCT four hours after endotoxin injection, followed by a plateau lasting from 8 to 24 hours. These kinetics have been reproduced in iatrogenic septic shock caused by *Acinetobacter baumanii* [8]. PCT could therefore be a specific marker of bacterial infection. In the same study, the PCT peak was preceded by a peak in TNFα and IL-6. Injection of pro-inflammatory cytokines alone (notably TNFα and IL-6) may induce PCT release [9]. Only the study of PCT evolution kinetics could explain its potential to differentiate between infection and inflammation [10]. On the other hand, the reduction of nitrates to nitrites by certain bacteria could underlie the increase in PCT [11].

Table 10 shows a high rate of resistance to aminopenicillins (amoxicillin 92% and ampicillin 80%). An amoxicillin resistance rate of 61.2% has been reported in El Jadida (Morocco) [36]. Even higher rates of resistance to amoxicillin, up to 75%, have been reported in other studies. These high rates of resistance justify the fact that aminopenicillins are the most widely over-prescribed antibiotics, due to their affordability. The acquisition of resistance to AMC, a highly prescribed antibiotic in Morocco, is a worldwide phenomenon reported at highly variable rates [38].

The number of cephalosporin-resistant strains was 82% for cefotaxime, followed by 74% for ceftriaxone. This is probably due to the often empirical prescription of these molecules, particularly in outpatient medicine, or in many facilities where ECBU results are awaited, or to the virtual absence of this examination and of the bacteriology department.

Regarding fluoroquinolone resistance phenotypes, resistance rates of over 40% have been observed. This proportion is very high compared with other studies, such as that carried out in Morocco, which showed only 27% resistance [39]. This reflects the high level of fluoroquinolone resistance in our country. Several mechanisms could be responsible for this resistance: (1) impermeability of the bacterial wall through reduced expression or activation of the gene coding for porins, (2) mutation of genes in the QRDR region, coding for the gyrA subunit of DNA gyrase (gyrA/B genes) or topoisomerase IV (C/E gene), or (3) acquisition or superexpression of an efflux pump reducing the concentration of fluoroquinolones in bacteria. These resistances mainly arise through successive mutations in the chromosomal genes of quinolone targets: the “first step mutation” indicates a first level of resistance. It has now been established that quinolone resistance is correlated with ambulatory quinolone consumption, at state, hospital, general practice and community levels [39].

Strict compliance with antibiotic therapy recommendations for common infections should make it possible to drastically limit the use of quinolones in urinary tract infections, by limiting indications and treatment durations, and

by practicing therapeutic de-escalation when the antibiogram allows. A major change in prescribing practices is rapidly required, in order to safeguard this very useful therapeutic class in current practice [39].

The maximum value of GOT enzyme activity is 284.0 U/l with a minimum value of 13.0 U/l, this maximum value is higher than the normal value of Glutamo - oxaloacetic Transaminase enzyme activity (Reference values < 31 IU/l in women and < 38 IU/l in men) and the mean value of GPT enzyme activity is 57.73 U/l. This value is higher than the reference value for Glutamo-Pyruvic Transaminase (< 32 IU/L in women and < 40 IU/L in men). However, we found no literature that analyzed the severity of organ dysfunction and increased PCT levels, and there are no data available on the relationship of PCT concentrations and the severity of multiple organ dysfunction during systemic and liver failure-specific inflammation.

The mean urea value is around 50 mg/dl with a standard deviation of 32.97 mg/dl (15 - 45 mg/dl: reference values) and the maximum creatinine value is 6.40 mg/dl, which is higher than the normal creatinine value of 0.6 - 1.3 mg/dl in our laboratory. Several authors have demonstrated that, although there is renal secretion of PCT, this does not appear to be its principal mechanism of elimination. Renal function has little influence on PCT levels [12, 13, and 14].

We therefore suggest that in future studies we introduce scores. Indeed, these scores are systems that assess not only the severity of systemic inflammation, but also MODS or Multiple Organ Dysfunction Syndrome (MODS) should be assessed along with PCT concentrations. In this way, imbalances between groups in the severity of inflammation or MODS can be minimized.

PCT has several advantages over CRP in critically ill patients [15, 16]. On the other hand, PCT concentrations are quite low when only moderate organ dysfunction or a low systemic inflammatory response is present. Thus, CRP cannot provide information as to a further increase in organ dysfunction and inflammatory progress, respectively, as it is already increased to its maximum values during a less severe stage of disease. Other advantages of PCT are its faster kinetics; PCT responds more rapidly than CRP to both increased and decreased inflammation. A more rapid increase in PCT was also observed in this study. This observation has already been described by several authors. For example, after the experimental administration of lipo - polysaccharides [17,18] or the accidental application of a microbial contaminated infusion [20,21], where PCT increased within 6 hours of the initial stimulus and CRP did not increase significantly until 12h after the start of induction [22,23]. Furthermore, under clinical conditions, a more rapid increase in PCT compared with CRP has been described after the onset of severe inflammation [24]. The decline in PCT concentrations occurs more rapidly than that of CRP [2, 25, and 26]. However, PCT should not be used as a surrogate marker for MODS severity, as the correlation of PCT concentrations and score values is weak [27, 28].

In a clinical study, Gendrel D reports elevated PCT levels in patients with a poor prognosis already at disease onset [27]. Other studies support the notion that the course of PCT concentrations rather than the absolute height mirrors the systemic inflammatory response and plays a major role in prognosis [30]. A recent animal study by Nylen et al. suggests that PCT may be a significant lethal factor during sepsis. In this experimental study, PCT significantly increased mortality in a hamster model of endotoxin shock, and anti-PCT reactive antiserum was protective with regard to survival [31].

And so, PCT compared to CRP is characterized by its ability to be brought to very high serum concentrations also during advanced stages of MODS and severe systemic inflammation, respectively, whereas CRP is often already in the upper concentration range, even in patients with low severity. We plan to introduce scores in future studies. These scores can guide us in distinguishing between MODS and systemic inflammation when we have plasma CRP concentrations [33, 34, and 35].

In our study, all patients had a predominantly neutrophilic WBC count. Patients with neutropenia were excluded from our study, as there is an infection-induced release of PCT even in cases of immune deficiency or leukopenia. Several studies have shown that procalcitonin determination is influenced by neutropenia, so patients with a below-normal neutrophil count were excluded from our study in order to avoid bias [36].

5. Conclusion

Procalcitonin alone does not appear to be the absolute diagnostic marker of bacterial infection, and it is therefore necessary to combine it with other parameters to confirm the bacterial origin of an infection. PCT release is part of the host's response to aggression. Any situation generating inflammation with systemic repercussions appears to be a source of PCT elevation. Nevertheless, on the basis of current data, PCT currently appears to be one of the best markers available. What's more, its measurement is one of the simplest and quickest available. Its prognostic value on admission and during treatment, whether or not bacterial infection is present, seems to have been demonstrated in several studies

we have documented. Its diagnostic value in detecting bacterial infection appears to be one of the most specific. However, the diagnostic interpretation of PCT is difficult, and needs to take into account the systemic impact of the infection and/or the presence of an inflammatory state under the skin.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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