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RESEARCH ARTICLE

# THE VALUE OF PROCALCITONIN MEASUREMENT IN MENINGITIS PATIENTS

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**ABSTRACT**

Background: Meningitis is defined as inflammation of the membranes that surround the brain and spinal cord and can occur at any age, it is caused by infectious microorganisms include (bacteria, viruses, fungi, and parasites) and non infectious include (drugs, carcinoma and inflammatory disorder).
Objective: The objective of the present study was to evaluate the value of PCT levels to discriminate between bacterial and non-bacterial meningitis patients.
Methods: A total of 40 patients with meningitis admitted to emergency department of Baghdad teaching hospital and pediatrics emergency room in child welfare teaching hospital were followed in this prospective study. Cerebrospinal fluid (CSF) sample where collected from 40 patients and serum sample collected from these patients and healthy person. NHS real-time PCR technique using to identified the type of bacteria and serum levels of PCT were measured.
Results: The diagnosis of meningitis was based on clinical findings, gram staining, culture, and chemical analysis of CSF. Twenty-eight of patients were diagnosed as bacterial meningitis and the other twelve patients as non-bacterial meningitis.
The mean PCT level in patients with bacterial meningitis was 658.00 pg/ml, and the lower level was 21. Pg/ml, while the higher level in patients with non-bacterial meningitis was 11.00 pg/ml (mean level, 5.30 pg/ml). It is clear from the range of serum PCT level that there are no overlapping values seen for serum PCT in both groups.
Conclusion: Serum PCT levels can be used in the early diagnosis of bacterial meningitis and is more valuable marker than the other predictive marker. Similarly, they may be useful in differential diagnosis of bacterial and non-bacterial meningitis to assess treatment efficacy.

**Keywords:** Meningitis, Procalcitonin

## INTRODUCTION

Meningitis defined as inflammation of the protective membranes that covering the brain and spinal cord, known collectively as the meninges [1], it may develop in response to number of causes, like most prominently bacterial as *streptococcus pneumonia*e, *Neisseria meningitis*, *Haemophilus influenzae,* are most commonly associated with bacterial meningitis [2,3] also Escherichia Coli Group B .streptococci , viruses, physical injury, cancer and drugs [4], and the incidence of meningitis disease during the first year of life is 20 times higher than in older children and adults [5], and 70% of cases occurring in children under age of 5 years [6]. Meningitis is characterized by the presence of fever, headache and neck stiffness, nausea, vomiting, photophobia, phonophobia and progressive lethargy, stupor or coma, and epileptic activity may develop [7].

Routine laboratory analysis of cerebrospinal fluid (CSF) is not efficient enough to discriminate between both bacterial and viral meningitis, especially in the early phase of the disease [8, 9].

Procalcitonin it is a 116 amino acid long peptide having a molecular weight of 13 KDa [10]. As the name suggests, it is a precursor of calcitonin, produced by the C-cells of thyroid under the control of the calcitonin gene related peptide 1 *(CALC-1)* gene [11].

Normally, the expression of the gene is found in the neuroendocrine cells of the thyroid and the lung. However, during microbial infections there is increased *CALC-1* gene expression in various extra-thyroid tissues and cells including kidneys, liver, pancreas, leucocytes, and adipose tissue with concomitant release of PCT throughout the body [12].

The secretion of PCT was found to increase in the presence of bacterial lipopolysaccharides and cytokines that are associated with sepsis [13, 14]. So the normal physiological level of PCT in serum is less than 0.1 ng/ml which can increase several folds in systemic bacterial infections [15], this increase and especially the course correlates with the severity of the condition and with mortality [16, 12].

## MATERIALS AND METHODS

A total of 40 patients aged from 18 days to 55 years, with meningitis disease who were admitted to emergency department of Baghdad teaching hospital and pediatrics emergency room in child welfare teaching hospital were followed in this prospective study. Twenty-eight patients were diagnosed as bacterial meningitis and the other twelve as non-bacterial Meningitis. The control group was revealed by 40 healthy individual whose age range was between 5 to 53 years.

Patient divided into groups infected with viral and bacterial meningitis by using and PCR technique with laboratory finding of cells, biochemical tests, and microbiology examination.

Blood serum samples were taken from all cases, peripheral leukocyte count, PCT in blood serum samples and the protein, glucose and number and type of cells in CSF samples were simultaneously investigated. Sign & Symptoms of patients and findings at the time of diagnosis, demographical data also were reported.

Procalcitonin levels were measured by using ELISA technique. Its detection when the value more than 10 pg/ml and the level in healthy individual as determined with this assay, are <10 pg/ml. CSF proteins, CSF glucose and CSF cell counts where determined by routine methods.

Statistical analysis of data was carried out in a windows setting using the SPSS version 21.0 and excel program. Differences between groups in continuous variables were tested for significance with the t-test. A p-value of $\leq 0.05$ was regarded as statistically significant.

## RESULT

### Clinical and prevalence features of all groups

The mean age group of all cases was (11.63±14.78%), ranging from 18 days-55 years and it was (25.17±12.31) for control group, ranging from 5-53 years as shown in table (1).

There was a highly significant difference between meningitis groups in respect to mean age ($p < 0.0005$).

From 40 cases with meningitis, 21 (52.5%) were males and 19 (47.5%) were females while those for control, 16(45.7 %) were males and 24 (53.3 %) were females. There was no significant difference in infection between male and female ($p < 0.05$).

Clinical presentations (e.g., fever, vomiting, and headache ) were of little assistance in differentiating bacterial from nonbacterial meningitis, The most common symptoms at the time of diagnosis in all study groups were fever (100%) of the patient followed by nausea or vomiting (62.5%) and headache (37.5%).

**Table 1: Clinical and prevalence features of all groups.**

| Study group → | Bacterial group no. 20 | | | Viral group No.=12 | Control group No.=12 |
|---|---|---|---|---|---|
| **Variable** | **S. pneumoniae** | **H. influenzae** | **Others** | | |
| Age Range (years) | (0.25-49) | (1.50-9) | (0.05-35) | (0.01 -55 ) | (5 -53 ) |
| Mean ± SD | 18.68± 16.61 | 3.75± 2.99 | 5.65±11.14 | 13,66±16.62 | 25.17±12.31 |
| Gender NO (%) | | | | | |
| Female | 7 (20.0%) | 3 (8.6%) | 4 (11.4%) | 5 (14.3%) | 16 ( 45.7 % ) |
| Male | 5 (11.1%) | 4 (8.9%) | 5 (11.1%) | 7 (15.6% ) | 24 (53.3 % ) |
| Clinical finding | | | | | |
| Fever | 22.5% | 17.5% | 30.0% | 30.0% | 0% |
| Nausea or vomiting | 32.0% | 20.0% | 16.0% | 32.0% | 0% |
| Headache | 6.7% | 2.0% | 46.7% | 46.7% | 0% |

**The laboratory findings of studied groups**:

CSF analysis of the studied patients also showed significant difference between the two groups of patients (viral and bacterial groups).

Cerebrospinal fluid finding of patients with bacterial and viral meningitis were presented in Table (2).

The mean of CSF neutrophil was detected highly significant differences ($p < 0.05$) between all groups.

Among all bacteria groups neutrophils in meningitis that cause by *S. pneumoniae* was showed highest mean (128.86±26.239), While the lymphocyte is predominantly in CSF showed in *S. pneumoniae* and *H. influenzae* were convergent (77.08± 99.784), (74.00± 76.241) respectively, also the mean of lymphocyte in other bacterial and viral groups was convergent (44.22±32.957), (31.92±29.519) respectively. So the CSF lymphocyte in all groups was increased significantly ($p<0.05$).

Elevated CSF protein (>50 mg/dl) was present in 71.4% of patients with bacterial meningitis, versus 25% of patients with nonbacterial meningitis

So mean of CSF protein was highly elevated in *S. pneumoniae* and other bacteria (103.08± 83.012) and (124.44± 88.61) respectively, followed in *H. influenzae* was (65.14± 39.334) while in viral group the mean level of protein was low (42.25± 29.407).

Decreased CSF glucose values (<45 mg/dl) were found in 50% and 70% of patients with bacterial and nonbacterial meningitis. But there was no significant differences among studied groups regarded to CSF glucose concentration at ($P > 0.05$**)** because the mean level in all groups was convergent.

Also leukocyte count >10,000 cell/mm3 is no significant differences between all studied groups ($P>0.05$).

So the CSF glucose and peripheral WBC appeared to be less efficient in the diagnosis the cause of meningitis infection.

**Table 2: The laboratory findings of studied groups.**

| Study group → | Bacterial group No.=20 | | | Viral group No.=12 | P-value |
|---|---|---|---|---|---|
| **Variables** | **S. pneumoniae** | **H. influenzae** | **Others** | | |
| CSF Neutrophil count (cells/mm$^3$) Mean ± SD | 128.86±26.239 | 19.75±33.540 | 7.00±4.000 | 1.00±0.00 | 0.010* |
| CSF Lymphocyte count (cells/ mm3) Mean ± SD | 77.08±99.784 | 74.00±76.241 | 44.22±32.957 | 31.92±29.519 | 0.013* |
| CSF Protein Lymphocyte count (cells/ mm3) Mean ± SD | 103.08±83.012 | 65.14±39.334 | 124.44±88.616 | 42.25±29.407 | 0.010* |
| CSF Glucose ( mg/ dl) Mean ± SD | 60.92±33.533 | 43.57±24.144 | 51.00±27.377 | 41.50±13.118 | 0.200** |
| WBC cells/ mm3 Mean ± SD | 17333.3±6110.1 | 18571.4±8753.2 | 19111.1±9636.4 | 17550.0±9195.7 | 0.200** |

***p value <0.05 significant ,**p value >0.05 non significant**

**Serum levels of PCT in all studied groups**

Serum PCT in all groups are summarized in Table (3) and at the time of diagnosis, PCT levels were statistically significantly elevated in patients with bacterial meningitis in comparison to PCT levels in patients with non bacterial meningitis that were low {P< 0.005}. A similar comparison between bacterial meningitis and control groups also revealed increased serum PCT levels in bacterial meningitis patients {p</0.005}.

**Table 3: Serum levels of PCT in all studied groups.**

| | Group | | | | | |
|---|---|---|---|---|---|---|
| | **S. pneumoniae** | **H. influnzae** | **Other Bacteria** | **Virus** | **Control** | **Total** |
| (PCT <10) Count | 0 | 0 | 0 | 11 | 33 | 44 |
| % within PCT | 0.0% | 0.0% | 0.0% | 25.0% | 75.0% | 100.0% |
| (PCT ≥10) Count | 12 | 7 | 9 | 1 | 7 | 36 |
| % within PCT | 33.3% | 19.5% | 25.0% | 2.8% | 19.4% | 100.0% |
| Total Count | 12 | 7 | 9 | 12 | 40 | 80 |
| % within PCT | 15.0% | 8.7% | 11.3% | 15.0% | 50.0% | 100.0% |

**DISSCUSION**

Meningitis is one of the most emergency diseases because it is a major cause of morbidity & mortality in all over world [17]. The use of biological markers, especially cytokines and acute phase proteins, have been proposed to facilitate the accuracy of the initial diagnosis of meningitis but none of them are used in clinical routine work**.**

At the time of diagnosis, the age of patients ranged from 18 days to 55 years its symmetrically to study by Tunkel et al.,2004 [18] , while the other study appeared the effect of meningitis disease only in children [19, 20, 21].

We take all ages to show what the organism is most common and what the age is more effect by meningitis diseases.

This study include 40 meningitis patients, 21 (52.5%) were males and 19 (47.5%) were females, it was found that male to female ratio is 1:1 this frequency is comparable to some extent with that of study by Al-Naddawi et al., 2008; Hamedi et al., 2012 [21, 22]

While another study appears the male more effect than female like Haider, 2013; Nashwan, 2000 and Saleem, et al., 2009 [23,24,25], this difference may be due to the difference in the nature of the society; more direct evidence for the hypothesis must come from comparative studies of the immune mechanism in the two sexes [26].

In this study, fever was the most frequent presenting symptom (70%) of bacterial meningitis, 30% of viral meningitis following the Nausea or vomiting (68.0%), (32.0%) and Headache was (55.4%), (46.7). The clinical presentation of the present study resembled to that found by Huda et al., 2012 [27], who found fever and vomiting by 100% and 61% respectively. This appears the concept role of immune system against the infection.

The typical CSF findings may not present in every patient who has bacterial meningitis and may even show a normal WBC in the CSF and/or lymphocyte predominance, especially if early in the disease [28].

Protein level in CSF in bacterial meningitis patients was higher than viral meningitis and control groups with significantly differential at p = 0.01.

The CSF glucose concentration is <40 mg/dl in approximately (50%–60%) of meningitis patients [29], and in our study the CSF glucose concentration level was decreased in all patients with bacterial meningitis and was lower than the glucose level in viral group and this agrees with the result of other study like [19,30].

One of the important results of the present study was the significant increase of PCT levels in patients with bacterial meningitis than in those with aseptic meningitis, Our findings showed a significant elevation in serum PCT levels in patients with bacterial meningitis S. pneumoniae was (328.09 ± 385.0834 pg/ml), H. influenzae was (54.06 ± 23.599 pg/ml) and other bacteria was (275.85± 443.203pg/ml) compared to aseptic meningitis (5.30 ±3.173pg/ml) and controls (16.72 ± 2.850 pg/ml).

These results are agreement with many study, one in Egypt by Eman A. El- Shami et al., 2008; and in Iran by Hamid et al.,2013, and Ray et al., 2007 in USA [31, 22, 32], considered that PCT level is higher in bacterial meningitis than in viral meningitis.

Procalcitonin (PCT) serum concentration increases in a setting of systemic bacterial infection, while patients with viral infections have normal or slightly elevated. An explanation for increased PCT levels in bacterial meningitis was a global increase of the first calcitonin gene (CALC I gene) expression and a cardinal release of PCT from all parenchymal tissues and differentiated cell types throughout the body induced by a microbial infection [12].

Also PCT is produced ubiquitously in response to endotoxin or mediators released in response to bacterial infections (that is, interleukin (IL)-1b, tumor necrosis factor (TNF)-a, and IL-6) and strongly correlates with extent and severity of bacterial infections [33]. But IFN gamma released in response to viral infection can cause a down-regulation of PCT, this makes PCT a more specific marker for bacterial infection [34].

In conclusion, Procalcitonin was a good marker for differentiating bacterial from viral infections, which is probably the most frequent dilemma encountered in clinical practice and it was the faster marker in emergency department. Further studies on large scale are needed to support our result.

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