Serum procalcitonin and C-reactive protein as a significant indicator in differentiation between bacterial and viral meningitis

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Abstract:

Background: In patients with infection of meningitis, it's difficult to determine the cause of infection. Thus, the studies continue to develop novel and fast diagnostic methods to distinguish bacterial from viral meningitis. Patients and methods: 60 meningitis patients (38 out of 60 were diagnosed with bacterial meningitis and 22 with viral meningitis), were enrolled in our study, the ages range were between 15 to 65 year, 20 healthy individuals (free any diseases) involved in the study and ages range were between 15 to 65 year. Both patients and control undergo to PCT and CRP levels assessment.

Results: The results showed 3 bacterial meningitis, 19 viral meningitis patients and 19 healthy control presented with low PCT (less than 2ng/ml) level, while 35 bacterial meningitis, 3 viral meningitis patients and 1 healthy control presented with high PCT level and the P-value was < 0.0001. Moreover, 5 bacterial meningitis, 20 viral meningitis patients and 18 healthy person appeared with low CRP level, but 33 bacterial meningitis, 2 viral meningitis patients and 2 healthy person found with high CRP (more than 10 mg/l) level, and the P-value was < 0.0001. Conclusion: We revealed to the serum PCT and CRP level test consider good differential method between bacterial and viral meningitis.

Keywords: bacterial meningitis, viral meningitis, procalcitonin and C-reactive protein.

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Introduction

Meningitis is an inflammatory reaction involving pia, arachnoid mater and the subarachnoidal space [1]. It may cause by infectious microorganism such as (bacteria, virus, mycobacteria, parasite and spirochete), other causes involve drugs induced hypersensitivity meningitis, carcinomatous, lymphomatous meningitis, or associated with inflammatory disorder e.g. sarcoidosis, Behçet's disease, systemic lupus erythematosus, Sjögren syndrome[2].

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Because of the implications of belated diagnosis of bacterial meningitis to be squeaky, others suggested that the diagnostic tool should gain about 100% sensitivity [3]. Clinical parameters, gram staining test, and presence of bacterial antigen in cerebrospinal fluid (CSF), further the using of WBC count in blood or CSF (protein level, glucose level and WBC count) which utilized alone don't displayed 100% sensitivity and specificity to recognize bacterial and aseptic meningitis [3]. In addition, distinguishing the frequently viral agents through polymerase chain reaction (PCR) isn't constantly conceivable in all organizations [4]. Consequently, intensive studies were performed in order to discover new and fast diagnostic methods to differentiate and diagnose bacterial and viral meningitis [5].

Serum procalcitonin found to has a role in viral and bacterial meningitis [1], as well as C-reactive protein consider a part of diagnosis many diseases, and monitoring of CRP levels can also play a role in determining how well a patient is responding to a particular medication [6]. Procalcitonin (PCT), a calcitonin propeptide, is believed to be synthesized in thyroid gland C cells and secreted from peripheral blood leukocytes. PCT secretion was noticed to elevate in existence of sepsis-associated bacterial lipopolysaccharides and cytokines [7, 8]. Previously, serum PCT level has been shown to increase during bacterial, parasite, or fungal infections. Previously, serum PCT levels have been shown to increase during bacterial, parasite, or fungal infections, but still normal or mildly elevated in non-infectious inflammatory reactions and viral infections [8, 9].

C-reactive protein (CRP) is one of the many proteins which can be found in human blood at varying levels [6]. This protein is produced by the liver and the fat cells in the body. The body makes C-reactive protein in response to infection, which means that elevated CRP levels can suggest a systemic infection. The concentration in the blood tends to rise with the severity of the infection, reaching a peak and then declining as the body breaks the protein down once the infection has been dealt with medications used to manage systemic infections and inflammations should cause a decrease in CRP levels [6, 10].

Patients and Methods

1- Cases and healthy individuals’ selection

The study was conducted since October 2013 up to December 2014. 60 patients presented with meningitis admitted to Baghdad teaching hospital, medical city complex, Baghdad, Iraq, were enrolled in our study. The ages range was between 15 to 65 years and mean ± SD (46.2 ± 3.27 years). 38 out of 60 were presented with bacterial meningitis also 22 presented with viral meningitis, the patients diagnosed according to the common criteria which is used in hospitals. Control group included 20 free diseases individuals with ages range between 15 to 65 years with mean ± SD (33.8 ± 1.93 years). The university and teaching hospital ethical committee approval has been obtained to carry the study, moreover, Informed consent was gained from the patients and healthy individuals to engage them in the current research.
2- Assessment of Procalcitonin (PCT) level

2 ml of blood sample were drawn from both patients and healthy control, and then sent to laboratory. Serum procalcitonin was evaluating before antibiotic injection, level of serum PCT were assessed via Analyzer luminometer apparatus using the Lumi test kit (Lumitest PCT kits BRAHMS Diagnostica, Berlin, Germany). PCT > 2 ng/ml considers positive.

3- Assessment of C-reactive protein (CRP) level

2 ml were collected from patients and healthy control subsequently sent it to laboratory, the CRP level was analyzed by CRP-latex slide agglutination method using CRP-latex by SPINREACT. CRP positive was taken at level ≥ 10 mg/l.

4- Data analysis

The data analysis was performed using software (SPSS), version 22. The frequency of ages was expressed as a Mean ± SD, otherwise the One-Way ANOVA was used to correlate the levels of PCT and CRP among patients and control. The significance level was taken at value $P \leq 0.05$.

Results

Overall, the results showed that the rates of clinical manifestation in bacterial meningitis patients higher than viral meningitis patients, as well as the features of fever, headache and meningeal irritation in both bacterial and viral meningitis patients were greater than seizure and FND as shown in Figure 1.

![Figure 1: Rate of clinical manifestation in bacterial meningitis and viral meningitis](image-url)

Lowest number 3 (7.9%) of bacterial meningitis patients appeared with low PCT (less than 2ng/ml) comparison to viral meningitis patients which were 19 (86.4%) and control which were 19 (95%), while PCT levels seemed to be high in 35 (92.1%) bacterial meningitis patients, but 3 (13.6%) viral
meningitis patients showed with high PCT level, the less number found to have high level of PCT was among control group 1(5%), the significance was ($P < 0.0001$) Table 1.

Table 1: PCT level among bacterial meningitis, viral meningitis and control group

<table>
<thead>
<tr>
<th>variables</th>
<th>Bacterial meningitis</th>
<th>Viral meningitis</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Low Procalcitonin less than 2ng/ml</td>
<td>3</td>
<td>7.9%</td>
<td>19</td>
<td>86.4%</td>
</tr>
<tr>
<td>High procalcitonin</td>
<td>35</td>
<td>92.1%</td>
<td>3</td>
<td>13.6%</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>100%</td>
<td>22</td>
<td>100%</td>
</tr>
</tbody>
</table>

The low CRP level found in 5 (13.2%) patients diagnosed with bacterial meningitis, 20 (90.9%) patients diagnosed with viral meningitis and 18 (90%) healthy control, otherwise the high CRP (more than 10 mg/l) manifested in 33 (86.8%) patients presented with bacterial meningitis, 2 (9.1%) patients presented with viral meningitis and 2 (10%) healthy control, the $P$ -value was ($< 0.0001$) Table 2.

Table 2: CRP level among bacterial meningitis, viral meningitis and control group

<table>
<thead>
<tr>
<th>variables</th>
<th>Bacterial meningitis</th>
<th>Viral meningitis</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Percentage</td>
<td>No.</td>
<td>Percentage</td>
</tr>
<tr>
<td>Low CRP</td>
<td>5</td>
<td>13.2%</td>
<td>20</td>
<td>90.9%</td>
</tr>
<tr>
<td>High CRP more than 10 mg/l</td>
<td>33</td>
<td>86.8%</td>
<td>2</td>
<td>9.1%</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>100%</td>
<td>22</td>
<td>100%</td>
</tr>
</tbody>
</table>

Discussion

For many years, the biomarkers utilization to differentiate among patients with meningitis caused by bacterial infection or viral infection followed without significant changes in such patients’ daily evaluations. In addition, the disastrous effects of having a misdiagnosis in such a situation indicate that every single test is unlikely to be confident of reliably differentiating aseptic from bacterial meningitis.

The order of frequency of CNS infections in the present study are in order of frequency; bacterial meningitis (63.6%), viral meningitis (36.7%). These rates were different from a study of Polkowska A. was carried in Poland who found that 35% of his series were bacterial infections and 49.42% per year were viral infections [11]. The higher rate of cases for viral over bacterial infections in the study of Polkowska A. is most likely due to many cases of tick-borne meningoencephalitis (Ixodes ricinus ticks) which were endemic in the north-eastern part of that country. The absence of Ixodes ricinus ticks’ incidence rate in Iraq making the bacterial infections of CNS more common than viral infections in the present study.

The present study showed that the presence of fever (more than 37.8C) occurred in 100% of patients with bacterial meningitis, 90.9% of patients with viral meningitis. Also that the fever rate in case of
bacterial meningitis was consistent with the results of Naumova EN et al., study (95%) [12]. In viral meningitis the fever rate was slightly less than Fan HW et al study (97%) [13]. The seizures rate was 7.9% in bacterial meningitis, 4.5% in viral meningitis in the present study.

This rate for bacterial meningitis was differ from the results of Pizon AF et al., study (40%) [14]. In case of viral meningitis the seizures rate was differ from the results of Power, C. study (75%) [15], the rates was less this because early treatment and diagnosis in our cases and the study of Power, C. deal meningoencephalitis more than meningitis alone and large number study.

Meningismus occurred in 86.8% of bacterial meningitis, 81.8% of viral meningitis in the present study. The meningismus rate in bacterial meningitis in the present study approximate similar the results of the study of Van de Beek, D. et al., (80%) [16]. In the present study meningismus in viral meningitis was differ from the results of DeBiasi, R. L. et al., (20%) [17].

The present study showed that the rate of focal neurological deficits on presentation was 5.3% of bacterial meningitis, 4.5% of viral meningitis. This rate was differ from the results of Thigpen MC et al., study in case of bacterial meningitis [18].

In this study showed significant PCT level among bacterial & viral meningitis as well as control group in which PCT level more than 2 ng/ml in 92% (35 from 38 patients) of bacterial meningitis, where is that high PCT was in viral meningitis 13.6% (3 from 22 patients) and in control 5% (1 from 20 patients), and this study the same as in study Taskin E et al[1] and Dubos F et al., [3].

In Cassady KA et al., study showed there is may be PCT positive more than 2 ng/ml in viral meningitis initially but with time return to normal as in this study there are 13.6% high PCT in viral meningitis but in this study concern with initially level [4].

Also, there is 5% (1 from 20 patients) control group PCT was high may be due to osteoarthritic changes or hidden infections not showed by done investigations.

About CRP, the study showed significant CRP level among bacterial & viral meningitis as well as control group in which PCT level (more than 10 mg/l) in 86.8% (33 from 38 patients) of bacterial meningitis, where is that high CRP was in viral meningitis 9.1% (2 from 22 patients) and in control 10% (2 from 20 patients), and this study the same as in Singh UK et al., study [6] and Meisner M et al study [8].

In Gendral D. et al., study showed there is may be CRP positive (more than 10 mg/l) in viral meningitis initially but with time return to normal as in this study there are 9.1% high CRP in viral meningitis but in this study concern with initially level[10].

In control group, there is 10% (2 from 20 patients) control group CRP was high may be due to osteoarthritic changes or hidden infections not showed by done investigations.
In this study the sensitivity and specificity of PCT to be positive (more than 2ng/ml) in bacterial meningitis was 92.1% and 86.4% respectively in compares with viral meningitis, which differ from the study of Alkholi UM et al., in which sensitivity 100% and specificity 66% [19].

In this study also sensitivity and specificity in CRP to be positive (more than 10mg/dl) in bacterial meningitis was 86.8% and 90.9% respectively in compares with viral meningitis which is approximately similar to study Alkholi UM found that sensitivity and specificity in CRP to be positive (more than 10mg/dl) in bacterial meningitis was 90% and 62% respectively [19].

**Conclusion**

The level of serum PCT and CRP gives a best diagnostic and prognostic indicator to distinguish between bacterial and viral meningitis rather than traditional methods such as WBC count in blood or CSF analysis.

**References**


