

## Epidemiological study of Meningitis and Role of Neopterin in its Diagnosis

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### Abstract

**Background:** Meningitis is inflammation of the meninges. The inflammation may be caused by infection, and by certain drugs. Neopterin better with C- reactive protein is suited to support the differential diagnosis of viral versus bacterial infections.

**Aim:** The study aimed at determination of epidemiological profile of admitted cases of meningitis (from two to twelve years old) and to evaluate the role of serum neopterin in differentiation between septic& aseptic meningitis.

**Patients& Methods:** Nignty meningitis cases admitted in Imbabah Fever Hospital in one year (May 2012- May 2013) and eighty one meningitis cases admitted in 1 year (May 2013- May 2014). The following had been done for all patients Full medical history and Clinical examination, Laboratory investigation including a- CBC, and Serum neopterin by ELISA of the second phase. c- CSF analysis, and Statistical analysis SPSS.

**Results:** risk factors among cases of meningitis are age<5 years, males more affected (63.3%) in the 1st phase in comparison to the 2nd phase (56.8%), there was a statistical significant difference as regard contact to ill relative with a higher percent in the 1st phase 66.2% in comparison to the 2nd phase 33.8%. There was a higher percent of viral meningitis in the 2nd phase (67.9%) in comparison to the 1st (47.8%). CSF culture: no growth (32.2% in the 1st phase comparison to the 2nd phase 14.8%), followed by St. pneumonia (9.9% in the 2nd phase comparison to the 1st phase 5.6%), then H influenza (7.8% in the 1st phase in comparison to the 2nd phase 2.5%), the lowest percentage was TB meningitis with a percent of 1% and 0% in 1st and 2nd phase respectively. There was positive correlation between the bacterial meningitis occurrence and the higher level of serum neopterin.

**Conclusion:** Meningitis is increasing worldwide in an alarming rate. Neopterin is a diagnostic marker to differentiate between viral and bacterial infections.

### دراسة انتشار التهاب السحايا ودور النيوبترين في تشخيصه

**المقدمة:** التهاب السحايا هو التهاب الأغشية الواقية التي تغطي المخ والحبل الشوكي، قد يكون سبب الإلتهاب عن طريق العدوى، من قبل بعض الأدوية. النيوبترين لوحده أو الأفضل أن يصاحبه البروتين سى التفاعلى مناسب جدا لدعم التشخيص التفريقى بين العدوى الفيروسية من العدوى البكتيرية.

**الهدف:** وصف طريقة انتشار مرض الحمى الشوكية بين كل الاطفال المحجوزة من سن (٢-١٢) فى فترة زمنية محددة فى مستشفى حميات امبابه، وتقييم الدور المحتمل للنيوبترين فى الدم للتفريق بين التهاب السحايا الصدئى والغير صدئى.

**الافراد وىرق البحث:** المرضى: تم اجراء هذه الدراسة بقسم الحمى الشوكية بمستشفى حميات امبابه وقد تضمنت هذه الدراسة مرحلتين: المرحلة الاولى حالات الالتهاب السحائى المحجوزة بالمستشفى خلال سنة (مايو ٢٠١٢- مايو ٢٠١٣)، والمرحلة الثانية حالات الالتهاب السحائى المحجوزة بالمستشفى خلال سنة (مايو ٢٠١٣- مايو ٢٠١٤).

**ىرق البحث المستخدمة:** المجموعتين: التاريخ الطبى الكامل والفحص السريرى لجميع الأجهزة، وتحليل معملية روتينية كصورة دم كامله، والنيوبترين فى الدم فى المجموعة الثانية، تحليل السائل النخاعى، والتحليل الإحصائى: تم جمع البيانات وتسجيلها على أشكال محددة.

**نتائج البحث:** ولقد وجدنا ان من اكثر عوامل الخطورة فى هذه الدراسة: السن اقل من ٥ سنوات، الذكور اكثر اصابة من الاناث، الاتصال بالحالات، الحالات فى المدارس واختلاف الفصول وخاصة فى الربيع والشتاء. نسبة الإصابة بالتهاب السحايا الفيروسي فى المرحلة الثانية اكبر من المرحلة الاولى. نتيجة تحليل السائل النخاعى هى: No growth، متبوعا ب St. pneumonia، ويليها H influenza، ويليها N. meningitides، والاقال نسبة TB meningitis ويوجد علاقة ايجابية بين التهاب السحايا البكتيرى وارتفاع نسبة النيوبترين.

**Introduction:**

Meningitis is inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges. The inflammation may be caused by infection with viruses, bacteria, or other microorganisms, and less commonly by certain drugs.<sup>(3)</sup>

In the early phases of acute bacterial and viral meningitis, signs and symptoms are often non- specific and it is not always possible to make a differential diagnosis on the basis of routine examination of CSF. In untreated bacterial meningitis, gram staining of CSF reveals bacteria in about 50- 80% of cases, and cultures are positive in at least 85% of cases. However, sensitivity of both tests is less than 50% in patients who are already on antibiotic treatment.<sup>(5)</sup> Therefore, intensive research has been carried out to find new and rapid diagnostic methods for differential diagnosis of bacterial and aseptic meningitis. Increased neopterin concentrations demonstrate an activated cell mediated immune system.<sup>(6)</sup> Neopterin alone or even better in combinations with C- reactive protein is very well suited to support the differential diagnosis of viral versus bacterial infections.<sup>(4)</sup>

**Aim Of The Study:**

1. Determination of epidemiological profile of all admitted cases of meningitis in the age group (2- 12) years old in selected period of time (5/ 2012- 5/ 2014), in Embaba Fever Hospital.
2. To evaluate the potential role of serum neopterin level in differentiation between septic& aseptic meningitis.

**Subjects And Methods**

**Design Of The Study:**

Retrospective study of the first phase and cross- sectional study of the second phase.

**Subjects:**

The present study will be conducted at the meningitis department, Embaba Fever Hospital and it will include two phases:

- ☒ First phase: Will represent meningitis cases admitted in the hospital in one year (2012- 2013).
- ☒ Second phase: Will represent the admitted meningitis cases in a period of one year (2013- 2014).

1. Inclusion criteria:

- a. Age: (2- 12 ) years.
- b. Gender: Both sexes.

2. Exclusion criteria: Patients with the following conditions will be excluded:

- a. Clinical picture suggestive of cerebro- vascular disease.
- b. Clinical and laboratory findings suggestive of tuberculous meningitis.
- c. Malignancies (including brain tumors) and other neurological insults.
- d. Autoimmune diseases as SLE and RA.
- e. Other causes of fever.
- f. Other causes of coma.
- g. Drug induced meningeal irritation.
- h. Patients receiving antibiotics.

**Methods:**

1. Full medical history and Clinical examination.
2. Laboratory investigation including:
  - a. CBC.
  - b. Serum neopterin by ELISA of the second phase.
  - c. CSF analysis

3. Statistical analysis the data were coded, entered and processed on computer using SPSS.

Ethical consideration: The objective of the study and the possible complications were explained to all patients and they were asked to sign a consent form.

**Statistical Methodology**

Data Management And Analysis: The data were coded, entered and processed on computer using Statistical Packaged for Social Science(9). The level  $P \leq 0.05$  was considered the cut- off value for significance.

**Results:**

Risk factors among cases of meningitis are age< 5 years, males more affected (63.3%) in the 1st phase in comparison to the 2nd phase (56.8%), contact to ill relative, cases attending school and seasonal variation with high percent in winter and spring. There was a higher percent of viral meningitis in the 2nd phase (67.9%) in comparison to the 1st (47.8%). CSF culture: no growth(there was higher percent in 1st phase 32.2% in comparison to the 2nd phase 14.8%), followed by St. pneumonia (there was a higher percent in the 2nd phase 9.9% in comparison to the 1st phase 5.6%), then H influenza(there was a higher percent in the 1st phase 7.8% in comparison to the 2nd phase 2.5%), the lowest percentage was TB meningitis with a percent of 1% and 0% in 1st and 2nd phase respectively. There was positive correlation between the bacterial meningitis occurrence and the higher level of serum neopterin.

Table (1) Risk factors among cases of meningitis

	First Phase (90)	Second Phase (81)	P Value	Odd Ratio	95% Ci Lower- Upper
Age< 5years	35 (53%)	31 (47%)	0.934	1.026	0.554- 1.902
Gender: Male	57(55.3%)	46 (44.7%)	0.383	1.314	0.711- 2.429
Case Attending School	56 (52.8%)	50 (47.2%)	0.947	0.979	0.528- 1.817
Case Contact	43 (66.2%)	22 (33.8%)	0.006*	0.408	0.215- 0.774
Winter	35 (54.7%)	29 (45.3%)	0.677	0.876	0.471- 1.631
Spring	33 (55%)	27 (45%)	0.648	0.864	0.46- 1.622
Summer	12 (48%)	13 (52%)	0.616	1.243	0.531- 2.905
Autumn	10 (45.5%)	12 (54.5%)	0.471	1.391	0.566- 3.418

There was a statistical significant difference as regard case contact between both phases with a higher percent in the 1st phase 66.2% in comparison to the 2nd phase 33.8%.

Table (2) Clinical Presentation among studied patients

	First Phase (90)		Second Phase (81)		X <sup>2</sup>	P
	no	%	no	%		
Fever	60	66.7	64	73.0	3.260	0.071
Stiff Neck	56	62.2	60	74.1	2.745	0.098
Seizure	41	45.6	41	49.4	0.438	0.508
Photophobia	35	38.9	2	2.5	33.350	<0.001**
Nausea, Vomiting	60	66.7	58	71.6	0.486	0.486
Abdominal Pain	30	33.3	13	16.1	6.766	0.009*
Pharyngitis	38	42.2	30	37.1	0.479	0.489
Headache	60	66.7	30	37.1	15.012	<0.001**
Rash	4	4.4	1	1.2	1.547	0.214
Petichiea	4	4.4	1	1.2	1.547	0.214

There was a statistical significant difference as regard photophobia with a higher percent in the 1st phase 38.9% in comparison to the 2nd phase 2.5% and headache with a higher percent in the 1st phase 66.7% in comparison to the 2nd phase 37.1%.

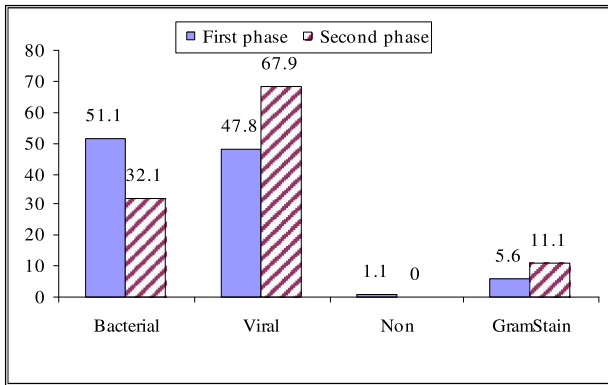


Figure (1) Causative agent among cases of meningitis.  
Table (3) CSF culture among cases of meningitis

	First Phase (90)		Second Phase (81)		X <sup>2</sup>	P
	no	%	no	%		
Staph	1	1.1	2	2.5	0.456	0.499
St. Pneumoniae	5	5.6	8	9.9	1.133	0.287
N. Meningitides	3	3.3	2	2.5	0.112	0.738
No. Growth	29	32.2	12	14.8	1.250	0.264
H. Influenza	7	7.8	2	2.5	2.410	0.121
TB Meningitis	1	1.1	0	0.00	0.905	0.341

There was a higher percent of no growth followed by St. pneumonia then H Influenza. Then N. meningitides, the lowest percentage was TB meningitis.

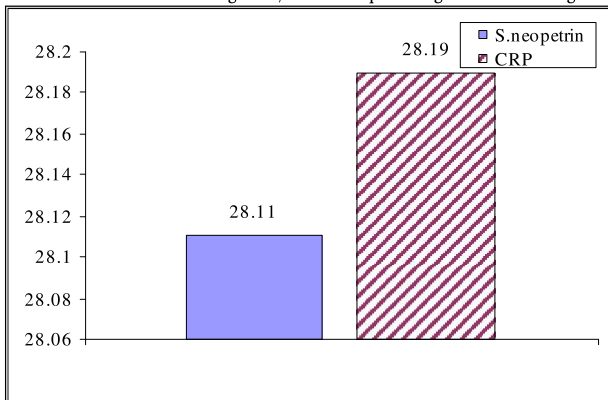


Figure (2) Serum Neopterin and CRP among the second phase of patients

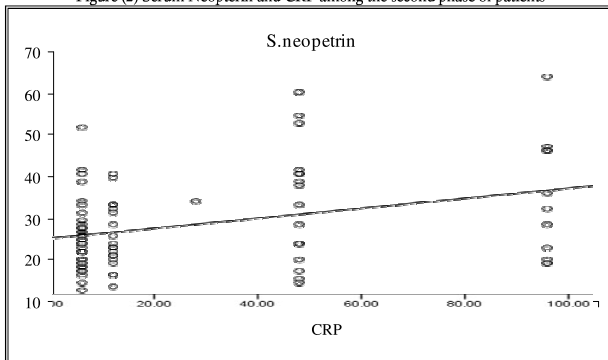


Figure (3) Positive correlation between the serum Neopterin and CRP  
Table (4) Prognosis among cases of meningitis

	First Phase (90)		Second Phase (81)		X <sup>2</sup>	P
	no	%	no	%		
Improved	66	73.3	64	79.1	0.754	0.385
Death	8	8.9	6	7.4	0.124	0.724
Neurological Complications	14	15.6	11	13.6	0.133	0.715

**Discussion:**

In the current study the age ranged from (2- 12) years with a mean of 7.2±

3.39 in the first phase in comparison to the second phase with a mean of 6.74± 3.18.

This is agreed with a study done by,<sup>(1)</sup> which stated that age is a major risk factor of meningitis: extremes of age: elderly (age> 60 years); young children); especially infants and neonates study the percentage of males was higher than females. The percentage of males was higher (63.3%) in the first phase in comparison to the second phase (56.8%), while the percentage of females was higher (43.2%) in the second phase in comparison to the first phase (36.7%).

This is agreed with a study that stated that the male predominance seen as (male: female ratio 1.8: 1) it is similar to several previous reports but it may not reflect true disease incidence. Instead, it may indicate the greater potential contact exposure of men to community cases of meningitis in particularly, and gender- based health care attitudes and practices in general, in this traditional Muslim society.<sup>(2)</sup>

In the current study we found that there was a statistical significant difference (p=0.0 06) between both phases regarding cases were in contact to ill relative, the percentage was (47.8%) in the first phase in comparison to the second phase (27.2%).

Close contact with meningitis patients, contiguous infection as sinusitis, mastoiditis and otitis media.<sup>(1)</sup>

In the current study we found that there was no statistical significant difference between both phases regarding seasonal variation, there was a higher percentage in winter (38.9%, 35.8%) in first and second phase respectively followed by spring (36.7%, 33.3%) in first and second phase respectively, while in summer were (14.4%, 14.8%) in first and second phase respectively and in autumn were (11.1%, 14.8%) in first and second phase respectively.

Cold seasonality was confirmed for meningococci and.<sup>(11)</sup> Incidence of meningitis is highest during cold months because of the greater frequency of upper respiratory tract infections (which damage the mucosal barrier or diminish the local immunity of the pharynx), closer personal contacts and poor indoor ventilation.<sup>(12)</sup>

In the current study: There was a higher percentage (67.9%) of clear CSF indicating non bacterial cases in the second phase in comparison to the first phase (48.9%) with a statistical significant difference between both phases, and there was a higher percentage (51.1%) of turbid CSF indicating bacterial cases in the first phase in comparison to the second phase (32.1%) with a statistical significant difference between both phases, while the bloody CSF indicating tuberculous cases represent only 1.1% in the first phase in comparison to the second phase (0.00%).

This goes with a study done by<sup>(10)</sup> which conclude that unlike other reports where aseptic meningitis accounted for 70- 80% of all cases of meningitis, only 50% of the children included in that study had aseptic meningitis. Most of these cases peaked during summer and early fall, a time consistent with previous reports of enterovirus meningitis.<sup>(7)</sup>

In the current study as regard CSF culture there was a higher percentage (32.2%) of no growth in the first phase in comparison to the second phase (14.8%), followed by St. pneumonia (9.9%) in the second phase in comparison to the first phase (5.6%), then H influenza (7.8%) in the first phase in comparison to the second phase (2.5%), then N. meningitides (3.3%) in the first phase in comparison to the second phase (2.5%), the lowest percentage was TB meningitis (1.1% and 0.00%) in the first and second phase respectively.

This goes with a study done by<sup>(8)</sup> which conclude that among different pediatric series, the most important causative organisms of BM are *S. pneumoniae*, *N. meningitidis*, and Hib.

In the current study the mean± SD of serum neopterin and CRP were (28.11± 12.01) and (28.19± 31.34) respectively among the second phase of patients.

There was a statistical significant positive correlation between the bacterial meningitis and the higher level of serum neopterin.

There was a statistical significant correlation between the serum neopterin and CRP.

This goes with a study done by<sup>(6)</sup> which conclude that increased neopterin concentrations demonstrate an activated cell mediated immune system. Neopterin alone or even better in combinations with C- reactive protein is very well suited to support the differential diagnosis of viral versus bacterial infections.<sup>(4)</sup>

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