Journal of Antivirals & Antiretrovirals

Ghuneim N et al., J Antivir Antiretrovir 2016, 8:1
http://dx.doi.org/10.4172/jaa.1000132

Research Article Open Access:

Epidemiology of Different Types of Meningitis Cases in Gaza Governorates, Occupied Palestinian Territory, December 2013- January 2014

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Received date: February 09, 2016; **Accepted date:** March 17, 2016; **Published date:** March 27, 2016

Abstract

Background: Meningitis remains one of the most significant infections in children. In Gaza Strip (GS), meningitis is endemic and the incidence is fluctuating from 22 to 94/100000 population. There was an outbreak of aseptic meningitis in 1997, 2004 and 2013 resulting in an elevation of the rate to higher than 100/100000.

Aim of the study: To determine and characterize the epidemiology of meningitis in GS in order to design adequate management, prevention and control strategies.

Methods and material: This study is a cross sectional descriptive study of meningitis in GS. From December 1, 2013 through January 31, 2014, data of all registered cases of meningitis in Ministry of Health pediatric hospitals were collected and analyzed. 20 cerebrospinal fluid samples (CSF) were sent to Norway through the institute of public health for viral study.

Results: During the study period, a total of 129 cases with meningitis were reported in GS. The majority of cases were male (57.4%) with a male:female ratio of 100: 74. The mean age was 28 months and infants were the most affected age group (48.8%). The majority of cases (62%) were diagnosed as non-specific meningitis and 38% as bacterial meningitis. The majority of CSF and blood cultures for bacteria were negative (96% and 97% respectively). 3 cases were diagnosed as Neisseria Meningitides by Gram staining. All these patients were hospitalized and received parenteral antibiotics. Out of 20 samples sent to Norway, seven samples (35%) were positive for enterovirus. No deaths were reported among all reported cases.

Discussion: However, we found in our study very large differences in CSF lab testing parameters with similar studies or even with the globally used cut-off between bacterial and aseptic meningitis. In GS except CSF culture no available lab tests for distinguishing different types of meningitis. Different statistical significant differences were found between the types of meningitis and different CSF or blood tests but it is not a reliable to differentiate the types of meningitis. These findings are due to the lack of a clear standard guideline for dealing with suspected cases of different types of meningitis and management of the disease.

Conclusion: Aseptic meningitis is the most prevalent type of meningitis in GS where children and infants are more at risk. No available unified and adequate standard guidelines for dealing with meningitis and the available CSF lab tests are not fully reliable for differentiation of meningitis types.

Introduction

Meningitis remains one of the most significant infections in children and despite the availability of newer antibiotics and preventive strategies, it remains an important cause of morbidity and mortality in developing countries. Meningitis is usually a complication of a primary bacteremia and has a peak incidence in children between birth and 2 years of age [1].

The incidence of meningitis during the first year of life is 20 times higher than in older children and adults [2]. More recently, the literature has reported a decline in overall incidence of meningitis from 2.00 cases/100,000 in 1998-1999 to 1.38 cases/100,000 in 2006–2007, representing a 31% drop. Incidence fell significantly in all age groups except infants aged < 2 months.

Despite advances in prevention and treatment, there are still one million cases of meningitis worldwide each year, leading to more than 200,000 deaths. The mortality rate is 3 to 19% even with treatment, and up to 54% of survivors have some neurologic disability (Figure 1) [3].

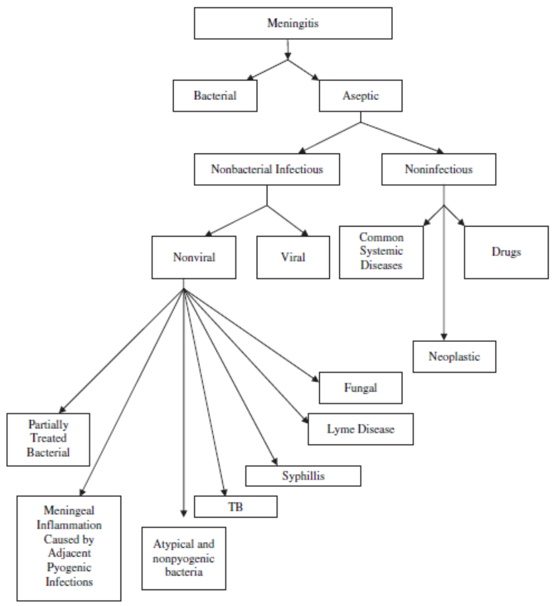

Figure 1: Causes of Meningitis.

A variety of infectious agents can cause meningitis, including bacteria, viruses, fungi, and mycobacteria (Figure 1) and may also be a manifestation of noninfectious diseases [4]. Most pathogens are specific to certain age groups, immune status, seasonality, living conditions, travel history and overall health of the individual. Viral and bacterial meningitis cannot be differentiated properly. However examination of cerebrospinal fluid could result in excluding bacterial meningitis (Table 1), and identification of the specific viral causes [5].

CSF parameters	CSF normal values	CSF values for bacterial meningitis	CSF values for aseptic meningitis
Gross appearance	clear and colorless	Purulent or cloudy	clear
CSF opening pressure	50–180 mm H_2O	Elevated (> 250 mm H_2O)	Usually normal or elevated
Glucose	40–85 mg/dL.	less than 40 mg/dL	Higher than 60% serum glucose
Protein (total)	15–45 mg/dL.	greater than 50 mg/dL	greater than 50 mg/dL
Lactate dehydrogenase	1/10 of serum level.	Highly elevated	elevated
Leukocytes (WBC)	0–5/μL (adults / children); up to 30/μL (newborns).	greater than 1000 cells/mL	10-1000 cells/mL
Gram stain	negative	Positive	negative
Culture	sterile	Positive for bacteria	Positive for viruses
Differential	60–70% lymphocytes; up to 30% monocytes and macrophages; other cells 2% or less.	Greater than 80% polymorphonuclear neutrophils	Predominance of lymphocytes

Table 1: Normal CSF values.

Bacterial meningitis

Bacterial or pyogenic meningitis is an acute meningeal inflammation secondary to a bacterial infection that generally evokes a polymorphonuclear (PMN) response in the CSF. The disease can occur at any age, but infants, the elderly and immunocompromised patients are at higher risk [6]. Although the occurrence of negative consequences of bacterial meningitis in developed countries is strongly reduced by vaccination strategies, antibiotic treatment and good care facilities, bacterial meningitis is still responsible for substantial morbidity and mortality in both developing and developed countries [7]. Bacterial meningitis can cause serious complications and its severity depends not only on the causal microorganism, but also on host immune factors, immunization status, and geographic region. The most common etiological agents are Neisseria Meningitidis and Streptococcus Pneumoniae, the latter being associated with a higher rate of severe and permanent sequelae, and mortality. The etiology of bacterial meningitis is affected most by the age of the patient. In neonates, the most common etiologic agents are group B streptococci and gram-negative enteric bacilli [6] *Escherichia coli* and other gram-negative enteric bacilli, including *Klebsiella*, *Enterobacter*, and *Salmonella*, cause sporadic disease. Other pathogens that occasionally cause meningitis in neonates, especially during outbreaks, include *Listeria monocytogenes*, *Enterobacter sakazakii*, and *Citrobacter koseri* (formerly *Citrobacter diversus*). In infants and young children worldwide, *Streptococcus pneumoniae*, *Neisseria meningitides*, and Heamophilus Influenza group b (Hib) are the most common causes of bacterial meningitis. Among children older than 5 years of age and adolescents, *S. pneumoniae* and *N. meningitidis* are the predominant causes of bacterial meningitis. The epidemiology of bacterial meningitis has changed significantly, primarily because of widespread immunization with new vaccines. Before the introduction of these vaccines, H influenza accounted for nearly half of all bacterial meningitis cases (45%), followed by *S pneumoniae* (18%) and then *Neisseria meningitidis* (14%). After the introduction of the Hib vaccine, the most common pathogens were *S pneumoniae* (47%), *N meningitidis* (25%), group *B streptococcus* (12%), and *Listeria monocytogenes* (8%).

The clinical triad of meningitis is fever, neck stiffness, and altered mental status (repeated vomiting) is, unfortunately, present in less than half of adult patients who have bacterial meningitis. Furthermore, certain patient populations, such as infants (especially neonates) and the elderly, often have a subtle presentation with nonspecific signs and symptoms. As the early symptoms and signs of bacterial meningitis are non-specific, up to 50% of cases may initially receive oral antibiotics. This partial treatment may delay the child's presentation to hospital and result in a diagnostic dilemma. The CSF findings may be altered; Gram stain and growth of organism may be negative, however antibiotics rarely interfere with CSF protein or glucose. In this situation CSF should be sent for both Polymerase Chain Reaction (PCR) and bacterial antigen detection, as these are not affected by prior antibiotic administration.

Standard case definition of meningococcal meningitis:

1. Suspected case of meningococcal meningitis:

- Sudden onset of fever (> 38.5°C rectal or 38.0°C axillary), headache, vomiting.
- Stiff neck with/ or altered consciousness or convulsion and bulging fontanel in small babies and infants.

2. Probable case of meningococcal meningitis:

- A suspected case as defined above and turbid CSF (with positive Gram stain) or clinical purpura fulminans in the absence of a positive blood culture or ongoing epidemic and epidemiological link to a confirmed case.

3. Confirmed case of meningococcal meningitis:

- A suspected or probable case with laboratory confirmation by isolation of *Nisearea meningitidis* by CSF, blood or pitechial rash culture.

Standard case definition of Other Bacterial Meningitis:

1. Suspected case of other bacterial meningitis:

- Sudden onset of fever (> 38.5°C rectal or 38.0°C axillary), headache, vomiting.
- Stiff neck with/ or altered consciousness or convulsion and bulging fontanel in small babies and infants.

2. Probable case of other bacterial meningitis:

- A case with turbid CSF or a positive antigen test in CSF.

3. Confirmed case of other bacterial meningitis:

- A suspected or probable case with laboratory confirmation by isolation of causative agent from CSF.

Aseptic meningitis

Aseptic meningitis is the most common type of meningitis caused by infections other than bacteria and viruses are the most common causes. Viral meningitis should be differentiated from the broader category of aseptic meningitis. Although patients with aseptic meningitis by definition have negative bacterial cultures, the clinical picture of meningitis is not always caused by a virus and is not always infectious [8]. Viral meningitis is often assumed to be a largely benign disease. Aseptic meningitis is subdivided into two categories: nonbacterial meningeal infections (typically viral or fungal meningitis), and noninfectious meningeal inflammation from systemic diseases (such as sarcoidosis), neoplastic disease (leptomeningeal carcinomatosis or neoplastic meningitis), or drugs [9]. Distinguishing between bacterial and aseptic meningitis in children in the emergency department could contribute to limiting unnecessary antibiotic use and hospital admissions. However, studies attempting to document the timing of transition from CSF PMN to mononuclear cells report conflicting results. Whereas some suggests that the transition occurs 8 to 24 h after presentation, others failed to find a correlation between the duration of symptoms and CSF PMN predominance [10].

The exact incidence is difficult to determine since many cases of viral meningitis are not reported to public health authorities and many cases are probably undiagnosed because this self-limited disorder often resolves without progression of symptoms. Viral meningitis occurs with a peak monthly incidence of 1 per 100,000 persons in temperate climates. Viral meningitis is more common in the summer and early fall. Most cases of viral meningitis (75-90%) are caused by viruses called "enteroviruses" with both epidemic and endemic patterns, in patients of all ages [11]. The enterovirus genus includes coxsackievirus, echovirus, poliovirus, and human enteroviruses 68 to 71. Adenovirus, mumps, measles, herpes simplex virus-2 (HSV-2), varicella, and arboviruses can also cause meningitis. Humans are the reservoir for enteroviruses, mumps, measles, herpes simplex, and varicella viruses. Person-to-person transmission varies, depending on the particular virus, and may include fecal-oral (enteroviruses), through airborne (measles, varicella), respiratory droplet (enteroviruses, mumps), and direct contact (mumps, measles, herpes simplex, varicella). The virus is frequently spread to others by contact with feces, especially among small children who are not toilet trained and to adults who change diapers of an infected infant. The virus is present in the feces of an infected person for weeks. The incubation period for viral meningitis is variable. For most enteroviruses, it is 3–6 days. For most arboviruses, it is 2-15 days. Viral meningitis is usually self-limited and resolves without treatment, although case reports suggest that treatment is indicated and beneficial in certain clinical scenarios.

Standard case definition of Aseptic Meningitis:

1. Suspected case of aseptic meningitis:

- A case of fever (> 38.5°C) and neck stiffness with/ or altered consciousness or convulsion and bulging fontanel in small babies and infant.

2. Probable case of aseptic meningitis:

A suspected case with one or more of the following:

- Normal CSF glucose and normal or mild increase in CSF protein (> 50 mg/dl), moderate increase CSF cells (< 500/mm^3) and lymphocyte predominance (> 50%).
- Epidemiological link to a confirmed case or ongoing epidemic.

3. Confirmed case of aseptic meningitis:

- A suspected or probable case with laboratory confirmation or negative culture from CSF.

Situation in Gaza Strip

Palestine consists of two geographically separated areas: West Bank (WB) and Gaza Strip (GS). Palestine as other countries in the Middle East falls in the region where meningitis is endemic. The Gaza strip is considered as a risky area for high endemecity of different aspects of meningitis due to overcrowding where the population density is around 4429 inhabitants per sq km. During the last four years, there was a clear increase of the reported cases of all types of meningitis. According to the epidemiological sheet, meningitis classified as meningococcal, hemophillus influenza type B, other bacterial and aseptic meningitis. The situation of all types of meningitis in GS as the following:

Meningococcal diseases

The situation of meningococcal diseases in the Eastern Mediterranean Region varies considerably from one country to the other. The disease is endemic in many countries including Palestine. In West Bank (WB), sporadic cases are reported with an incidence varies from 0.1 to 0.8 per 100.000. But in GS, the disease is endemic and the incidence varies from 6.8 to 10 per 100.000 (Figure 2). The majority of cases were Meningococcemia with high CFR (from 8-25%) and comparing to the reported incidence in WB, there still a big gap between the incidence in WB and GS. And till now, the epidemiology of meningococcal disease in Palestine is incompletely understood.

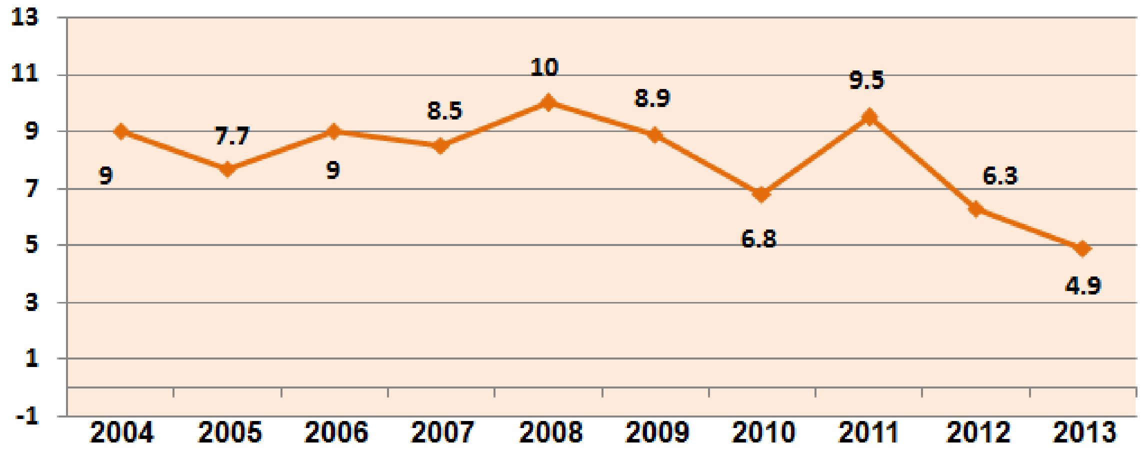

Figure 2: Annual incidence rate per 100.000 of Neisseria Meningitides diseases in GS, years 2004-2013.

Hemophillus Influenza B meningitis

In GS, since the introduction of conjugate Hib vaccine in the national EPI in 2007 (three doses at 2, 4 and 6 months), Hib meningitis registered cases dramatically decreased and had nearly been eliminated. Before 2007, the incidence reached 1.46 per 100.000 population but after this date it decreased to zero in some years (Figure 3). During 2013, a total of 4 cases were reported among adults and infant who did not received the vaccine.

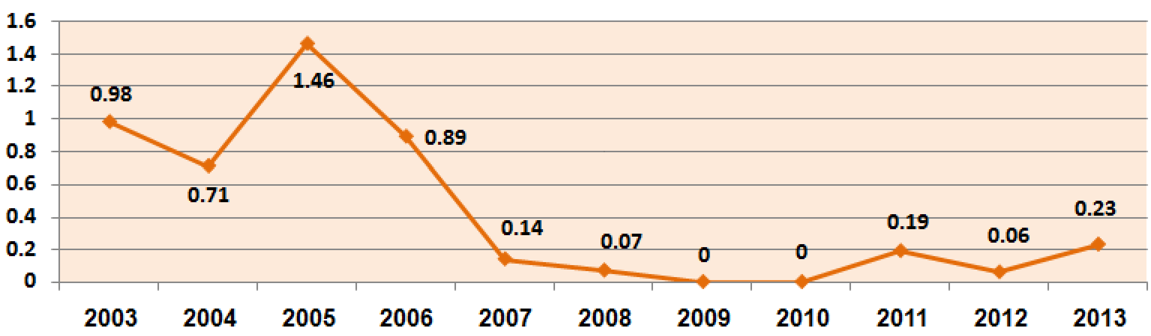

Figure 3: Annual incidence rate per 100.000 of Hemophillus Influenza B Meningitis in GS, years 2003-2013.

Other bacterial meningitis

There was an increase of reported cases of other bacterial meningitis during the years 2011-2012 (Figure 4) in Gaza governorates. All cases were diagnosed clinically with elevation of preliminary lab tests (CSF WBC, protein and glucose) but the majority of cultures were negative. In 2013, a slightly decrease of reported cases was noticed.

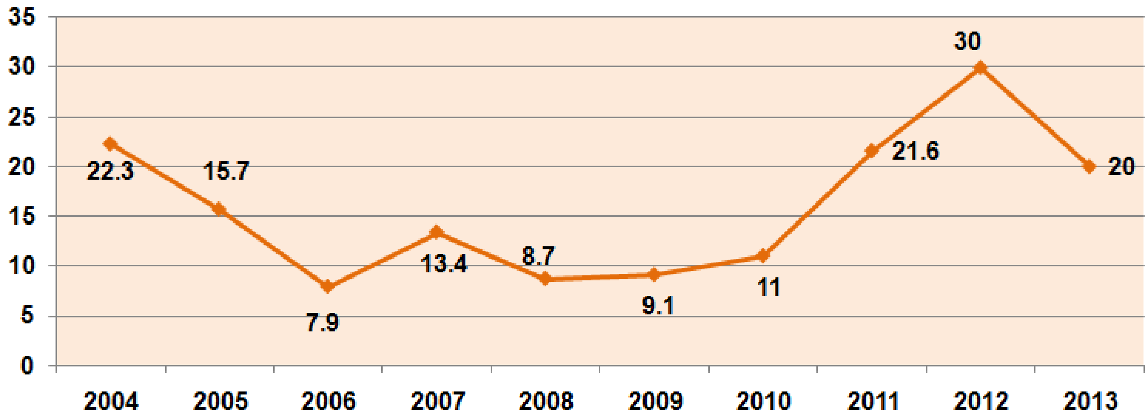

Figure 4: Annual incidence rate per 100.000 of other bacterial Meningitis diseases in GS, years 2004-2013.

Viral meningitis

Viral meningitis is considered one of the endemic diseases in Palestine with some seasonal variation. The majority of viral meningitis cases (more than 72%) are reported in spring and summer seasons. The incidence of the disease in Gaza Strip is increasing during the last 5 years (Figure 5). In 2008 the incidence was 13.3 increased to 159 in 2013.

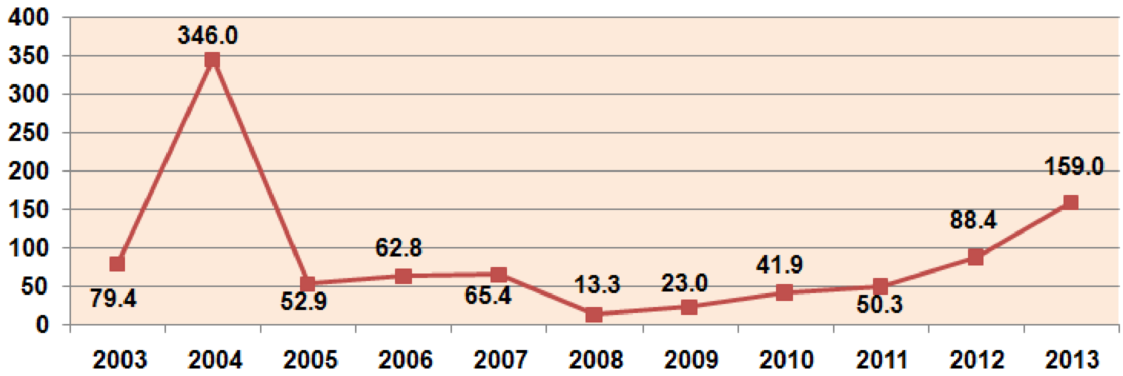

Figure 5: Annual incidence rate per 100.000 of viral meningitis in GS, years 2003-2013.

All reported cases were diagnosed based on clinical picture, CSF findings (measurement of cells, protein and sugar levels), negative CSF culture and for some cases gram stain was negative. As there is no confirmatory tests in Gaza strip for this disease, all cases were considered as probable aseptic meningitis cases. Some specimens were sent to Israeli hospitals for viral study but no viruses were isolated.

Although the majority of cases most probably are viral, there are also cases with a classic clinical picture of bacterial meningitis, but with a negative blood and CSF cultures. Whether this is a false negative examination or other cause is unclear. In order to identify the epidemiology of meningitis and to make the study useful, a collaboration with Norwegian Institute of Public Health (NIPH) was established.

Aim of the Study

This study aims to identify and characterize the different aspects of meningitis in Gaza Strip in order to design adequate management, prevention and control strategies.

General objective

To study the epidemiology of different aspects of Meningitis in GS.

Specific objectives

- To determine the most etiological agents of meningitis in GS.
- To determine the most affected age groups.
- To determine the geographical distribution of different aspects of Meningitis in GS.
- To evaluate the adopted guidelines for diagnosis and management of meningitis in GS.

Methodology

Study design

This study is a cross sectional study because cross sectional study is relatively easy to conduct, economical, carried out over a short period of time, and useful for investigating of different exposures as well as interventions.

Study population

The study population included all patients with meningitis disease who were admitted to the main pediatric hospitals in Gaza Strip.

Time of the study

The study was conducted from December 1, 2013 to January 31, 2014.

Place of the study

The study was carried out at Gaza Strip where the main four pediatric hospitals were included in the study. An ethical written letter was sent to the Directors of the Hospitals asking to facilitate the task for collecting the needed data from the files. These hospitals are El-nasser, Naser, European Gaza Hospital (EGH) and Kamal Edwan.

Sample size

All patients admitted to the hospitals and diagnosed with meningitis were included in the study as a sample size. According to the hospitals records, there were 129 patients.

Selection criteria

Inclusion criteria:

All reported meningitis cases during the period from December 1, 2013 – January 31, 2014 who were admitted in all pediatric hospitals in Gaza Strip are eligible to be included in the study.

Data collection

Data were collected by administering the questionnaire prepared by MOH for reporting meningitis cases. All patients who were admitted to the hospital as meningitis and underwent lumbar puncture as part of their diagnostic evaluation were followed. For all cases demographic, clinical and laboratory data (for CSF: cell count with differentiation, glucose, total protein, culture and for blood: WBC, glucose and culture) were collected.

For CSF culture: Specimens are usually collected in there sterile Tubes, labeled 1, 2 and 3 in the order in which they are drawn, tube 1 for chemistry and serology , while tube 2 is used for cell count and differential and tube 3 for microbiology. CSF specimen cultures on blood, MacConkey, Chocolate agar and Thioglycolate broth. Then the plates incubated for 24 hrs at 37°C in CO_2 incubator.

For blood culture: Blood should be collected before antimicrobial treatment has been started. Specimens are usually collected in two bottles, aerobic and anaerobic. The bottles then incubated for 24 hour before plating to enhance the growth of bacteria. Then aerobic bottle plate on blood agar, MacConkey and chocolate in CO_2 Incubator for 24 hour. Anaerobic bottle incubates anaerobically on blood agar for 48 hours. The negative bottle should be re-incubated and tested after one week before discarded as negative culture.

Data entry

Over-viewing of the questionnaires was the first step prior to data entry. The useable number of questionnaires was 129. This step was followed by designing an entry model using the computer software Statistical Package for Social Sciences (SPSS), version 13. Data cleaning was done through checking out a random number of questionnaires and through exploring descriptive statistics and frequencies for all variables.

Data analysis

The researcher used SPSS version 13 for analysis, many different statistical tests were used through frequency of the study items, description of the study population. Frequency, and Cross-tabulation of the results were used to demonstrate the study items. Appropriate advanced statistical analysis was conducted to explore the potential relationships between variables. Therefore, an independent T-test, Chi-square and One way ANOVA (Including LSD-Post Hoc test) tests were carried out to investigate the relationships between variables.

Ethical matters

1. An official letter of approval to conduct the research was obtained from the Helsinki Committee-Gaza Strip (Ethical committee).

2. An ethical written letter was sent to the Directors of the Hospitals asking about facilitating the task of collecting needed information from the files.

3. All the relevant ethical concepts were considered: Respect for people and respect for truth.

4. Anonymity and confidentiality was maintained.

Results

From December 1, 2013 through January 31, 2014, a total of 129 meningitis cases were reported in GS from pediatric hospitals. Among these cases, aseptic meningitis was most common where 62% (80 cases) of cases were diagnosed, followed by other bacterial meningitis 24.8% (32 cases) and 13.2% (17 cases) as meningococcal meningitis. The majority of cases (57.4%) were male with a male:female ratio of 100:74. Infants were more affected age group (48.8%), followed by age group 1-5 years (36.4%) and age group more than 5 years (14.7%). Age varied between 2 weeks to 151 months (12.5 years). Mean age was 28 months and median age was 16 months (Table 2).

Variables	Category	Meningococcal Meningitis		Bacterial meningitis		Aseptic meningitis	
		No	%	No	%	No	%
Month of notification	Dec-13	8	47.1	21	65.6	39	48.8
	Jan-14	9	52.9	11	34.4	41	51.3
Sex	Male	10	58.8	22	68.8	42	52.5
	Female	7	41.2	10	31.3	38	47.5

Age group	Infants	7	41.2	15	46.9	41	51.3
	1-5 years	5	29.4	12	37.5	30	37.5
	More than 5	5	29.4	5	15.6	9	11.3
Residency	North	5	29.4	0	0	3	3.8
(Governorate)	Gaza	3	17.6	9	28.1	32	40
	Mid-Zone	3	17.6	2	6.3	18	22.5
	Khan-Younes	6	35.3	6	18.8	22	27.5
	Rafah	0	0	15	46.9	5	6.3

Table 2: Socio-demographic characteristics of the study population.

The majority of cases (34.1%) were reported in Gaza governorate followed by Khan-Younes governorate (26.4%). In North governorate only 6.2% of cases were reported.

Patients presented with the following major clinical symptoms: fever (85.3%), vomiting (48.8%), drowsiness (25.6%), headache (16.3%), diarrhea (7.8%), skin rash (5.4%), neck rigidity (4.7%) and plugging fontanel (2.3%).

The majority of CSF and blood cultures for bacteria (96% and 97% respectively) were negative. All these patients were hospitalized and received parenteral antibiotics.

During the study period, out of 20 CSF samples which were sent to Norway through NIPH for viral study, seven samples revealed enterovirus and no other microorganisms were isolated.

Meningococcal meningitis

During the study period a total of 17 (13.2%) cases were positive for Neisseria meningitidis. The majority of reported cases (53%) were diagnosed as meningococcal septicemia while 47% were diagnosed as meningococcal meningitis. There was a male predominance (59%) with a male:female ratio of 100: 70. Age varied from two months to 12 years. The mean age of cases was 43 months while the median age was 38 months and the age distribution showed that it occurred mainly among infants (41%). The disease was reported mainly in Khan-Younes (35.3%) and northern (29.4%) governorates. The main symptom was fever (94%). Skin rash were noticed among 41.2% of cases. CSF cells vary from 800 to 40.000 cells/mm^3 with a mean CSF cells of 10.884 with 63% neutrophiles. The mean CSF sugar was 26 mg/dl and CSF protein was 222 mg/dl. The majority of cases were diagnosed by skin smear (41.2%) or gram stain (29.4%). Out of 17 CSF cultures, only three cultures were positive. Serogrouping was done for 3 cases (17.6%) and showed only serogroup B. The mean blood WBC was 12*109/l. Blood sugar varied from 70 to 181 mg/dl with a blood sugar mean of 96 mg/dl. Two cases with meningococcal septicemia among males were died with a case fatality rate (CFR) among all cases of 11.7% (22.2% among meningococcal septicemia, zero% among meningococcal meningitis).

Other bacterial meningitis

A total of 32 children were diagnosed as other bacterial meningitis (24.8%). There was a male predominance (68.8%) with a male: female ratio of 100:45. Age varied from less than one month to 12 years. The mean age of cases was 30 months while the median age was 16 months and age distribution showed that it occurred mainly among infants (46.9%). The disease was reported mainly in Rafah governorate (46.9%) followed by Gaza governorate (28.1%). The main symptoms were fever (84.4%) and vomiting (40.6%). CSF cells varies from 12 to 25.600 cells/mm^3 with a mean CSF cells of 2020 cells/mm^3 with 44% neutrophiles. The mean CSF sugar was 60 mg/dl and CSF protein was 76 mg/dl. Appropriately, all specimens were cultured and no bacterial growth was shown; only 2 CSF cultures were positive (one aged one month with Pseudomonus spp. and the second aged two months with Klebsella). Blood WBC varied from 3 to 19*109/l with a mean blood WBC of 9.7*109/l. Blood sugar varied from 54 to 132 mg/dl with a mean of 92 mg/dl. Only one blood culture was positive (a case aged one month with *E.coli*). The majority of cases were diagnosed clinically or by exclusion. No deaths were reported among these patients.

Aseptic meningitis

A total of 80 children were identified with aseptic meningitis (62%). There was a male predominance (52.5%) with a male: female ratio of 100: 90. Age varied from less than one month to 12 years. The mean age of cases was 24 months while the median age was 12 months. The disease was reported mainly in Gaza (40%) and Khan-Younes (27.5%) governorates. The main symptoms were fever (83.8%) and vomiting (52.5%). CSF cells vary from 2 to 4.100 cells/mm^3 with a mean CSF cells of 271 cells/mm^3 with 52% neutrophiles. The mean CSF sugar was 57.8 mg/dl and CSF protein was 52 mg/dl. Blood WBC varied from 3 to 24*109/l with a mean blood WBC of 10*109/l. Blood sugar varied from 55 to 135 mg/dl with a blood sugar mean of 88 mg/dl. The majority of cases were diagnosed clinically or by exclusion. No deaths were reported among these patients (Table 3).

Variables	**Bacterial Meningitis**	**Aseptic meningitis**	**P value**
	No = 49	No = 80	
Age (months)	34 ± 39	24 ± 29	0.009
Gender (M/F)	32/17	42/38	0.15
CSF WBC count (106/1)	5095 ± 8434	271 ± 557	0
Percent Neutrophils in CSF	51 ± 30	52 ± 19	0
CSF protein (mg/dL)	127 ± 214	52 ± 42	0.002
CSF glucose (mg/dL)	48 ± 29	57 ± 15	0
Leukocyte count (109/1)	10.5 ± 5.6	10 ± 5	0.115
Blood glucose (mg/dL)	93 ± 39	87 ± 18	0
CSF/blood glucose ratio	0.58 ± 0.37	0.67 ± 0.20	0.003

Table 3: Patients' characteristics of blood and CSF findings of bacterial and viral meningitis (mean, standard deviation and p-value).

Discussion

The study revealed that most cases of meningitis in children are aseptic caused by enterovirus. Despite that no specific treatment for enteroviral aseptic meningitis is available and most patients completely recover on their own, all children in our study were treated by antibiotics for 5-7 days. This constitutes a source of high hospital occupancy rates, increased health costs and parental stress. On the other hand, the up use of antibiotics will increase the possibility of occurrence of resistant bacterial strains, failure to promptly diagnose and treat bacterial meningitis can have devastating consequences.

According to our results, children and mainly infants are more at risk for meningitis and male were more susceptible but there was no significance differences between the two genders. The study shows that for all patients suspected as having meningitis, CSF and blood samples are sent to the laboratory for testing. For clinicians, clear consensus guidelines are exist for management of bacterial meningitis, but not for aseptic meningitis, which are most of the patients had. The ultimate confirmation of this diagnosis is CSF bacterial culture. However, physicians make treatment decisions before culture results are available, and they don't change their decision according to the cultures results.

Despite that a statistical significant differences were found between types of meningitis and different preliminary CSF or blood tests, the study revealed that the CSF and blood preliminary lab results (WBC, protein and sugar) alone cannot reliably differentiate bacterial and enteroviral meningitis. Several studies showed that the CSF preliminary lab results alone could not reliably differentiate bacterial from other types of meningitis. Patients with meningitis exhibited a wide range of CSF values for WBC, glucose and protein, and these values overlapped significantly between bacterial and aseptic meningitis. Lindquist study showed that WBC count, total protein and glucose levels were often unreliable tools for differential diagnosis. The study confirms that no CSF test is fully reliable in distinguishing bacterial meningitis from other forms of meningitis [12].

Other study found that CSF WBC count was significantly higher in patients with bacterial meningitis compared to patients with aseptic meningitis. The study concluded that a cutoff value of 321 CSF WBC count was found to be a useful and rapid diagnostic test to distinguish between bacterial and non-bacterial meningitis in children [13].

In their study, Graham and Murdoch concluded that enteroviral meningitis frequently occurs in the absence of either CSF pleocytosis or elevated protein levels, especially in young infants which reinforce earlier observations that the CSF profile alone cannot reliably differentiate enteroviral and bacterial meningitis and the value of performing an enteroviral polymerase chain reaction (PCR) as an additional rapid diagnostic test should be emphasized, regardless of the CSF profile [14].

However, we found in our study a very large differences when testing CSF parameters with a similar studies or even with the globally used cut-off. CSF findings showed a higher mean of CSF WBC count in all types of bacterial than aseptic cases (5095 vs. 271 cells/mm^3; P< 0.000). The globally used CSF WBC cut-off differentiating bacterial from viral meningitis is 1000 cells. In our study for bacterial meningitis, only 40% had a CSF WBC count higher than 1000 and for viral meningitis, about 95% had a CSF WBC count lower than 1000. Using one sample T-test to compare diagnosis with the CSF WBC count at cut-off of 1000 was highly statistical significant of 0.000. The fact that this parameter was statistically significant was a surprise to us as it is not a reliable factor to differentiate the types of meningitis.

In actual practice based on our study, the diagnosis of bacterial meningitis is recommended at a cut-off value of CSF WBC less than 2650 cells/mm^3 (using one sample T-test) and the diagnosis of aseptic meningitis is recommended at a cut-off value of CSF WBC more than 400 cells/mm^3. This cut-off is far away from the internationally accepted values and they are not sufficient to include all cases of suspected even bacterial or aseptic meningitis.

Hidetaka et al. studied CSF/Blood sugar ratio as an indicator for bacterial meningitis. The study concluded that this ratio may be a better single indicator for bacterial meningitis and it should be considered as a timely diagnostic indicator of bacterial meningitis and it may prove reliable even after patients have received antimicrobials prior to a lumbar puncture [15]. Using independent samples T-test to compare diagnosis with the CSF/Blood sugar ratio was also highly statistical significant of 0.003. The globally used CSF/Blood sugar ratio cut-off differentiating bacterial from viral meningitis is 0.4. For bacterial meningitis about 62% had the ratio higher than 0.40 but for viral meningitis, about 94% had a ratio higher than 0.40.

A study held by Abro et al. noticed significant increase in CSF protein level in bacterial meningitis as compared to the viral meningitis, an observation which is also reported by the other investigators [16]. Mulford et al. found that value of CSF protein levels was not a good predictor of enteroviral central nervous system infection, with low sensitivity and specificity for diagnosis in all age groups, whether used by itself or when interpreted in conjunction with the CSF white cell count [17]. Based on our study, the CSF protein level was high in bacterial than viral meningitis patients, with a mean of 127 ± 214 vs. 52 ± 42 mg/dl and this difference was statistically significant (p value < 0.002).

Our study confirms that no CSF preliminary tests are fully reliable in distinguishing bacterial meningitis from aseptic meningitis. Other blood tests were also performed but the results were nonspecific. Almost none of the blood chemistries showed any significant difference. These finding could be due to the lack of a clear standard guideline for different types of meningitis.

Conclusion

Our study concluded that:

- Aseptic meningitis is more common than bacterial meningitis and, although rarely life-threatening, it can negatively affect public health status.
- Data about the real situation of aseptic meningitis (mainly viral) in GS still poor.
- No unified guideline for using clinical findings and preliminary lab tests in differentiation of bacterial and aseptic meningitis.
- Lack of accurate tools (highly sensitive lab tests) differentiating bacterial from aseptic meningitis leads to overuse of antibiotics and high hospital beds occupancy rates.
- Because no single laboratory value can differentiate bacterial and aseptic meningitis, multivariable approaches combining clinical picture, CSF analysis results with a serum laboratory values, patient age and month of presentation in necessary.

Recommendations

- Adoption of a unified guideline for dealing with different types of suspected meningitis.
- Introducing of highly sensitive and specific diagnostic tools for accurate diagnosis of bacterial and aseptic meningitis
- Conducting a prospective operational study with a larger sample size for good estimation and differentiation of different types of meningitis disease.
- Improving of the personal and environmental hygiene to decrease prevalence of Aseptic meningitis.

Acknowledgement

This work was supported by the Palestinian Health Research Council (PHRC) through a grant from the Arab Medical Union to support the Applied health Researches. The researchers would like to thank PHRC and the Arab Medical Union for their support.

References

1. John O, Cline D, Tintinalli E, Kelen G, Stapczynski J (2007) Emergency Medicine Manual, Sixth edition. American Collega of Emergency Physicians. The McGraw-Hill companies.
2. Vokshoor A (2004) Viral meningitis: Article by MD, Staff, Department of neurosurgery, Woodland Hills, medical Center.
3. Scolnik N, Albert R (2008) Essential Infectious Disease Topics for Primary Care. Human press, USA.
4. Mandle G, Bennett J, Dolin R (2005) Principles and Practice of Infectious Diseases, Sixth edition. Elsevier's Health Sciences Rights Department, USA.
5. Mamishi S (2013) Direct Serotyping of Enteroviruses in Cerebrospinal Fluid of Children With Aseptic Meningitis. Jundishapur J Microbiol 9: e7852.
6. Chávez-Bueno S, McCracken GH Jr (2005) Bacterial meningitis in children. Pediatr Clin North Am 52: 795-810, vii.
7. De Jonge RC, van Furth AM, Wassenaar M, Gemke RJ, Terwee CB (2010): Predicting sequelae and death after bacterial meningitis in childhood: A systematic review of prognostic studies. BMC Infect Dis 10.
8. Traint V (2005) Viral Meningitis. The Health Care of Homeless Persons-Part 1-Viral Meningitis.
9. Sharon E (2008) Acute Bacterial Meningitis. Emergency Medicine Clinics of North America 38: 281-317.
10. Shah S, Hodinka R, Turnquist J, Elliott M, Coffin SE (2006) Cerebrospinal fluid mononuclear cell predominance is not related to symptom duration in children with enteroviral meningitis. J Pediatr 1: 118-121.
11. MDPH (2006) Guide to Surveillance, Reporting and Control. Massachusetts Department of Public Health, Bureau of Communicable Disease Control, Jamaica.
12. Lindquist L, Linne T, Hansson L, Kalin M, Axelsson G (1988) Value of cerebrospinal fluid analysis in the differential diagnosis of meningitis: a study in 710 patients with suspected central nervous system infection. EJCMID 7: 374-380.
13. Águeda S, Campos T, Maia A (2013) Prediction of bacterial meningitis based on cerebrospinal fluid pleocytosis in children. Braz J Infect Dis 17: 401-404.
14. Graham AK, Murdoch DR (2005) Association between cerebrospinal fluid pleocytosis and enteroviral meningitis. J Clin Microbiol 43: 1491.
15. Hidetaka T (2013) Cerebrospinal fluid/blood glucose ratio as an indicator for bacterial meningitis. Am J Emerg Med, Elsevier Inc.
16. Abro A, Abdou A, Ali H, Ustadi A, Hasab A (2008) Cerebrospinal Fluid Analysis: Acute Bacterial versus Viral Meningitis. Pak J Med Sci 24.
17. Mulford W, Buller R, Arens M, Storch G (2004) Correlation of Cerebrospinal Fluid (CSF) Cell Counts and Elevated CSF Protein Levels with Enterovirus Reverse Transcription-PCR Results in Pediatric and Adult Patients. J Clin Microbiol 9: 4199.