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Original Article

Epidemiology and Risk Factors Associated with Developing Bacterial Meningitis among Children in Gaza Strip

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Abstract

Background: Bacterial meningitis is still the leading cause of high morbidity and mortality among the children. The present study was conducted to determine the epidemiology, clinical characteristics of bacterial meningitis and to evaluate the risk factors associated with developing the infection.

Methods: This cross sectional study was conducted in three hospitals of Gaza strip –Palestine during the period 2009. All the children with clinical diagnosis of meningitis /meningoencephalitis admitted to these hospitals were included in the study. They were subjected to clinical examination as well as CSF bacteriological and serological investigations.

Results: During the period (2009), 1853 patients were admitted to the hospitals with suspect of meningitis by pediatricians, 73 (3.9%) proved by culture to be acute bacterial meningitis, of these patients 62% were males and 38% were females. The common isolated pathogens were *Neisseria meningitides* (47.9%), *Streptococcus pneumonia* (15.1%), *Haemophillus influenza* (13.7%), *E. coli* (11.0%), *Enterobacter* spp. (6.8%), *Citrobacter* spp. (2.7%), *Providencia* spp. (1.4%), and *Pseudomonas aeruginosa* (1.4%). The common recorded symptoms were fever (78%), neck stiffness (47%), vomiting (37%), poor feeding (19%), and irritability (16%). Statistical analysis showed that there was statistical significance associated developing of infection with malnutrition (low hemoglobin level), high house crowdness and irritability (P-value <0.05). The ANOVA statistical analysis showed that *S. pneumonia* has an impact on developing low hemoglobin level and leukocytosis.

Conclusion: *N. meningitides* is still dominant and needs vaccination. The risk factors should be taken into consideration in any future plan.

Keywords: Meningitis, Septic meningitis, Risk factors

Introduction

Acute bacterial meningitis (ABM) is an important cause of childhood mortality and those who survive are at a higher risk of developing permanent neurological disability. Worldwide meningitis was estimated to cause 1, 73, 000 deaths in 2002, most of them were children from the developing world (1). In the high-mortality countries of the eastern Mediterranean region bacterial meningitis accounted for 23,000 (2.5%) of the 0.96 million deaths caused by infectious diseases in the region and contributed 13.3% of death due to meningitis worldwide (1). The annual incidence of bacterial meningitis in USA before the introduction of Hib conjugate vaccines was between 30-70/100 000 (2). Bacterial meningitis affects 35.000 Europeans each year and has a mortality rate of about 20% (3). In 2011 in Poland, it was recorded 2915 cases of meningitis and/or encephalitis. This included 1438 cases of viral etiology, 888 of bacterial etiology (4). There is variation in the incidence of bacterial etiological agents in different countries. A study conducted in Europe and Mediterranean region during 2007 found that *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* type b were most commonly associated with bacterial meningitis accounting for almost 90% of reported cases of acute bacterial meningitis in infants over 60 days of age and young children(5). In contrast, another study was carried out in eastern of Mediterranean region during 2005-2010 found that the most commonly isolated pathogens were *S. pneumoniae* (27% of confirmed cases), *N. meningitidis* (22%), and *H. influenzae* (10%) (6). In the Middle East region different studies have been carried out in order to estimate the rate of infection and to find out the etiological agents. Accordingly *N. meningitides*, *H. influenzae* and *S. pneumoniae* were the predominant pathogens with different proportions (7-10). During the last two decades witnessed major advances in the understanding of the etiology and pathophysiology of bacterial meningitis; however, the major breakthrough was in the prevention of meningitis with the introduction of the Hib conjugate vaccine in the early 1980s. This resulted in a significant decrease in the incidence of bacterial meningitis in areas where routine vaccination of infants was instituted (11-12). Although diagnostic performance has recently improved by using new diagnostic methodologies (13, 14), the immediate management is usually decided upon treatment before a certain diagnosis is known and started considering only simple findings of cerebrospinal fluid (CSF) examination. At this time, the emphasis is to firstly not miss a bacterial with antibiotics or inappropriately prescribe corticosteroids for an uncontrolled viral infection. This decision can be difficult to make since CSF results often overlap between the two categories (15, 16). In order to help to distinguish bacterial and viral meningitis, academic algorithms (17, 18) and scoring tools have been proposed (19).

In Gaza Strip, few studies conducted to emphasis the etiologic agents of bacterial meningitis with the risk factors, therefore this study aimed to find out the different bacterial agents and the risk factors might be contributed in the development of such infection.

Materials and Methods

From January to December 2009, active surveillance of acute bacterial meningitis among children admitted to Gaza strip pediatrics hospitals was undertaken. Gaza Strip was divided into 5 geographic areas (Governorates). North and middle geographic regions were selected to represent the population characteristics of the country. Two hospitals, Al Nasser and Al Dora hospitals were selected to participate in the survey. These centers serve ≈62% of the entire pediatric population of Gaza strip. Approval was obtained from the Ethical Committees of the participating centers and Ministry of Health. In each hospital, suspected cases of acute bacterial meningitis were identified by using inclusion Criteria used for of identification of bacterial meningitis cases, the presence of a clinical picture compatible with bacterial meningitis and cerebrospinal fluid (CSF) neutrophilic pleocytosis of at least 100 neutrophil per cubic mm (presumptive) and then confirmed positive CSF culture for bacterial agents (20).The clinical symptoms were diagnosed by a pediatrician based on the following criteria: any sign of meningitis: fever [axillaries measurement >38°C], vomiting [>3 episodes in 24 h], headache, meningeal irritation signs [bulging fontanel, Kernig or Brudzinski signs, or neck stiffness]) in children >1 year of age fever without any documented source; impaired consciousness (Blantyre Coma Scale <4 if <9 months of age and <5 if >9 months of age). For each suspected case, demographic data were recorded by using a standardized questionnaire approved by experts in Pediatrics.

Epidemiology and statistics

Demographic data collected included age and sex, house crowdness the residents in a house rooms with two categories a-<3individual per room and b->3individual per room, mother education (elementary, secondary schools and university), malnutrition (anemia), family income (low, moderate and high according to local master of living).

In the hospitals, sterile CSF was placed in suitable transport or holding media (usually trypticase soy broth or thioglycollate broth), and rushed to the hospital laboratory that works 24 hr a day.

All CSF samples received at the laboratory were processed immediately. The macroscopic appearance of the CSF was recorded. A total count of CSF cells and differential count were done using a haemocytometer and standard methods. The CSF samples were subjected to centrifugation, the resultant smear was Gram stained and examined microscopically. The procedure used for microbiological analysis was sediment from a centrifuged CSF specimen cultured on specific culture media, the isolated pathogens were identified by specific biochemical tests, API system and specific antisera. The biochemical tests used for detection of Bacterial meningitis in CSF were Glucose level and Protein level..The CSF-total-blood glucose and protein were computed. The Chi square and Odds ratio tests were applied to examine any significant association that may exists between each of the demographical, clinical development of Bacterial infection. Also Anova test was used to find out the impact of the three main pathogens on development of Anemia and Leukocytosis.

Results

Out of the 1853 suspected cases bacterial meningitis based on inclusion criteria with presence of cells >100 in CSF and were confirmed by culture in 73(3.9%) patients. Table 1 shows the age distribution and the Gender of the suspected cases.The data obtained demonstrated that there were 45(62%) males and 28(38%) females. Male to female ratio was 1.6:1.0, 42% of the cases were male less than 2 years while 80% of the cases were male less than 4 years. At the same time, 46% of the cases were female less than 2 years while 82% were female less than 4 years of age.

Table 2 illustrates the causative organisms *N. meningitides* (47.9%), *S. pneumoniae (15.1%), H. influenzae*(13.7%), *E. coli*(11.0%), *Enterobacter* sp. (6.8%), *Citrobacter* sp. (2.7%) *Providencia* sp. (1.4%) and *P. aeruginosa* (1.4%).

Table 1: Distribution of bacterial meningitis cases by age group and gender

Age group (yr)	Total number	Male Meningitis cases	%	Total number	Female Meningitis cases	%
1month-2 Y	602	19	3.16	409	13	3.18
2-4 Year	319	17	5.33	188	10	5.32
4-6 Year	131	5	3.82	77	3	3.89
6-8 Year	30	2	6.67	25	1	4.0
8-12 Year	47	2	4.25	25	1	4.0
Total	1129	45	3.98	724	28	3.87

Table 2: The isolated species from the clinical samples

Isolated Pathogens	n	%
N. meningitides	35	47.9
S. pneumonia	11	15.1
H. influenza	10	13.7
E.coli	8	11.0
Enterobacter spp.	5	6.8
Citrobacter spp.	2	2.7
Providencia spp.	1	1.4
Pseudomonas aeruginosa	1	1.4

Abbreviations. N=*Neisseria*, S=*Streptococcus*, H=*Haemophilus*

Table 3 illustrates the socio-demographic factors that might be contributed in developing of bacterial meningitis. The statically significance associated with developing of infection was obtained with malnutrition (low hemoglobin level) *P*-value<0.001and high house crowdness *P*-value 0.037. Simultaneously, the risk factors were represented by Odds ratio (>1.0), malnutrition showed a risk factor for developing of bacterial meningitis Odds ratio 2.7 followed by house crowdness odds ratio 1.7 and low family income odds ratio 1.6 (Table 3).

Table 4 illustrates the direct effect of the isolated pathogens on the development of anemia while Table 5 shows the effect of the same pathogens on development of leucocytosis in infected patients; both analyses demonstrated clearly that *S. pneumonia* was the significant factor in development of these pathological effects.

Table 6 illustrates the symptoms accompanied the meningitis cases, the fever was the most frequent symptom followed by neck stiffness and vomiting, other minor symptoms were poor feeding and irritability.

Table 3: The demographic characteristics and the risk factors associated with developing of bacterial meningitis

Variables	Total no cases	Meningitis cases	Percentage	*P*-value	Odds ratio	95%C.I
Malnutrition/(Hemoglobin)						
Yes	840	50	6.0	<0.001	2.62	1.58-4.31
No	1013	23	2.3			
Family income						
Low	1070	50	4.7	0.068	1.59	0.96-2.63
High Moderate	783	23	2.9			
House Crowdness						
Per room						
≤3.0						
>3.0	803	23	2.9			
	1050	50	4.8	0.045	1.66	1.01-2.74
Gender						
Male	1129	43	3.8	0.728	0.92	0.57-1.48
Female	724	30	4.1			
Mother education						
Elementary						
Secondary	660	30	4.5	0.34	1.26	0.78-2.03
University	563	20	3.6			
	630	23	3.7			
Other diseases/RTI						
Septicemia	300	14	4.7	0.98	0.99	0.51-1.94
UTI	370	20	5.4	0.40	1.32	0.69-2.53
	140	4	2.9	0.16	0.48	0..16-1.3

Abbreviations : RTI= Respiratory Tract Infection, UTI =Urinary Tract Infection/P-value: significant at 0.05, CI= Confidence interval

Table 4: Pairwise comparison among differences of three pathogens in anemic patients

Organism I	Organism J	Mean difference I-J	SE	*P*-value
N.meningitides	*H. influenza*	0.15857	0.32598	1.000
	S.pneumonia	0.79403	0.31367	0.043
H. influenza	*N.meningitides*	-0.15857	0.32538	1.000
	S.pneumonia	0.63545	0.39649	0.345
S.pneumonia	*N H. influenza*	-0.79403	0.31367	0.043
	.meningitides	-0.635456	0.39649	0.345

Abbreviations :STD= Standard deviation

Table 5: Pairwise comparison among differences of three pathogens in relation to leukocytosis in CSF

Organism I	Organism J	Mean difference I-J	STD Error	*P* value
N. meningitides	*H. influenza*	1904-286	1241.443	0.393
	S.pneumonia	-1972-987	1196.749	0.043
H. influenza	*N.meningitides*	-1904-286	1241.443	0.393
	S.pneumonia	-3877-273	1512.752	0.044
S.pneumonia	*N H. influenza*	1972-987	1196.749	0.315
	.meningitides	3877-273	1512.752	0.040

Table 6: The Clinical Symptoms associated of Bacterial meningitis

Clinical Symptoms	n	%
Fever	57	78
Vomiting	27	37
Neck stiffness	34	47
Irritability	12	16
Poor feeding	14	19

Discussion

An accurate laboratory confirmation of the etiology in acute bacterial meningitis (ABM) is essential to provide optimal patient therapy, appropriate case contact management, and reasoned public health actions, it also provides information upon which to base decisions regarding immunization programs, especially for countries without routine vaccination against the main acute bacterial meningitis pathogens (21, 22). The present cross sectional study showed the pattern of bacterial meningitis in children younger than twelve years of age and reported the pattern of the disease in district hospitals which may reflects the pattern of the disease in the central and north catchment areas of Gaza strip.

In our study, only 73 (4%) cases proved to contain viable bacterial pathogens out of 1853 confirmed cases by cells in according of inclusion criteria of probable ABM cases. The infection rate recorded is low in comparison to big number of suspected specimens by cells. Reasons as reviewed in other studies for low CSF culture yield are low bacterial load, use of antimicrobial agents prior to CSF collection, poor culture media (23), poor culture facility such as non-availability of special media, stored in unsatisfactory conditions, samples refrigerated before plating, delayed and faulty inoculation, lack of transport media and inadequacy in processing of CSF specimens (24), lack of 24 hours facility for processing CSF samples (25). In our study, the probable cause was the use of antibiotics prior hospitalization. It is well known that meningitis developed as a complication for initial infection like pneumonia, sepsis, and otitis. Therefore, these infections might unwell treated (26, 27). Forty five (62 %) of cases in our study were male. These results showed no sex significant difference with male infection higher than females. More infection was in the age group of 1-month-two years with frequency (44%), and 81% of confirmed bacterial meningitis belonged to age group 1-month-4 years, these age groups for the children have considered as development age and they are more susceptible to infection than elder one (28).

In diagnosis of acute bacterial meningitis, usually blood culture was carried out in parallel with CSF analysis which can be used as tool of diagnosis the bacteria has three steps to reach to the meninges, the second step is the invasion of the blood. Fifty seven percent of meningitis cases showed blood positive in our trial, also gram stain was carried out in parallel of cells excluding 12 cases which were positive only on gram-stain and not by culture. Similar results were obtained when a comparison was carried out between PCR, Gram and culture in which gram and PCR are not affected by antibiotics (29).

The main symptoms accompanied the meningitis cases were the fever followed by neck stiffness and vomiting. similar symptoms were recorded in some reports (30-32). It was noted that some cases have no fever which reflects the asymptomatic cases and this was recorded in some reports (33-35).

The latex agglutination test (LAT) was used in comparison with culture and with

some CSF negative culture which contain cells >100 cells. The results showed that out of 120 cases with negative CSF culture examined 18% were positive by LAT. This test result is used to inform the pediatricians for treatment of bacterial infection. Some studies demonstrated that LAT was more sensitive compared to conventional Gram stain and culture technique in identifying the fastidious organisms like *H. influenzae, S. pneumoniae* and Group B *Streptococcus* (36).

N.meningitides is the leading cause of meningitis in our area. No previous precise information to be compared in our past data. These etiological agents and their relative frequency may vary in different geographical areas. Tzanakaki &, Mastrantonio (2007) reported that the etiology of bacterial meningitis in Europe and in the Mediterranean region *N. meningitidis, S. pneumoniae* and *H. influenzae* type b were most commonly associated with bacterial meningitis accounting for almost 90% of reported cases of acute bacterial meningitis in infants and young children (5). Mani et al. reported that *S. pneumoniae* was the predominant pathogen accounting for 238 (61.8%) cases. *Haemophilus influenzae* and *N. meningitidis* accounted for 7 (1.8%) and 4 (1%) cases respectively in India (24). This difference in the frequencies of the causative agents may be attributed to the applying of vaccination regimen and other socioeconomically factors associated with target group of the study area. The introduction of vaccination regimen of *H. influenzae* and *S. pneumonia* and *N. meningitidis* in different countries induced great reduction of these pathogens from the community (37).

The risk factors associated with developing such an infection using Chi square test with *P*-value of <0.05 and Odds ratio with level 0>1.0 showed that there was statically significant association with the malnutrition (low hemoglobin level). These factors showed clearly that the anemic patients were highly susceptible to serious infection, and it is well known that the developing countries and Gaza strip are highly endemic with anemia with different causative agents (38, 39). Simultaneously, house crowdness encouraged the development of meningitis due to most of the detected pathogens are air transmission and the smoking in these houses played an important role in diminishing the capacity of epithelial cells covering the respiratory tract for prevention of acquiring infection in addition to the prevalence of healthy carriers of pathogens (40,41).

The Anova test demonstrated that the impact effect of the presence of the three main pathogens in the blood and CSF of the children, the test proved clearly that the presence of *S. pneumonia* caused hemolysis of the blood causing anemia and induced the development of leukocytosis in the blood of patients.

The study had several potential limitations. First, this is a cross sectional study analyzing only notified cases of meningitis; thus the true incidence of disease in the community may have been underreported. Second, detailed information before presentation of meningitis was missing, and cases of presumed viral meningitis could have represented cases of partially treated bacterial meningitis, thus affecting the results. A final limitation of our study is our inability to follow up and record the complications including the neurological ones in the survivor of acute bacterial meningitis.

Conclusion

The bacterial meningitis is still predominant among the children and *N. meningitides* is the dominant causative agent and needs vaccination. The risk factors should be taken in consideration in any future planning.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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