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Epidemiology of *Neisseria meningitidis* among Children in Gaza Strip

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Abstract

A laboratory-based descriptive and analytical study was carried out in Gaza Strip Palestine 2001-2002. The aim of this study is to identify the incidence, the distribution and risk factors of meningococcal disease among children less than 15 years, and to assess the association between certain laboratory results and the severity and prognosis of disease. Data was collected through structured questionnaire administered to 95 subjects' parents. Response rate was 100%. The incidence rate of meningococcal disease was 17.8/100,000 children. Clear variations were found in incidence according to sex, age groups, governorates and socio-demographic and economic status. The disease was prominent among children less than 5 years with percentage 79%. The risk age group was children less than 2 years (47.4%). Females less than 9 years old lived in North and Gaza governorates were more likely to have meningococcal disease than males. Low socio-economic status, families of high crowding index, parents of low educational level and with low income jobs were associated with the disease, and its severity. There was clear seasonal variation in incidence of disease with a peak in winter. The study showed that 74.7% of cases exposed to passive smoking. The case fatality rate of meningococcal disease was low (5.3%) in Gaza Strip in comparison with other countries. Meningococcemia was associated with hypocalcaemia (X^2 28.3, p-value 0.001) and with protein C deficiency (x^2= 23.5, p-value= 0.001). Leucopenia, thrombocytopenia and hyponatremia were also considered as indicators of poor prognosis. Serogroup B (77.2%) and serogroup W135 (22.8%) found to be the only

serogroups in Gaza Strip. There was variation in serogroups distributions according to governorates. Serogroup B was more prominent in North, Gaza and Rafah governorates, while serogroup W135 was more prominent in Khanyounis governorate. The study demonstrates strains resistant to penicillin (12.3%), Ampicillin (1.5%) and sulfonamides (47.7%). No any strain was resistant to cephalosporins, chloromphenicol, and rifampicin. No secondary cases reported during the period of the study. The study contributes in highlighting the major risk factors for implementing strategies that could help in prevention of meningococcal disease. The study recommended the need for application of vaccination programs against *N. meningitidis* serogroup W135 especially for risk group peoples, making serogrouping for all isolates in the health centers, conducting further studies for determining the causes of low incidence of *N. meningitides* in Southern governorates and West Bank, and study about the efficacy of protein C as therapeutic agent in case of meningococcal septecaemia.

ملخص الدراسة

هدف الدراسة

الهدف من هذه الدراسة هو التعرف على مدى انتشار بكتيريا النيسيريا المسببة لمرض التهاب السحايا لدى الأطفال الذين أعمارهم أقل من ١٥ سنة وكذلك عوامل الخطر المؤدية إلى حدوث المرض، وعلاقة بعض نتائج الفحوصات المخبرية مع تطور الحالة.

منهجية الدراسة

هذه الدراسة دراسة وصفية تحليلية تم إجرائها في قطاع غزة عام ٢٠٠١- ٢٠٠٢.

عينة الدراسة

تكونت العينة من ٩٥ طفلاً ممن يبلغون من العمر أقل من ١٥ عاماً والذين أدخلوا إلى المستشفيات بسبب إصابتهم بمرض التهاب السحايا وتسمم الدم الناتج عن بكتيريا النيسيريا المسببة للمرض و الذين تم توثيق تشخيصهم مخبرياً.

جمع المعلومات:

جمعت المعلومات بواسطة استبانة خاصة تم تصميمها بواسطة الباحث وفحص مدى ثباتها من قبل محكمين من ذوي الإختصاص، كذلك جمعت المعلومات من الملفات الطبية للمرضى ومن تقارير المختبرات وسجلات الطب الوقائي.

النتائج:

أظهرت الدراسة أن معدل حدوث مرض إلتهاب السحايا في قطاع غزة بلغ ١٧,٨/١٠٠٠٠٠ طفل. وأن هناك فروقات في معدل الانتشار بحسب الجنس و المجموعات العمرية والمحافظات والحالة الإقتصادية والإجتماعية. ولقد كان المرض أكثر انتشاراً بين الأطفال الأقل من ٥ سنوات (٧٩%) و أن الأطفال الأقل من سنتين هم الأكثر قابلية للإصابة بالمرض (٤و٤٧)% و كان المرض أكثر وضوحاً لدى الإناث اللاتي تقل أعمارهن عن ٩ سنوات ولدى الذين يقطنون في محافظتي شمال غزة وغزة. وأظهرت الدراسة أن هناك ارتباطاً بين الحالة الإقتصادية الإجتماعية المنخفضة وحدوث المرض وأنه ينتشر لدى العائلات ذوي الإكتظاظ العالي، و أن هناك ارتباطاً مع مستوى تعلم الآباء والدخل. لقد كانت هناك فروقات واضحة في معدلات حدوث المرض بسب اختلاف فصول السنة حيث وصل المرض ذروة حدوثه في فصل الشتاء. وأظهرت الدراسة أن ٧٤,٧% من الحالات تعرضوا لتأثير الدخين السلبي. وقد كان مرض التهاب السحايا الذي يصيب سائل النخاع الشوكي أكثر انتشاراً لدى الذكور (٥٨,١%) بينما كان تسمم الدم الناتج عن الإصابة بنفس الميكروب أكثر إنتشاراً لدى الإناث (٧١,٩%)، وأظهرت الدراسة أن معدل قاتلية المرض كان منخفضاً في قطاع غزة (٥,٣%) بالمقارنة مع دول أخرى وكذلك أظهرت الدراسة أن انخفاض

كرات الدم البيضاء وانخفاض الصفائح الدموية وكذلك انخفاض معدل الصوديوم في الدم لدى المريض هي من المؤشرات الخطرة للمرض.

أظهرت الدراسة أن تسمم الدم السحائي كان مرتبطاً بنقص الكالسيوم في الدم (إختبار كاي ٢٨,٣ ، القيمة المعيارية ٠,٠٠١)، وكذلك بنقص بروتين C (إختبار كاي ٢٣,٥ ، القيمة المعيارية ٠,٠٠١). وكانت سلالات الميكروب الموجودة في قطاع غزة من نوعي B (٧٧,٣%) و W135 (٢٢,٨%) وكان هناك فروقات في توزيع تلك السلالات بحسب المحافظات حيث كانت المجموعة B أكثر انتشاراً في محافظات الشمال وغزة ورفح بينما كانت المجوعة W135 أكثر انتشاراً في محافظة خانيونس. وأظهرت الدراسة أن هناك سلالات مقاومة للبنسلين (١٢,٣%) ولمركبات السلفا (٤٧,٧%) والأمبيسلين (١,٥%)، بينما لم تكن هناك سلالات مقاومة للسيفالوسبورين والكلورامفينكول والريفامبيسين.

التوصيات:

- زيادة وعي الجمهور حول أسباب وطرق انتشار وأعراض وعواقب مرض إلتهاب السحايا الناتج عن بكتيريا النيسيريا وذلك بالطرق المقروءة والمسموعة والمرئية.

- التركيز على الحاجة لتطبيق برامج تطعيم ضد السلالة W135 وخاصة للأشخاص الأكثر عرضة للإصابة بالمرض، وللمسافرين إلى المناطق المتفشي فيها المرض وذات الازدحام العالي مثل موسم الحج، و إعطاء علاجات وقائية للقادمين من تلك المناطق والمخالطين لهم.

- وضع بروتوكول عمل موحد ذو جودة عالية لتشخيص وتسجيل الحالات وكيفية التعامل معها في المراكز والمختبرات الصحية التابعة لوزارة الصحة و التركيز على تحديد السلالات لكل الميكروبات المعزولة في مختلف المستشفيات.

- تعزيز وتوفير جميع المواد والأدوات اللازمة لتشخيص المرض.

- تعزيز ودعم الخطط العلاجية الخاصة بالمرض والمتبعة في مستشفيات وزارة الصحة.

- عمل دراسة حول استخدام بروتين "C" في علاج حالات تسمم الدم الناتجة عن الاصابة ببكتيريا النيسيريا.

- عمل دراسات مستقبلية عن وبائية المرض في الضفة الغربية وكذلك دراسات لاستكشاف أسباب إنخفاض معدل حدوث المرض في المحافظات الجنوبية لقطاع غزة.

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CHAPTER (1)

Introduction

1.1 Background

Neisseria meningitidis (N. meningitidis) is a Gram-negative bacterium causes both endemic and epidemic meningococcal disease, principally meningococcal meningitis (meningitis) and meningococcemia (1), although there are other organisms which cause meningitis (2). Meningococcal meningitis is an infection which causes inflammation of the membranes covering the brain and spinal cord. Meningococcemia is an acute generalized infection of the blood stream and subsequent vasculitis. It is the more life-threatening form than Meningococcal meningitis. Case-fatality rates exceeded 50%, but with early diagnosis, modern therapy, and supportive measures, the case-fatality rate is between 5% and 15% (3).

Meningococcal disease is a contagious disease (4). The infection is transmitted from person to person through direct contact with nose and throat secretions (5), as in coughing, sneezing, kissing, and immediate sharing of unwashed eating utensils (6). As do overcrowding and climatic conditions such as dry season or prolonged drought and dust storms (7). Incubation period is from two to ten days, often three to four days (8).

Meningococcal meningitis occurs globally, the disease is endemic in temperate climates causing a steady number of sporadic cases or small clusters with a seasonal increase in winter and spring. The highest disease rates are found in

young children. During epidemics older children, teenagers and young adults are also affected (9). It is generally a very serious illness which can result in blindness, deafness, amputations, permanent brain damage, or even death. However, with proper treatment, many people recover fully (6).

1.2 Rationale of the study

In Gaza Strip, A notable number of positive cases of *Neisseria meningitidis* were obtained by the laboratory results of CSF and blood cultures and other specific laboratory examinations annually, which showed an increasing number of meningococcal cases in the recent years.

The nature of this disease and the mode of its transmission, make the disease one of the most serious types, and an important cause of childhood morbidity and mortality.

The geographical, social and economical conditions that are found in our region permit the spread of this microorganism.

Gaza Strip considered one of the highest overcrowded areas in the world with incomplete infrastructure and bad housing conditions.

In Gaza Strip Palestine, no previous studies carried out about *Neisseria meningitidis.*

So we need further study which is intended to discover more about the epidemiological factors related to this serious microorganism and to set some recommendations for better prevention policy which may be implemented in Gaza Strip.

1.3 Objectives

1- To determine the incidence and case fatality rates of Meningococcal disease among children less than 15 years old in Gaza strip, Palestinian 2001-2002.

2- To define the risk factors associated with Meningococcal disease.

3- To identify the serogroups of *Neisseria meningitidis.*

4- To determine antibiotics resistant strains of *Neisseria meningitidis.*

5- To identify the most common manifestations of the disease.

6- To examine the relationship between certain laboratory results and severity of the disease and prognosis.

1.4 Research questions

The researcher addresses the following questions:

1- What are the incidence and the case fatality rates of meningococcal disease among children in Gaza Strip?

2- What are the risk factors associated with of meningococcal disease?

3- What are the prominent serogroups of *Neisseria meningitidis* in Gaza Strip?

4- Is there any strain resists to commonly used antibiotics for treatment of meningococcal disease in Gaza Strip, and to which antibiotic they resist?

5- What are the common manifestations of the disease among children in Gaza Strip?

6- Is there an association between certain laboratory results and severity of the disease and prognosis?

Chapter 6

Conclusion and Recommendations

6.1 Conclusion

The current study described the socio-demographic and economic status of patients of meningococcal disease in Gaza Strip. The incidence and the mortality of meningococcal disease according to sex, age groups, governorates and health and nutritional status of the patients were studied. The relationship between clinical manifestations and laboratory results from one side and the three forms of meningococcal disease from other side has been investigated.

Results of the study revealed that the meningococcal disease was more prevalent among children of age less than 5 years old. The risk age group was less than 2 years. Female were more susceptible to infection with *N. meningitidis* than male especially in age group less than 9 years old, where the prominence of males appears in age group 9 years and over. The incidence rate of meningococcal disease was higher in North and Gaza governorates than in Southern governorates. The difference in incidence rates according to governorates was attributed to possible under reporting or weakness of diagnostic method in those governorates. There was no difference in incidence rates of meningococcal disease according to type of residency. Meningococcal disease was more prominent in cases with low socio- economic status, overcrowded areas, low family income and low educational levels of parents. The severity of disease which presented in meningococcemic cases was also more prominent in North and Mid-zone governorates. Furthermore, most of cases were exposed to passive smoking

at homes and more than one quarter of cases had a history of URTI preceding the oncet of the disease. Although malnutrition and anemia play an important role in decreasing the innate immunity of the individual, there was no significant association between nutritional status and occurrence of meningococcal disease. Meningococcemia was more prevalent among female children less than 2 years. The highest peak of incidence of meningococcal disease was in winter where the weather is cold and the viral infection occurrence increased.

The case fatality rate of meningococcal disease was low in comparison with the nature of disease and in comparison with international rates. This indicates that there are high quality of services in diagnosis and management of cases in hospitals of MOH in Gaza Strip. The possibility of under reporting of the sever fulminant cases is also to be considered especially in the south.

Meningococcal meningitis among children in Gaza was more manifested by fever, vomiting and stiff neck, while meningococcal septicemia was more manifested by fever, petechial rash, and shock. The results of CSF culture, gram stain, cell count, and chemistry was very important in diagnosis of meningococcal disease. There was high significant association between meningococcemia from one side and leucopenia, thrombocytopenia, hypocalcaemia, and protein C deficiency from other side; these disturbances were considered as indicators of poor prognosis. The only serogroups of *N. meningitidis* which found in Gaza Strip were serogroups B and W 135. Serogroup B was more prominent in North Gaza, Gaza, and Rafah where serogroup W135 was more prominent in Khanyounes. There were resistant strains of *N. meningitidis* to penicillins and sulfonamides. There were no strains resistant to cephalosporins, chloromphenicol, and rifampicin. No secondary cases

reported during the period of the study which indicates that the prophylactic measures taken by the preventive health department are effective.

6.2 Recommendations

- Increasing health awareness of public about the causes, mode of transmission, manifestations, and complications of meningococcal diseases.
- High index of suspicion is needed among the medical staff for early diagnosis and treatment of meningococcal disease.
- Enhancing and supporting the treatment plans and protocols which followed in MOH pediatrics' hospitals.
- Focusing on the need for application of vaccination programs against *N. meningitidis* serogroups W135 especially for risk group peoples and travellers to risk areas.
- Giving chemoprophylaxis for arrivals and the contacts to the arrivals from risk areas.
- Setting specific and general protocol for diagnosis, registration, and management of meningococcal disease cases in all health centers and laboratories of MOH.
- Focusing on making serogrouping and serotyping for all isolates in the health centers.
- Reinforcement the availability of all materials and instruments needed for diagnosis of the disease.

- Conducting study for proving the efficacy of protein c as a useful therapeutic agent in treatment of meningococcal septecaemia.
- Conducting studies in Southern governorates for determining the causes of low incidence of *N. meningitides* in comparison with other governorates.
- Further studies and researches about the epidemiology of *N. meningitidis* in West Bank.
- Conducting further researches and prospective studies about the outcomes of meningococcal disease among recovered children.