

Changes in epidemiological pattern of Meningococcal disease in Saudi Arabia

Does it constitute a new challenge for prevention and control?

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ABSTRACT

Objective: Meningococcal meningitis epidemics, which occurred in the Kingdom of Saudi Arabia (KSA) coincided with Hajj and Umra seasons; the 2 major pilgrims to Muslims. In many countries, the disease showed major changes of its epidemiological determinants, in particular to age and prevailing serogroup. This study was conducted to determine the epidemiological trend of meningococcal meningitis disease in KSA.

Methods: All confirmed meningococcal meningitis cases reported in KSA during the period from January 1999 to December 2002 were studied retrospectively. Confirmation of cases was based on isolation of the causative organism from cerebrospinal fluid (CSF) or blood culture or detection of antigen in the CSF. Personal, clinical and laboratory results were analyzed

using Epi info version 6 software. Categorical data were tested using X^2 test.

Results: A total of 729 cases were reported, 304 cases (42%) were among people coming from abroad for Hajj or Umra and 425 (58%) were among local population. Nearly half of the later (48%) were reported at the 2 holy areas of Makkah and Madinah, KSA. Thirty-nine percent of cases were children aged <2 years and 58% were <5 years of age. Proportion of cases affected with serogroup W135 increased over time (up to 95%) and significantly affected children aged <5 years ($p < 0.001$).

Conclusion: Continuous monitoring of epidemiological determinants is essential to guide vaccination policy.

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Meningococcal meningitis is known to be a seasonal disease with cyclic peaks every 3-5 years. It is endemic in what is known as the meningitis belt in Africa. In the Kingdom of Saudi Arabia (KSA), epidemics occur from time to time, usually coinciding with Hajj and Umra seasons (2 major religious pilgrimages of Muslims to Makkah, KSA). Serogroup A *Neisseria Meningitidis* was the

causative organism responsible for the outbreak witnessed during the year 1987 (1408 Hijra). A smaller outbreak occurred later during the year 1992 (1412 Hijra). In response to, KSA instituted requirements that all persons applying for visas for the Hajj or Umra should be vaccinated against meningococcal meningitis and the bivalent vaccine A/C was used at that time.¹⁻³ Differences in the

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course of invasive meningococcal disease prevalence, geographical and age distribution have been related to major serogroups. These differences and changes have been observed in many countries. In the United States the age distribution of susceptibility has shifted so that the disease is now common in children <2 years of age.⁴ In Europe, there is a shift in the age distribution towards teen ages and away from younger children.⁵ This is mainly due to the start of vaccinating children with the competent new conjugated vaccine for C serogroup, which is predominant in those countries. In Denmark, the highest rates of the disease were observed among the age groups 5-9 and 10-14 years.⁶ In other countries, such as Angola the age groups mostly affected were 15-29 years and 5-14 years with the circulation of serogroup A as a causative organism.⁷ Serogroups causing meningococcal disease is also changing over time. Among the 13 meningococcal serogroups defined, serogroups A, B and C are the most commonly associated with the disease worldwide, while other serogroups (for example X and Y) are of increasing importance.⁸ Reemergence of serogroup W135 was observed in many countries in the meningococcal belt as well as in KSA.^{9,10} Predominance of *Neisseria meningitidis* serogroup W135 was observed as a shift in the epidemic pattern of meningococcal disease during Hajj seasons of the years 2000 and 2001.¹¹ Mass vaccination was one of the causes of the change of the serogroups in Spain where it was observed that serogroup B was predominant in all areas where the vaccination was performed and not in those areas where vaccination has not been performed.¹²

Study of the epidemiological trends in meningococcal disease is important to understand infection dynamics and to develop timely and appropriate public health interventions. The aim of this study is to determine the epidemiological characteristics of meningococcal meningitis in KSA.

Methods. A retrospective descriptive study was conducted including all confirmed cases of meningococcal meningitis reported in KSA during the period from January 1999 to December 2002. The study population comprised the local population, citizens and expatriates, of 21.895 millions in addition to those coming from abroad for Hajj and Umra. Only cases occurred among local population was analyzed in details. Epi info version 6, a computer database and statistical program for epidemiology was used in analysis. χ^2 test was used to test categorical data while proportions were tested as percentages. Preventive Medicine Department at the Ministry of Health, Riyadh, KSA run a well established surveillance system as part of its Meningococcal Meningitis Control Program. The

surveillance includes immediate reporting by all health facilities of any suspected meningitis case to the concerned department in each of the 20 health directorates in the Kingdom. The latter follows the cases thoroughly for final diagnosis as well as implementing the preventive measures as soon as possible. Confirmation of cases is based on isolation of the causative organism from cerebrospinal fluid (CSF) or blood culture or detection of antigen in the CSF. Confirmed meningococcal meningitis cases are reported immediately from all health directorates to the central department followed later by a detailed case report that includes personal, clinical and laboratory data in addition to preventive measures taken.

Results. During a period of 48 months (January 1999 to December 2002) 729 cases of meningococcal meningitis were reported in KSA. The years 2000 and 2001 witnessed successive outbreaks of meningococcal meningitis, most of the cases were recorded during the months of March and April which coincide with the Hajj seasons. It was clear that 2 distinct population categories were affected; people coming from abroad for Hajj or Umra and local population of KSA. Three hundred and four (42%) cases were reported among the former category and 425 (58%) cases among the later (**Table 1**). The following analysis included only the 425 cases that occurred among local population of KSA. Approximately 50% of the cases (48%) were reported at the 2 holy areas of Hajj (Makkah and Madinah, KSA). They were the most affected areas. Riyadh with 20% and Jeddah with 14% were cities follow next. The former is the most densely populated city in the Kingdom and the later embrace the major entrance and exit ports for Hajjees coming from abroad. Only 19% of cases were reported from the rest of the country. Two hundred and fifty-two cases (59%) were among children aged <5 years, out of these 164 cases (39%) were below the age of 2 years. Seventy-eight cases (18%) affected children aged between 5 and 14 years, 95 cases (22%) were adults aged 15 years or more. Proportion of cases among children <5 steadily increased over time, from 33% in 1999 to 69% in 2001 and 57% in 2002 ($p=0.0005$). The same applied for <2 years age group, which increased significantly from 22-46% and 43% in the same years ($p=0.005$) (**Table 2**). Serogroup was determined in 255 specimens (60%) and not in the remaining 170 cases (40%), mostly due to negative culture or cases were not followed up. Among those identified, 213 (84%) were due to serogroup W135, 31 specimens (12%) were due to serogroup A, 7 cases were due to serogroups B and 4 cases were due to serogroups C. Out of those identified, proportion of cases caused by serogroup W135 was

Table 1 - Meningitis cases according to type of residency (Kingdom of Saudi Arabia, 1999-2002).

Residency	1999	2000	2001	2002	Total
Hajj	3	140	82	5	231
Umra	8	35	25	6	73
Local population	9	163	209	44	425
Total	20	338	316	55	729

Table 2 - Distribution of meningitis cases according to age group (Kingdom of Saudi Arabia, 1999-2002).

Age group (years)	1999 n (%)	2000 n (%)	2001 n (%)	2002 n (%)	Total n (%)
<2	2 (22)	47 (29)	96 (46)	19 (43)	164 (39)
2-<5	1 (11)	33 (20)	48 (23)	6 (14)	88 (21)
5-14	2 (22)	37 (23)	32 (15)	7 (16)	78 (18)
≥15	4 (45)	46 (28)	33 (16)	12 (27)	95 (22)
Total	9 (100)	163 (100)	209 (100)	44 (100)	425 (100)
Comparing proportions of (percentages) <2 years over time $p=0.005$ Comparing proportions (percentages) of <5 years over time $p=0.0005$					

high during 2000 (72%), and even higher (95%) during 2001. This indicates clearly the shift in the dominant serogroup to W135 throughout the years 2000 and 2001. The median age for the most dominant serogroup W135 was 3 years compared to 24 years for cases infected with serogroup A. Cases with unidentified serogroup were 65 (40%) during 2000 compared to 75 cases (36%) during 2001 (Table 3). Children <5 years were significantly more affected by serogroup W135 compared to adults aged >15 years (68% versus 14%, $p<0.001$) (Table 3). This with the steadily increase of <5 proportion over time (Table 2), revealed that this group was the most affected age group with meningococcal meningitis and more specifically with the serogroup W135.

DISCUSSION. Meningococcal meningitis peaks in KSA usually coincide with Hajj and Umra seasons and this is explained by the crowd, which occurs during those seasons where more than 2 million people gather in a relatively small area in the holy places. Three hundred and four cases were reported among people coming from abroad to Hajj and Umra including defaulters compared to 425 cases among those living in the Kingdom (Table 1). This difference could be due to the fact that cases, which occur among those going back to their countries after Hajj and Umra are not reported here, although some studies showed a high carriage rate among them,^{13,14} while all cases occur among those living in the Kingdom were reported. Approximately 50% of cases (48%) that occurred among local population were reported from Hajj areas (Makkah and Madinah). This is because residents of these areas are more exposed to the risk factors, which lead to the occurrence of cases;

Table 3 - Meningitis cases reported among local population in the Kingdom of Saudi Arabia during the years 1999 – 2002 according to serogroups and age group.

Serogroup	1999	2000	2001	2002	Age distribution							Total n (%)
					<5 years	5-14 years	≥15 years	Mean age	25% ile	50% ile	75% ile	
A	2	21	5	3	6	5	20	25	7	24	35	31 (12)
B	1	4	0	2	5	0	2	8.9	0.6	1.5	14.5	7 (3)
C	0	2	2	0	3	0	1	12.5	2.3	3	13.3	4 (1)
W135	0	71	127	16	145	39	29	7.3	1	3	6	213 (84)
Unidentified	6	65	75	23	93	34	43	10.2	1.4	3.8	14.8	170 (40)
Total	9	163	209	44	252	78	95	9.8	1.4	3	11	425 (100)
ile - percentile												

specially the exposure to travelers coming from other countries with different degrees of disease endemicity and the effect of travel is known to spread meningitis.¹⁵ One of the main changes in the disease epidemiology is the shift in the age distribution. The disease is significantly occurring among children <2 years of age, ($p=0.002$), and those <5 years ($p=0.0015$). Massive vaccination campaigns used to be implemented in the Kingdom were directed mainly to high risk groups as school children (aged >6 years) and adults, although the category of 2-5 years was within the targets. Similar increase in the disease incidence among children <4 years of age was observed in Spain 2-years after a massive vaccination.¹² The shift was not only in the age group but also affected the circulating serogroups. **Table 3** shows the continuous increase in the number of reported cases affected with serogroup W135. This can be explained by the fact that the vaccine, which was used earlier during the mass vaccination campaigns was the bivalent A/C vaccine. This shift raised the need to introduce the quadrivalent vaccine in the Kingdom and was decided upon as important prerequisites for all people coming for Hajj or Umra.¹⁶ This was accompanied by adoption of quadrivalent vaccine for local population in KSA. The same change to serogroup W135 was observed in Burkina Faso,¹⁷ and to X serogroup in Niger.¹⁸ Children <5 years of age are affected more by the serogroup W135 (**Table 3**), $p<0.001$.

The epidemiological and clinical profile of meningococcal disease appears to be rapidly evolving. After introducing the quadrivalent vaccine, outbreaks of serogroup B, C, X or others may emerge. The non-immunogenic effect of the polysaccharide vaccines in children <2 years will still remain as another challenge until the availing of the conjugate quadrivalent vaccine. Close and continuous monitoring of epidemiological determinants of meningococcal meningitis, particularly the prevailing serogroups, is required to modify the vaccination policy as needed.

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