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*For further information about this article or if you need reprints, please contact:*

A. Mehrabi Tavana
Health Research Center,
Department of
Medical Microbiology,
Faculty of Medicine,
Baqiyatallah(a.s)
University of Medical Sciences,
Tehran, Islamic Republic of Iran

# Meningococcal Meningitis Control in Iran: Five Year Comparative Study 2000-2004

A. Mehrabi Tavana and R.A. Ataee

The aim of this study was to compare the incidence and death rate of meningococcal meningitis among military and non military population in Iran from 2000 to 2004. All patients with clinical sign and symptoms of meningitis and para clinical findings were entered to the study from 21st March 2000 to 21st March 2004. Meningococcal meningitis was diagnosed on the basis isolation of the *Neisseria meningitidis* in culture. CSF samples were provided at admission before commencing antibiotic therapy. Based on laboratory standard procedure all isolates were identified and final analysis revealed total number of approved meningococcal meningitides. In this comparative study meningococcal meningitides were 65 and 1370 cases in military and non-military patients, respectively. However, the total recorded cases of death were 7 in military group and 173 in non-military population. The incidence rate were 1.22 and 0.6 in 100000 in non-military and military population, respectively. The incidence of meningococcal meningitis among military personnel shows a sharp decline due to compulsory vaccination at least 2 weeks before arriving to military training camps; nonetheless, sporadic cases of the disease do occur perhaps as a result of complement deficiency in patients themselves or very late vaccination (around 2-3 days before arriving to military training camps). The findings of this study, consistent time of vaccination could be effective factor in order to prevent the infection.

**Key words:** *Neisseria meningitidis*, meningococcal vaccination, intervention, time

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Health Research Center, Department of Medical Microbiology,
Faculty of Medicine, Baqiyatallah(a.s) University of Medical Sciences, Tehran,
Islamic Republic of Iran

## INTRODUCTION

*Neisseria meningitidis*, an etiologic agent of meningitis and sepsis, is a much feared public health emergency (Mayon-White and Heath, 1997; Singurdadottir *et al*., 1997). *Neisseria meningitidis* is divided into 13 serogroups defined by specific polysaccharides designated A, B, C, H, I, K, L, M, X, Y, Z, 29E and W135 (serogroup D is no longer recognized) and most infections are caused by organisms belonging to serogroups A, B, C, Y and W-135. Meningococci are further classified into 20 serotypes (on the basis of class 2 or 3 OMP antigens), 10 subtypes (identifying class 1 OMP antigens) and 13 immune types (on the basis of lipooligosaccharide antigens (Manchanda *et al*., 2006; Smith, 2008). The first vaccine, meningococcal polysaccharide vaccine (MPSV4 or Menomune, Sanofi Pasteur) has been available for more than 25 years (Cardinale, 1999). In spite of introduce the vaccine the disease could be seen sporadically and even in epidemic form (Booy *et al*., 2007). The Islamic Republic of Iran has been severely affected by the meningitidis epidemic during the last decade. It has been reported that morbidity and mortality from meningococcal disease can be significantly reduced by using currently available vaccines in groups at high risk, particularly during epidemics situation. Therefore, defining the risk factors for infection and continuing surveillance for the disease remain important public health goals for the control of meningococcal disease throughout the world. The annual incidence rates vary between 1 and 12 per 100,000 populations and incidence of the disease rising epidemics situation (Rosenstein *et al*., 2001; Riedo *et al*., 1995). Severe meningococcal meningitis as epidemics in the military have also been reported by Pollard and Levin (2000) and Siu *et al*. (2008). In the Islamic Republic of Iran, there is no nation-wide mass-immunization program against *Neisseria meningitidis*; nevertheless, vaccination has been recommended for high risk groups. Mass immunization of the military with divalent meningococcal vaccine is a strategy with the potential to provide active protection to soldiers before being dispatched to military training camps and pilgrims on their way to Mecca are also immunized with tetra divalent vaccine. The aim of this study was to introduce the role of time of vaccination as intervention in order to reduce the incidence of infection.

## MATERIALS AND METHODS

**Patients:** This retrospective descriptive study was carried out between 21st of March, 2000 and 21st of March, 2004. In this period, all the patients presented with clinical signs and symptoms of meningitis were included. Just before antibiotic therapy, lumbar puncture was performed by a medical specialist under aseptic condition and the laboratory test was carried out within 30 min. Lumbar puncture was performed by a medical specialist under aseptic condition. Usually, 2 tubes of CSF are collected for biochemistry and microbiology. The collection equipments for of CSF contain skin disinfectant solution, sterile gauze comprise band. Lumbar puncture needle: 22 gauge for adults and 23 gauge for children, sterile screw cap tubes and a transport container. The patient sits up or lies on one side with his or her back arched forward so the head touches the knees during the procedure. The skin is disinfected along a line drawn between the crests of the two ilia with 70% alcohol. Then a tincture of povidone-iodine is applied to the area. When the area is dry, the needle is inserted and drops of fluid (1 to 4 mL) are collected into sterile screw cap tubes. The specimens are labeled and carried to the laboratory immediately.

**Laboratory examination of CSF specimen:** After the CSF samples were collected, they were transported to the microbiology laboratory, where they were examined as soon as possible. Once the CSF samples arrived at the microbiology lab, depending on the turbidity of the samples, one of the tubes was centrifuged for 10-15 min at 2500 rpm. The supernatant was drawn off with a semiautomatic micro-pipette. The supernatant was refrigerated for further tests, such as antigen detection and viral assay. The sediment was vigorously vortexed and mixed. One drop of the sediment was used to prepare the smear, which was then stained by Gram stain and microscopically observed. Next, 100 μm of the sediment was inoculated into each supplemented plate of chocolate agar and then incubated at 36-37°C in 3% $CO_2$ condition for 24 to 48 h. After the incubation period, the plates were examined and a colonial growth was recognized by biochemical tests (oxidase, maltose and glucose fermentation). The other tube of the CSF sample was used for biochemical tests and cell counts (WBC, neutrophils, lymphocytes and RBC) and protein and glucose concentration was determined. Data on meningococcal meningitis in all the provinces of the Islamic Republic of Iran were collected and transferred to a data bank at the Center for Disease Control, affiliated to the Ministry of Health. Military cases of meningoccoal meningitis (as case) with at least 2 weeks time before arriving to military training camps were compared with national meningoccoal meningitis cases (without vaccination) as control from 21st March, 2000 to 21st March, 2004.

## RESULTS

Over the five year period of the study while 1370 cases of meningococcal meningitis leading to 173 deaths occurred in the non-military population (Table 1), there were 66 cases of the disease resulting in 8 deaths in the military population.

Within the period of the study, several outbreaks of the disease caused by *Neisseria meningitidis* were reported in different provinces of Iran. Patients with bacterial meningitis classically present with fever, headaches, meningismus and cerebrospinal disorders. In addition, this results revealed that the children and adolescents affected by *Neisseria meningitidis* were mostly less than 18 years of age. No serogroup was determined in all the specimens. The number of the cases of meningococcal meningitis in military patients by ages from 21st March, 2000 to 21st March, 2004 was shown in the Table 2. In addition the cases and incidences rate of meningococcal meningitis according to year and sex was shown in the Table 3.

## DISCUSSION AND CONCLUSION

The meningoccoal meningitis is world wide problem (Butler, 2006; Esposito *et al*., 2007). *Neisseria meningitidis* most commonly causes meningitis in children and adults and it is associated with mortality rate of <10% (Rendi-Wagner *et al*., 2005). In spite of mass vaccination from long time ago (Since, 1964) in different military forces such as USA Army sporadic cases occurred yet (US Army data, 1964-1998) (Department of Defense, 2000). In Iran the disease also occurred in 2000 to 2004 before 1999 as which are shown in Table 1-3. Based on our knowledge, after several clusters of meningococcal meningitis had been discovered among recruits to the Islamic Republic of Iran's Armed Forces, vaccination against serotypes A and C of *Neisseria meningitidis* was introduced for military recruits since 1982 (Ataee *et al*., 2005). Although no further clusters of meningococcal meningitidis have been reported ever since then. Laboratory investigation showed that the measurements of $CH_{50}$, $C_3$ and $C_4$ complement components were less than the normal range after 24 h

Table 1: The number of the cases of meningococcal meningitis in non-military patients by ages in five year

| | 2000 | | 2001 | | 2002 | | 2003 | | 2004 | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age group | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death |
| 0-4 | 31 | 5 | 66 | 12 | 59 | 10 | 35 | 5 | 41 | 3 | 232 | 35 |
| 5-9 | 45 | 3 | 64 | 11 | 56 | 4 | 38 | 4 | 48 | 2 | 251 | 24 |
| 10-14 | 25 | 5 | 69 | 7 | 45 | 3 | 32 | 1 | 37 | 2 | 208 | 18 |
| 15-19 | 28 | 6 | 57 | 7 | 50 | 3 | 34 | 1 | 43 | 2 | 312 | 19 |
| 20-24 | 23 | 7 | 65 | 8 | 46 | 9 | 40 | 5 | 54 | 6 | 228 | 35 |
| 25-29 | 9 | 2 | 17 | 1 | 19 | 1 | 13 | 2 | 17 | 1 | 75 | 7 |
| 30-34 | 3 | 0 | 16 | 0 | 11 | 1 | 8 | 2 | 9 | 1 | 47 | 4 |
| 35-39 | 1 | 1 | 7 | 0 | 6 | 1 | 6 | 1 | 5 | 2 | 25 | 5 |
| 40-44 | 1 | 0 | 6 | 3 | 6 | 1 | 8 | 1 | 6 | 1 | 27 | 6 |
| 45-50 | 1 | 1 | 3 | 0 | 5 | 1 | 6 | 1 | 5 | 2 | 20 | 4 |
| Up to 50 | 3 | 0 | 13 | 4 | 16 | 4 | 13 | 3 | 11 | 3 | 56 | 14 |
| Total | 170 | 30 | 384 | 53 | 319 | 36 | 231 | 26 | 276 | 28 | 1370 | 173 |

Table 2: The number of the cases of meningococcal meningitis in military patients by ages in five year

| | 2000 | | 2001 | | 2002 | | 2003 | | 2004 | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Age group | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death | No. Case | No. Death |
| 15-19 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 0 |
| 20-24 | 11 | 2 | 15 | 1 | 12 | 1 | 9 | 1 | 7 | 1 | 54 | 6 |
| 25-29 | 2 | 0 | 1 | 0 | 2 | 1 | 1 | 0 | 1 | 0 | 7 | 1 |
| 30-34 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 35-39 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 40-44 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 45-50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Up to 50 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 13 | 2 | 17 | 1 | 14 | 2 | 11 | 1 | 10 | 1 | 65 | 7 |

Table 3: The cases and incidences of meningococcal meningitis according to year and sex

| | 2000 | | 2001 | | 2002 | | 2003 | | 2004 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sex | N. Case | INC | N. Case | INC | N. Case | INC | N. Case | INC | N. Case | INC |
| Male | 142 | 0.45 | 274 | 0.86 | 247 | 0.78 | 163 | 0.51 | 198 | 0/61 |
| Female | 67 | 0.22 | 109 | 0.36 | 72 | 0.24 | 68 | 0/22 | 74 | 0.24 |
| Total | 209 | 0.67 | 383 | 1.22 | 319 | 1.01 | 231 | 0.73 | 272 | 0.86 |

INC: Incidence (Cases per 100000 population)

incubation at 37°C in 3% $CO_2$ condition which is supported by research (Jackson *et al*., 1995; Puricelli *et al*., 2004). In the military population, the serological and serotyping investigation revealed that *Neisseria meningitidis* isolated from CSF was serotype C strain. There are several reports associating the of mannose-binding lactin with meningococcal disease (Puricelli *et al*., 2004). The human genes also influence susceptibility to bacterial pathogenesis (Janet *et al*., 1999).

In conclusions it must be noted that, the total recorded cases of death were 7 in military group and 173 in non-military population in the period of study. The incidence rate was 1.22 and 0.6 in 100000 in non-military and military population at the same time of study respectively. In addition, meningococcal meningitis among military personnel shows a sharp decline due to compulsory vaccination at least 2 weeks before arriving to military training camps; however, a few sporadic cases of the disease do occur perhaps as a result of complement deficiency in patients themselves or very late vaccination. After time intervention very fortunately the diseases rate reduced sharply. Therefore, time of vaccination has a positive role in Iran in order to prevent the disease. Further studies must be done to find out the different aspect of the meningoccoal meningitis to overcome the problem completely.

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