

1 *Neisseria meningitidis* Nasopharyngeal Carriage during the Hajj: a cohort study
2 evaluating the need for ciprofloxacin prophylaxis

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24 **Abstract:**

25 **Background:** The annual Muslim pilgrimage has the potential of increase risk for
26 acquisition of *Neisseria meningitidis*. Here, we evaluate the Hajj impact on the
27 prevalence of *N. meningitidis* carriage in a paired and non-paired cohort of pilgrims.
28 Secondary objectives were to calculate the compliance with recommended vaccination.

29 **Methods:** This a prospective paired (arriving and departing), non-paired arriving and
30 non-paired departing cohort study with the collection of nasopharyngeal samples at the
31 start and the end of the Hajj.

32 **Results:** The study included unpaired arriving pilgrims at King Abdul Aziz International
33 Airport (N=1055), unpaired departing cohort (N=373), and a paired cohort (N=628) who
34 were tested on arrival and departure. Meningococcal vaccination was received by all
35 pilgrims, 98.2% received quadrivalent polysaccharide vaccine (ACWY), and 1.8%
36 received meningococcal quadrivalent conjugate vaccine (MCV4). Only 1.61% and
37 23.03% received pneumococcal and influenza vaccines, respectively. Of the 1055
38 arriving unpaired pilgrim, 36 (3.4%) tested positive for nasopharyngeal carriage of *N.*
39 *meningitidis*, and 24 (66.7%) of these were serogroup B, the remainder were non-
40 groupable. *Haemophilus influenza* was detected among 45 (4.3%), and 11 (1%) carriers
41 were positive for both *N. meningitidis* and *H. influenzae*. Out of 373 in the unpaired
42 departing cohort, 6 (1.61%) tested positive for *N. meningitidis*, and 34 (9.1%) were
43 positive for *H. influenzae*. Of the 628 paired cohort pilgrims, 36 (5.7%) pilgrims were
44 positive for *N. meningitidis* at arrival and 16 (2.5%) pilgrims were positive after the hajj.

45 **Conclusion:** This the largest study of the epidemiology of *N. meningitidis* among
46 pilgrims. The study showed a significant difference in the carriage between pilgrims from
47 high endemicity and other pilgrims with a predominance of serogroup B. The continued
48 use of ciprofloxacin as prophylactic antibiotics should be reconsidered as well as the
49 consideration to add serogroup B as a required vaccination.

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68 **Introduction**

69 Meningococcal disease is a major cause of morbidity and mortality worldwide [1].
70 Meningococcal disease occurs at a rate of 0.5 -10 cases per 100.000 and may reach a rate
71 of 1,000 in epidemic countries [2]. *Neisseria meningitidis* is classified into 12 serogroups,
72 Only 6 serogroup (A, B, C, W, Y, X) are responsible for most invasive meningococcal
73 disease [3]. Meningococcal disease is the most common presentation of invasive
74 meningococcal infection and causes a substantial burden and death among all age groups
75 [4]. Mass gatherings are associated with outbreaks of respiratory infection diseases
76 including meningococcal disease [5–9]. In 1987, the first international meningococcal
77 disease outbreak following the Hajj occurred and was caused by *N. meningitidis*
78 serogroup A [10–12], and serogroup W¹³⁵ [13]. The prevalence of asymptomatic *N.*
79 *meningitidis* carriage ~~increases~~ increased more than 80% and contributed to outbreaks
80 during Hajj in 1987 and 2000-2001 [9,10]. Due to these outbreaks, the Ministry of Health
81 in Saudi Arabia adopted the mandatory vaccination for all ~~hajj~~ Hajj pilgrims, annual
82 vaccination campaigns for all the residents living in the area near the pilgrimage site and
83 mandatory oral ciprofloxacin prophylaxis for all the pilgrims coming from sub-Saharan
84 African meningitis belt countries [1,10,14–16].

85 Mass gatherings continue to draw larger crowds from around the Globe [13]. These
86 events offer a great potential for a health legacy through intense periods of unprecedented
87 focus and funding for improvement in health systems. However, these events also pose
88 several significant public health challenges within the host country and abroad [17].
89 ~~Meningococcal disease has been associated with the Hajj.~~—Of factors that increase
90 acquisition of *N. meningitidis* is the Hajj pilgrimage due to crowding and the gathering of

91 millions in a small place [8,9]. Taking effective preventive measures by the Saudi
92 Ministry of Health, in recent years, curtailed the development of meningococcal
93 outbreaks since the W outbreak in 2000 [7,9,10]. Of those preventive measures,
94 mandatory vaccination of domestic and international pilgrims is required using
95 quadrivalent meningococcal vaccine ~~and as well as the~~ administration of a single dose of
96 ciprofloxacin as chemoprophylaxis against *N. meningitidis* carriage to pilgrims from sub-
97 Saharan African meningitis belt [14]. These practices are based on the evidence of
98 distribution pattern of *N. meningitidis* in the world. Outbreaks in sub-Saharan Africa were
99 caused by serogroup C, W and X meningococcal but most of epidemics were due to
100 serogroup A [18]. Meningococcal serogroup W caused an outbreak in Saudi Arabia
101 among pilgrims during Hajj season 2000 and spread to contacts after returning back to
102 home countries [6,19]. Epidemics related to serogroup B meningococcal disease were
103 reported in Norway and Cuba since 1976 [20]. Late in 1980 group B meningococcal
104 disease spreading from Cuba to São Paulo in Brazil and in 2000 in New Zealand [21,22].
105 Prophylactic ciprofloxacin can decrease the carriage rate from 8.1% to 0% before and
106 after the Hajj [23]. The recent epidemiologic changes of *N. meningitidis* infection in
107 Africa and other parts of the world; the improvement in vaccination practices among
108 pilgrims; and recent development of conjugate vaccine permit the policy Maker in
109 Ministry of Health, KSA, to re-evaluate aspects of *N. meningitidis* epidemiology and to
110 re-assess the prevention measures that applied during hajj.

111 In this study, we evaluate the Hajj impact on the prevalence of *N. meningitidis* carriage in
112 pilgrims. Secondary objectives were to calculate the compliance with recommended

113 vaccination and to re-evaluate the recommendations of a chemoprophylaxis applied
114 during Hajj.

115 **Methods:**

116 **Study Area:** King Abdul Aziz International Airport (KAAIA) in Jeddah occupies an area
117 of 105 km² and is located 70 kilometers west of the holy city of Makkah, where the
118 pilgrims perform the religious rituals. There are three passenger terminals: the North
119 terminal handles all foreign air carriers, the South terminal handles local flights, and the
120 Hajj Terminal handles pilgrims traveling to Makkah. The KAAIA Hajj terminal is the
121 gateway to Makkah and is designed in the form of tents occupying an area of 465,000
122 m². KAAIA can receive about 80,000 pilgrims in 36 hours during the ~~hajj~~-Hajj season.
123 Twelve teams from preventive medicine consisted of physicians, nurses and health
124 inspectors and were distributed in each arrival hall to assess pilgrims, check the
125 vaccination cards, administer chemoprophylaxis (single dose of ciprofloxacin tablets) for
126 pilgrims arriving from the sub-Saharan meningitis belt countries and perform other
127 preventive measures, in accordance with international health regulation for pilgrimage
128 posted yearly by Ministry of health , Saudi Arabia [14,15,24].

129 **Mina:** is a small city located inside a valley in the province of Makkah, about 8 km to the
130 east of the Holy city of Makkah. It covers an area of approximately 20 km². There are
131 more than 100,000 air-conditioned tents in Mina providing temporary accommodation for
132 three million pilgrims. The tents are constructed of fibber glass coated with Teflon in
133 order to ensure high resistance to fire. In these tents Hajj pilgrims stay overnight for five
134 days as part of the Hajj season.

135 **Ethical Approval:**

136 The study was approved by the institutional review board (IRB) of King Fahd Medical
137 City, Riyadh, Saudi Arabia.

138 **Study Population:**

139 The study included unpaired cohort of arriving pilgrims at KAAIA (N=1055), unpaired
140 departing cohort (N=373), and a paired cohort (N=628) who were tested on arrival and
141 departure. Arriving pilgrims were recruited at KAAIA on October 2-October 7, 2014,
142 and departing pilgrims were sampled after performing the ~~hajj~~-Hajj in Mina tents
143 (October 16-October 24, 2014). Nationality of pilgrims was chosen based on the level of
144 meningococcal meningitis endemicity of respective countries. The annual incidence per
145 100,000 population of >10 cases, 2–10 cases, and < 2 cases represent high, moderate, and
146 low endemicity, respectively [25,26]. To obtain adequate sample size, only countries
147 with more than 5,000 pilgrims were included in the study. We included pilgrims who
148 were 18 years of age and older and verbal consent was obtained. If a pilgrim refused to
149 participate then next pilgrims was asked to take part in the study.

150 **Laboratory testing:**

151 Nasopharyngeal swabs were collected in accordance with WHO guideline, from pilgrims
152 upon arrival and departure. Samples were collected in a charcoal swab with transport
153 media, and were transported in cold boxes at temperature 2-8° C, and were sent to KAIA
154 laboratory within 2 hours of collection at arrival time and to Hira'a General hospital in
155 Makkah laboratory at departure time. Identification of Neisseria species was determined

156 by biochemical testing, polymerase chain reaction (PCR) and genotyping in Special
157 Infectious Agent Units at King Fahd Medical Research Center of King Abdulaziz
158 University [27,28].

159 **Cultures:**

160 Samples were cultured immediately using direct plating to non-selective and selective
161 media, enriched chocolate agar and 5 % sheep blood agar plates. Samples were directly
162 inoculated on labeled fresh culture plates and streaked for isolation with a sterile
163 disposable loop. All plates were incubated at 36°C in humidified 5-10% CO₂ incubator.
164 Plates were examined for growth and typical colonies after 18-24 hours of incubation and
165 again after 48 hours and were examined for colonies with consistent *Neisseria*
166 morphology. All suspected *Neisseria* species were subculture for purity on both chocolate
167 and sheep blood plates.

168 **Sample transportation and storage:** Frozen samples transported to Special infectious
169 Agents Unit King Fahd Medical Research Center –Jeddah and stored at -80°C for DNA
170 extraction, QIAamp DNA kit(Qiagen), were used following the manufacturer’s protocol
171 specifically developed for extraction of DNA from Pharyngeal swab and the extracted
172 DNA was stored at -80°C for PCR analysis.

173 **Polymerase chain reaction (PCR)**

174 In this study we have used *N. meningitidis* species-specific assays *ctrA* considering the
175 probes and guidelines of CDC. The capsule transport gene, *ctrA*, is highly conserved
176 among isolates responsible for invasive meningococcal infections [27,29]. It is, however,
177 not found in all carriage isolates as capsular null (cnl) meningococci are found in carriage

178 though only very rarely cause disease in immunocompromised patients and thus are not
179 the focus of this current study [30].

180 In paralleled to the above RT-PCR, a dual-labelled Multiplex Real-Time PCR based FTD
181 bacterial meningitis kit (Luxembourg) were used for detection of *N. meningitidis*, and
182 *Haemophilus influenzae* from extracted DNA of each sample following the
183 manufacturer's protocol. The test is fully validated with fast-track master mix (Fast-track
184 Diagnostics) and AgPath ID™ One-Step RT-PCR kit (life technologies™). The test
185 contained one positive control and one negative control in each run. The 7500 fast real
186 time PCR instrument (Applied Bio System) was used for this project. Each sample was
187 tested individually in a single tube for the *N. meningitidis*, and *H. influenzae*.

188 We performed genogrouping of the positive samples of *N. meningitidis* for the detection
189 of A, B, C, W and Y. In this study, we have used real time Singleplex PCR strategy to
190 identify the six *N. meningitidis* genogroups from the *N. meningitidis* positive samples
191 following genogroup-specific primers and the protocol described by Wang et al [28].

192 **Results:**

193 The study included unpaired cohort of arriving pilgrims at KAAIA (N=1055), unpaired
194 departing cohort (N=373), and a paired cohort (N=628) who were, tested on arrival and
195 departure.

196 **Unpaired Arriving Pilgrims:**

197 Of 1055 unpaired arriving pilgrims, 23.03% (n=243) were 18-40 years, 641 (60.76%)
198 were 41–65 years, 149 (14.12%) were >65 years and a mean age of 50 years. Male
199 constituted 63% (n=665) of this cohort. Of those pilgrims, 25.69% (n=271) were from

200 high endemic countries (the sub-Saharan meningitis belt), 53.2% (n=562) from medium
201 endemic countries, and 21% (n=222) were from low endemic countries (Table 1). In
202 relation to meningococcal vaccination, 98.2% received quadrivalent polysaccharide
203 vaccine (ACWY), and 1.8% received meningococcal quadrivalent conjugate vaccination
204 (MCV4) vaccination. From the unpaired arriving pilgrims, 36 (3.4%) tested positive for
205 *N. meningitides*. The positivity rate was 8.9% among individuals from high endemic
206 region, and 2.3% from medium endemic region (Tables 1) (P 0.0001). Out of the 36
207 positive samples, 28 (85.71%) were male, 8 (14.29%) were female. Of the 36 *N.*
208 *meningitidis* isolates, 24 (66.7%) were serogroup B, and the remaining were non-
209 groupable. In addition, 45 (4.3%) were positive for *H. influenzae*, and 11 (1%) were
210 positive for both *N. meningitidis* and *H. influenzae* (Table 1).

211 **Unpaired departing cohort**

212 Of 373 unpaired departing cohort, 140 (37.5%) were from the high endemicity
213 (meningitis belt) countries, 164 (43.9%) from medium endemic countries, and 69
214 (18.49%) from low endemic countries (Table 2). Male constituted 60% of this cohort
215 with a mean age of 48 years. All received meningococcal vaccines, 3% received
216 pneumococcal conjugate vaccine and 22% received influenza vaccine. Of the 373
217 pilgrims, 6 (1.6%) tested positive for *N. meningitides* (two were *N. meningitidis*
218 serogroup B and four were non-groupable). Of the 373 pilgrims, 34 (9.1%) were positive
219 for *H. influenzae*.

220 **Paired cohort results:**

221 A total of 628 paired cohort pilgrims were tested on arrival and on departure. Out of
222 those, 124 (19.75%) were 18 - 40 years, 384 (61.15%) were 41 - 65years, 112 (17.83%)

223 | were > 65 years of age. There were 63.697% male and 36.31% female. Of those
224 | pilgrims, 136 (21.6%) were from high endemic countries, 365 (58.1%) from medium
225 | endemic countries, and 127 (20.2%) were from low endemic countries (Table 2). All
226 | received meningococcal vaccines: 98.1% received polysaccharide meningococcal vaccine
227 | (ACWY), 1.9% received MCV4 vaccine. In addition, 2.2% received pneumococcal
228 | conjugate vaccine and 25.6% received influenza vaccine.

229 | Out of the 16 (2.5%) pilgrims in the paired group who tested positive for *N. meningitides*
230 | on arrival, only one (0.15%) remained positive after the hajj. On the other hand, eight
231 | (1.3%) tested positive on departure and out of those, only 1 (~~4.30.15~~%) was positive on
232 | arrival (P = 0.0003). Thus, the acquisition rate (negative before and positive after) was 7
233 | (1.1%).

234 | Of the paired cohort, 17 (2.7%) tested positive for *H. influenzae* at arrival and only 5
235 | (0.8%) remained positive at the end of the Hajj (P = 0.013). Of those who tested negative
236 | for *H. influenzae* at arrival, 37 (5.9%) tested positive at the end of the hajj.

237 | **Comparison of *N. meningitides* Carriage among Arriving Pilgrims:**

238 | In the unpaired arriving pilgrims, *N. meningitidis* was detected in 7.1% and 1.9% of those
239 | from high endemic countries and other pilgrims respectively (P = 0.001). Among the
240 | paired cohort, the rate of *N. meningitidis* among arriving pilgrims was 3.6% in pilgrims
241 | from high endemicity and 2.2% from other pilgrims (P = 0.035), Figure 1. Of all arriving
242 | pilgrims, the carriage rate was 6.3% among pilgrims from high endemic areas compared
243 | to 2% in those from other countries (P = 0.0001) (Figure 1).

244 **Discussion:** Colonization by *N. meningitidis* can be a major potential source of infection
245 [31,32]. Acquisition of *N. meningitidis* among pilgrims is of concern for the potential
246 spread of this organism into the pilgrims' home countries globally [24,33]. The rate of *N.*
247 *meningitidis* among arriving pilgrims was low even among pilgrims coming from
248 endemic countries (6.3%). The risk of adverse events of chemoprophylaxis may
249 outweigh the benefits. Evaluation of returning pilgrims to Kuwait did not reveal any
250 colonization among 177 participants [34]. In a study from the United States, the carriage
251 rate of serogroup W was 0.8% among pilgrims and 0.9% among non-pilgrims and thus no
252 prophylactic antibiotic was recommended for returning Pilgrims [35,36]. In a paired
253 cohort group, the prevalence of *N. meningitidis* was 2.5% on arrival and 1.3% on
254 departure, indicating no increase in the acquisition rate of carriage of meningococci
255 [35,36]. The use of oral ciprofloxacin was evaluated in returning Iranian pilgrims, the
256 carriage rates of *N. meningitidis* was 5.2% before and 4.6% after pilgrimage (P = 0.65) in
257 those who did not receive ciprofloxacin compared to the carriage rate of 8.1% and zero
258 before and after pilgrimage in those who had ciprofloxacin on return [23]. In accordance
259 with the Saudi Ministry of Health, mandatory oral ciprofloxacin prophylaxis is given to
260 all pilgrims coming from sub-Saharan African meningitis belt countries [1,10,14–16].
261 In the paired cohort in this study, 2.5% pilgrims tested positive for *N. meningitidis* on
262 arrival and only 0.15% of them remained positive after the hajj. Data on the possibility of
263 increased carriage among returning pilgrims are variable. Few studies showed no increase
264 in the carriage rate [23,37,38]. In a cohort study, the acquisition rate of *N. Meningitides*
265 was 0.3% among paired cohort and 0.6% among non-paired cohort [39]. In another
266 cohort of French Hajj pilgrims, none of them had *N. Meningitides* on arrival or departure

267 | [40]. A recent review indicated that carriage rates were higher in Hajj pilgrims compared
268 | to Umrah pilgrims and that most studies showed the carriage rates to be comparable to
269 | the rates in non-epidemic settings [41]. The use of antibiotics during the Hajj may reduce
270 | the carriage rate [23]. Another important finding of the study is the fact that *N.*
271 | *meningitidis* serogroup B was isolated among pilgrims. *N. meningitidis* serogroup B is
272 | reported in many parts of the world including Europe, Australia, and north America
273 | [26,42]. *N. meningitidis* serogroup B represents 50% of all meningococcal cases and
274 | caused multiple outbreaks [43,44]. The quadrivalent meningococcal vaccine became a
275 | mandatory requirement for all pilgrims in 2001 [9,14]. A serosurvey of pilgrims showed
276 | that the majority of pilgrims were vaccinated and protected against meningococcal
277 | serogroups A, C, W, and Y [45]. There is a concern of the continued change in the
278 | epidemiology of invasive meningococcal disease and the fear of the development of
279 | outbreaks related to serogroups B or X. The availability of serogroup B *N. meningitidis*
280 | vaccine is an added advantage to be used in cases of outbreaks [46]. The recommendation
281 | to use this vaccine for all pilgrims would require further studies of the epidemiology of *N.*
282 | *meningitidis* in pilgrims.

283 | In conclusion, this the largest study of the epidemiology of *N. meningitidis* among
284 | pilgrims. The study showed a low rate of carriage and a predominance of serogroup B.
285 | The use of ciprofloxacin as prophylactic antibiotics should be reconsidered as well as the
286 | consideration to add serogroup B as a required vaccination especially for pilgrims coming
287 | from endemic areas.

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425

Table 1: Characteristics and Carriage Rates of *N. meningitidis* and *H. influenzae* of Unpaired Arriving Pilgrims

	Number of Nasopharyngeal swabs	Influenza vaccination n (%)	Pneumococcal vaccination n (%)	Carriage <i>Neisseria meningitidis</i> n (%)	Serogroup B, n (%)	Non-groupable, n (%)	Carriage <i>H. influenzae</i> on arrival, n (%)	Carriage <i>N. meningitidis</i> and <i>H. influenzae</i> on arrival, n (%)
High Risk Countries								
Nigeria	85	0 (0)	0 (0)	14(16.47)	5(5.8)	9(10.5)	2 (2.3)	2(2.3)
Ethiopia	93	0 (0)	0 (0)	6 (6.5)	4(4.3)	2(2.1)	12 (13.1)	1(1.0)
Tanzania	95	0 (0)	0 (0)	1 (1.0)	1(1.0)	0(0)	13 (3.1)	1 (1.0)
Subtotal	273 (25.9)	0 (0)	0 (0)	21 (8.78)	10 (3.6)	11 (4.0)	17 (6.2)	4(1.4)
Medium Risk Countries								
India	100	4 (4.0)	0 (0)	0 (0)	0(0)	0 (0)	3(3)	0
Pakistan	98	93 (94.89)	0 (0)	1 (1.0)	1(1.0)	0 (0)	0(0)	0
Bangladesh	79	60 (75.94)	0 (0)	2 (2.5)	2(2.5)	0 (0)	2(2.5)	1 (1.2)
Egypt	98	3 (3.0)	0 (0)	1 (1.02)	1(1.0)	0 (0)	4(4.0)	0
Somalia	98	0 (0)	0 (0)	7 (7.29)	6(6.25)	1(1.4)	4(4.1)	3 (3.1)
Subtotal	467 (44.2)	160 (34.3)	0 (0)	11 (2.3)	10 (2.1)	1 (0.1)	13 (2.8)	4 (0.8)
Low Risk Countries								
Indonesia	98	56 (57.14)	0 (0)	2 (2.0)	2(2.0)	0(0)	7(7.1)	1 (1.0)
Malaysia	95	15 (15.78)	15 (15.7)	0 (0)	0(0)	0(0)	0(0)	0
Albania	30	0 (0)	0 (0)	0 (0)	0(0)	0(0)	1(3.5)	0
USA	92	5 (5.49)	2 (2.1)	2 (2.1)	2(2.1)	0 (0)	7(7.6)	2 (2.1)
Subtotal	315 (29.9)	76 (24.1)	17 (5.4)	4 (1.3)	4 (1.3)	0(0)	15 (4.7)	3 (0.9)
Grand Total	1055	236 (22.36)	17 (1.6)	36 (3.4)	24 (2.27)	12 (1.1)	45(4.2)	11(1.0)

Table 2: Characteristics and Carriage Rates of *N. meningitidis* and *H. influenzae* of Paired Pilgrims

	Number of Nasopharyngeal swabs	Previous influenza vaccination n (%)	Previous pneumococcal vaccination, n (%)	Carriage <i>Neisseria meningitidis</i> at arrival, n (%)	Carriage <i>Neisseria meningitidis</i> at departure, n (%)	Genogroup B <i>Neisseria meningitidis</i> at arrival, n (%)	Genogroup B <i>Neisseria meningitidis</i> at departure, n (%)
High Risk Countries							
Ethiopia	64	0 (0)	0 (0)	4(6.2)	0(0)	3(4.6)	0(0)
Tanzania	72	0 (0)	0 (0)	1(1.3)	2(2.7)	1(1.3)	2(2.7)
Subtotal	136 (21.6)	0 (0)	0 (0)	5(3.6)	2(1.4)	4(2.9)	2(1.4)
Medium Risk Countries							
India	73	1(1.3)	0 (0)	0(0)	0(0)	0(0)	0(0)
Pakistan	89	84(94.3)	0 (0)	1(1.1)	0(0)	1(1.1)	0(0)
Bangladesh	27	18(66.6)	0 (0)	1(3.7)	1(3.7)	1(3.7)	1(3.7)
Egypt	86	3 (3.4)	0 (0)	1(1.1)	1(1.1)	1(1.1)	1(1.1)
Somalia	50	0 (0)	0 (0)	6(12.0)	1(0)	5(10.0)	1(2.0)
Subtotal	325 (51.7)	106 (32.6)	1 (0)	9 (2.7)	3 (0.9)	8 (2.4)	3 (1.0)
Low Risk Countries							
Indonesia	59	34(57.6)	0 (0)	1(1.6)	0(0)	1(1.6)	0(0)
Malaysia	68	12(17.6)	12(17.6)	0(0)	1(1.4)	0(0)	1(1.4)
USA	40	2 (3.4)	2 (5.0)	1(2.5)	1(2.5)	1(2.5)	2(5.0)
Subtotal	167 (26.6)	48 (28.7)	14 (8.34)	2 (1.2)	2 (1.2)	2 (1.2)	3 (1.7)
Grand Total	628 (100)	154 (24.5)	14(2.2)	16(2.5)	8(1.2)	14(2.2)	8 (1.2)

Figure 1: Percentage of Arriving Pilgrims with *N. meningitides* based on the Study Group and Endemicity

