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► **To cite this version:**

Seif S Al-Abri, Musallam Yunus Abuhasan, Soha Shawqi A. Albayat, Xilian Bai, Hamad Bastaki, et al.. Meningococcal disease in the Middle East: A report from the Global Meningococcal Initiative. *Journal of Infection*, 2024, 88 (2), pp.71-76. 10.1016/j.jinf.2023.10.011 . pasteur-04266742

**HAL Id: pasteur-04266742**

**<https://pasteur.hal.science/pasteur-04266742v1>**

Submitted on 8 Nov 2024

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## Review

## Meningococcal disease in the Middle East: A report from the Global Meningococcal Initiative



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## ARTICLE INFO

## Article history:

Accepted 18 October 2023

Available online 20 October 2023

## Keywords:

Meningococcal disease

Serogroup

Middle East

Vaccination

Surveillance

## SUMMARY

This review details recent findings from the Global Meningococcal Initiative's (GMI) recent meeting on the surveillance and control strategies for invasive meningococcal disease in the Middle East. The nature of case reporting and notification varies across the region, with many countries using bacterial meningitis as an IMD case definition in lieu of meningitis and septicaemia. This may overlook a significant burden associated with IMD leading to underreporting or misreporting of the disease. Based on these current definitions, IMD reported incidence remains low across the region, with historical outbreaks mainly occurring due to the Hajj and Umrah mass gatherings. The use of case confirmation techniques also varies in Middle Eastern countries. While typical microbiological techniques, such as culture and Gram staining, are widely used for characterisation, polymerase chain reaction (PCR) testing is utilised in a small number of countries. PCR testing may be inaccessible for several reasons including sample transportation, cost, or a lack of laboratory expertise. These barriers, not exclusive to PCR use, may impact surveillance systems more broadly. Another concern throughout the region is potentially widespread ciprofloxacin resistance since its use for chemoprophylaxis remains high in many countries.

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## Introduction

The Global Meningococcal Initiative (GMI) was formed in 2009 as a multidisciplinary group of experts with expertise in public health,

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epidemiology, paediatrics, infectious disease, vaccinology, immunology, and microbiology. As its primary objective, the GMI was created to prevent meningococcal disease worldwide through research, education, and international cooperation.

Invasive meningococcal disease (IMD) is caused by the Gram-negative bacterium, *Neisseria meningitidis*, which is spread through airborne transmission and carried asymptotically in the nasopharynx.<sup>1</sup> IMD usually presents as septicaemia or meningitis or both. Approximately 10% of a healthy population may carry the bacteria.<sup>2</sup> Pathogenic *N. meningitidis* are covered by a polysaccharide capsule, the presence of which is the main source of its virulence.<sup>3</sup> Differences in the polysaccharide capsule have led to the identification of 12 *N. meningitidis* serogroups, six of which cause most invasive disease (A, B, C, W, X, and Y).<sup>3</sup>

To understand the epidemiology and control strategies for IMD, 15 previous GMI meetings have been held in various regions worldwide.<sup>4–7</sup> This latest regional meeting was held virtually between 21 and 23 March 2023, and explored surveillance and IMD prevention in the Middle East. Delegates from this region and GMI steering committee members attended the three-day meeting, with the following principal objectives: (i) To determine the epidemiology and control strategies for IMD in the Middle East; (ii) To highlight the role of the World Health Organization (WHO) Collaborating Centers (WHOCC) in supporting regional laboratory capacity and testing; (iii) To raise awareness of ongoing meningitis advocacy efforts across the Middle East and globally; and (iv) To review the potential spread of IMD at mass gatherings in the Middle East, particularly during the Hajj and Umrah.

This review summarises the key points raised during the meeting, as well as a detailed overview of IMD epidemiology and control strategies in the Middle East.

## The surveillance, epidemiology, and prevention of IMD in the Middle East

### Surveillance of IMD

Accurate IMD case reporting and confirmation remain critical in understanding disease epidemiology, as well as the potential for disease outbreaks and evolving bacterial strains.<sup>8</sup> Coordinated surveillance networks help to address this need, with local hospitals/units notifying regional or national centres of any new cases through standardised reporting mechanisms. This framework is well-established in many countries globally, but practices vary owing to a range of limitations. This is a scenario that is equally applicable throughout the Middle East.<sup>9</sup>

Meningitis is notifiable in the majority of countries in the Middle East, with a few notable exceptions. The effects of ongoing civil conflict, exacerbated by recent natural disasters, in Syria have created difficulties in obtaining any data on communicable diseases, barring some sporadic case reports.<sup>10</sup> Despite this, WHOCC has been able to secure a number of isolates from the country that have been subsequently characterised. Recent data from the country has indicated an increase in suspected meningitis across three governorates in the region.<sup>11</sup>

Established meningitis reporting is in place in the Republic of Türkiye (Turkey), Qatar, the Kingdom of Saudi Arabia (KSA), Lebanon, Cyprus, Oman, Jordan, Iraq, Bahrain, Kuwait, Palestine, and the United Arab Emirates (UAE). Cases are typically reported to a national center for disease control (CDC) or Government ministry.<sup>12</sup> The robustness of such reporting mechanisms vary and their completeness is not evaluated. For instance, in Iraq and Lebanon, a paper-based notification system is used; these case report forms will include information on patient demographic data, clinical presentation, vaccination status, laboratory confirmation, and clinical outcomes. Qatar have made progress in moving away from a paper-based report system, with the introduction of the Surveillance &

Vaccine Electronic System (SAVES) in 2020.<sup>13</sup> In establishing an electronic-based notification network, real-time laboratory notifications of confirmed cases have increased.

In the UAE, any suspected case of bacterial meningitis is reported to the relevant Emirates' Department of Health, as well as the national Ministry of Health and Prevention. Public health specialists from the Emirates' local CDC will conduct a face-to-face investigation for each case, collating information on clinical presentation, potential source of infection, vaccination status, and disease outcome among other data. The country also has a dedicated national antimicrobial resistance surveillance database. In Oman, it is also mandatory to notify all meningitis cases from both private and government institutions through an electronic notification system (Trassud).<sup>14</sup> In Palestine, meningococcal disease has been included within the epidemiological sheet (group A). A disease within this group must be immediately notified by telephone and follow an active surveillance system protocol.

Despite the presence of established surveillance networks across the Middle East, the completeness and representativeness of the reporting system is still suboptimal. Although the aforementioned SAVES system in Qatar has streamlined processes for healthcare providers (HCPs), the country still predominantly operates a less exhaustive meningitis surveillance framework. This may reduce costs and save time, but risks underreporting potential IMD cases. In Lebanon, the Ministry of Public Health has mandated the reporting of all meningitis cases, irrespective of aetiology. Samples from patients (cerebrospinal fluid [CSF], serum, blood) are supposed to be sent to the Ministry of Health (MOH) for further processing and verification. A MOH-epidemiology surveillance officer will directly contact the reporting physician for details, with national statistics reported weekly on the MOH website. However, a number of HCPs may not send samples for further testing, often due to a lack of resources or means of transportation. This may again lead to mis- or underreporting of IMD cases.

IMD underreporting is not exclusive to surveillance system frameworks; how a country defines IMD may also adversely impact case reporting. Bacterial meningitis is often used as the case definition for IMD in many Middle Eastern countries, including the UAE, Bahrain, Iraq, Syria, and Jordan. The consequence of such an approach will be that other clinical presentations of IMD may be overlooked leading to the underreporting of the condition.<sup>15</sup>

As part of surveillance efforts across the Middle East, case confirmation methodologies vary significantly across the region. Standard diagnostic assays (e.g., Gram staining, bacterial culture) are used on CSF specimens, but these have a number of requirements, including the need of sufficient CSF volume, adequate specimen storage and transportation, and the presence of non-viable bacteria due to, for example, previous antibiotic administration or a delay of sample culture.<sup>16</sup> A limited number of countries use, or have access to, PCR assays, which detect bacterial DNA and therefore do not require viable bacteria. Globally, there are multiple PCR assays available (including real-time PCR [rt-PCR]) with a number potential targets for the detection of meningococci.<sup>16</sup> However, such methods may be expensive and complex to operate in some regions.<sup>17</sup> As a result, PCR assay use varies.

Only a small number of countries have access to PCR assays in the Middle East, including Cyprus, KSA, Lebanon, Oman, Kuwait, and the UAE. Specific challenges remain in Syria owing to the civil conflict. In 2022, through WHO's headquarters in Geneva, a WHOCC (Institut Pasteur in Paris, France) sent two, ready-to-use rt-PCR kits to Damascus (Syria) and Gaziantep (Turkey) to detect *N. meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*. In terms of training, there was a first virtual meeting (19th July) to discuss the protocol with both laboratories; and a second virtual meeting (29th July) addressed technical issues. However, ongoing PCR support has been difficult to maintain under the current circumstances, with

transportation/storage issues being exacerbated by the recent earthquake.

As mentioned, PCR is available in some countries through reference laboratories. In Cyprus, PCR assays form part of the mandatory notification system. Once a suspected case has been notified to the MoH, diagnosis is confirmed through referral of CSF specimens to the reference laboratory for multiplex rt-PCR diagnosis. However, this is only offered at the reference laboratory at the Nicosia General Hospital. Isolates are also sent to this laboratory for serogrouping and may also be sent to the Greek National Meningitis Reference Laboratory in Athens for further molecular characterisation (e.g., sequence types and clonal complexes).

Potential alternatives to PCR assays may help to reduce the burden associated with high costs, expertise, and assay sensitivity. Loop-mediated isothermal amplification (LAMP) may be one such alternative. Easy-to-perform and rapid, LAMP is a nucleic acid amplification technology that works in an isothermal context<sup>18,19</sup>. LAMP uses a special polymerase that is able to separate the double-stranded DNA in a specimen without the need for a temperature change. This means the assay can be carried out in a common water bath or a thermal heating block.

### Incidence of IMD

Owing to the nature of case reporting and surveillance systems across the Middle East, information on IMD incidence across the region varies. In particular, and as previously mentioned, many countries report meningitis with other clinical manifestations of IMD being potentially overlooked.

WHO reported a decreasing number of IMD cases in the Eastern Mediterranean region between 1986 and 1996.<sup>20</sup> Some countries have reported similar or lower meningococcal disease incidence rates to the average EU/EEA rate of 0.6 cases per 100,000 reported in 2018.<sup>21</sup> There has been a low incidence of meningococcal disease in Cyprus, with a recorded incidence of 0.2 cases per 100,000 in 2019. Between 1998 and 2011, IMD cases have been decreasing in Cyprus.<sup>22</sup> Following a peak in 2012, cases reached a higher plateau, fluctuating between 0.2 and 0.6 cases per 100,000 population. Such data may be hard to interpret given the introduction of multiplex PCR assays from 2017 in Cyprus, which have increased the detection of pathogens in CSF specimens.

Incidence rates have also been historically low in Syria, albeit estimates are based on very limited data. Prior to 1995, the WHO reported incidence rates of < 5 cases per 100,000.<sup>23</sup> The only other publicly available rate was noted in 2005 (0.07 cases per 100,000).<sup>24</sup> Broadly similar incidence rates were reported at that time across the Middle East. KSA, Oman, Iran, and Iraq reported rates of 0.09 (2006), 0.10 (2007), 0.14 (2005) and 0.18 (2005) cases per 100,000, respectively.<sup>24</sup> However, a few countries within the Middle East and North Africa (MENA) region were experiencing higher incidence rates. Sudan, in particular, recorded an IMD incidence of 13.26 cases per 100,000 in 2006.

In Palestine, the annual incidence of meningococcal disease across both the West Bank and the Gaza Strip has fluctuated between 0.3 and 10 cases per 100,000 between 2003 and 2022. The total number of cases over this period was 1682. The age of the cases varied from 3 months to 80 years. The mean age of those with meningococcal disease was 4.3 years (median: 3 years), with the highest incidence rate being those < 5 years (75%).

In terms of age distribution, IMD cases are frequently reported in children and young adults. In KSA, between 1999 and 2011, IMD was most prevalent among those aged between 15 and 45 years (n = 371; 19% of cases); with a significant proportion of cases being in those aged 1–4 years (9%; n = 214) and those < 1 year (7%; n = 117). More recent data has indicated a shift in the age distribution of IMD cases in KSA.<sup>15</sup> During the period 2012–2021, 48 IMD cases were reported

to the MoH, with 33% occurring in those < 5 years and 33% in those aged between 5 and 14 years.<sup>15</sup> IMD cases have also been reported in Turkiye; a significant proportion of cases were reported in those < 1 year (34.8%) and those aged between 1 and 4 years (27%) (2015–2018).<sup>25</sup>

In a study from 2007 in the UAE, 35% of bacterial meningitis cases reported in Al-Ain were caused by *N. meningitidis*.<sup>26</sup> Of these cases, the majority were recorded in the 21–30 (10 cases) and 31–40 age groups (5 cases). IMD case numbers peaked in 2001 (during the period 2000–2005). In a separate analysis, 48 IMD cases were reported to the MoH in UAE in 2008, with 79% occurring in those aged 15–44 years.<sup>12</sup>

More recent data has been collated in Iraq through a hospital-based surveillance survey that also highlighted IMD cases reported among specific age groups.<sup>27</sup> It was reported that a total of 2314 patients with suspected meningitis were admitted to 18 designated hospitals in four Iraqi governorates between 1st June 2018 and 30th May 2020. The age of these suspected cases ranged between 3 days and 91 years, with a median of 2 years. In total, 370 cases (16.0%) had confirmed bacterial meningitis with 215 (58.1%) caused by *N. meningitidis*. Patients with IMD were aged between two months and 36 years, with a median of 5 years (mean (SD) = 6.5 (6.6)). The majority (82.8%) were aged between 1 and 14 years.

A number of bacterial meningitis cases have been reported among young adults in Qatar.<sup>28</sup> The study found 117 cases of bacterial meningitis between 2009 and 2013, with 11 being attributable to *N. meningitidis*. Six out of the eleven *N. meningitidis* cases were in the 15–34 age group. From 2013 to 2018, a total of 39 IMD cases were reported to the MoH in Qatar. Most of these cases involved meningococcal bacteremia or overt meningitis, with 68% being attributable to those aged 15–44 years.<sup>29</sup>

### Serogroup distribution

Countries across the Middle East have serogrouping capabilities and a number of studies have elucidated the serogroup distribution of IMD in recent years. There does not appear to be a prevalent serogroup across the region, perhaps due to the differing nature of vaccination policies and preventative measures in different countries ( Fig. 1).

In Turkiye, MenB has been the most prevalent serogroup between 2015 and 2018. MenW cases have fallen over the period after being the dominant serogroup between 2009 and 2013. More specifically, during 2017–2018, MenB has been the most prevalent serogroup (54.7%) among IMD cases, although for 30.2% of the cases the serogroup had not been determined.<sup>25</sup>

*N. meningitidis* carriage rates have also been recorded in Turkiye among adolescents and young adults (in 2015).<sup>30</sup> The highest carriage rate (11%) was among those aged 17 years. By age group, the highest carriage rate was in the 21–24 year age group and was significantly higher than the rates in other age groups (p < 0.05). Serogrouping for samples isolated from nasopharyngeal specimens showed MenA in 5 specimens (5.2%), MenB in 9 specimens (9.4%), MenW in 64 specimens (66.6%), and MenY in 4 specimens.

Invasive MenB cases have also been prevalent in Iraq. In the aforementioned hospital-based surveillance survey,<sup>27</sup> among the identified meningococci, the most common serogroup was MenB (n = 167, 77.7%), followed by MenW (n = 39, 18.1%) and MenX (n = 9, 4.2%).

In contrast to MenB prevalence in Turkiye and Iraq, MenW was the dominant serogroup in Qatar. In a study of 39 IMD isolates identified from 2013 to 2018, the most common serogroup was MenW (n = 19; 49%), with 8% attributed to both MenB and MenA.<sup>29</sup> However, when considering cases per year, MenW cases have fallen from 7 in 2016 to 1 in 2018, with no MenW cases in 2017.

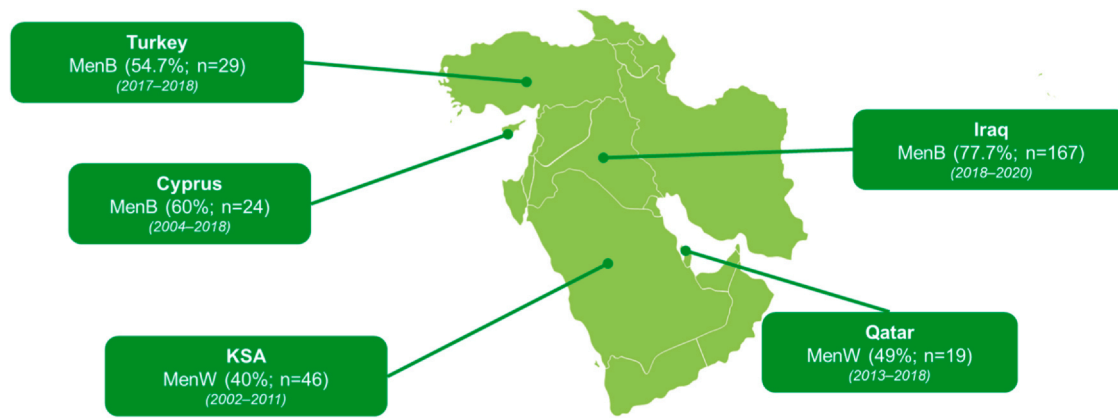


Fig. 1. Serogroup distribution across the Middle East region, with the most predominant serogroup indicated in each country<sup>21,24,26,28,30</sup>.

Between 1995 and 2011, 1103 IMD cases were reported in KSA. Serogroup data were available for 62.5% of all cases (2002–2011); MenW accounted for 40.0% cases, MenA (35.7%), and MenB (16.5%).<sup>31</sup>

#### Prevention and control strategies

IMD control strategies vary across the Middle East owing to infrastructure, resources, antibiotic use, and the extent of IMD burden.<sup>12</sup> A concern throughout the region is the reliance on chemoprophylaxis using antibiotics, with overuse of these medications potentially leading to increased antimicrobial resistance.

In the Gaza Strip, antibiotics are prescribed for certain exposed individuals (e.g. close contacts) using ciprofloxacin, rifampicin, or trimethoprim. Equally, no meningococcal vaccinations are available in Gaza, so chemoprophylaxis is preventively used. However, efforts are being made to introduce an IMD vaccine through the Expanded Program of Immunization.

Chemoprophylaxis is also leveraged in Bahrain, where outbreak control is managed using targeted chemoprophylaxis of close contacts. There are similar policies in place in Oman and Qatar, with chemoprophylaxis for contacts given for any confirmed IMD case; however, in Qatar, vaccination is also administered for close contacts. It should be noted that either rifampicin or ceftriaxone is used for chemoprophylaxis of close contacts of an IMD case in Kuwait. Rifampicin (four doses) or ciprofloxacin (one dose) is also given to contacts within 24 h of a reported case in Cyprus.

Cyprus also has a robust vaccination policy for IMD. Historically, there have been two vaccination schemes in place relating to public and private healthcare. In 2019, the establishment of the National Health System in Cyprus was designed to offer health care equally to all citizens. Following this, a common National Immunization Technical Advisory Group (NITAG) was established, with members from the public and private sectors. That same year, the two immunisation schemes were finally integrated into one common immunisation scheme.

There have been long established IMD vaccination programmes in those countries relating to the Hajj and Umrah pilgrimages. Given IMD outbreaks relating to these events in the past,<sup>32</sup> there is high awareness around the disease in KSA. A meningococcal quadrivalent conjugate vaccine (MCV4) was incorporated into KSA's National Immunisation Programme (NIP) in 2013 for those aged 9 and 12 months.<sup>32</sup> This was followed by the introduction of an additional dose in March 2020 for those aged 18 years.

In KSA, both domestic or international travellers (adults and children aged over 1 year) arriving for Umrah, Hajj or for seasonal work in Hajj zones, are required to submit a valid vaccination certificate. Travellers must have received a quadrivalent (MenACWY) meningococcal vaccine at least 10 days prior to the planned arrival to

Hajj and Umrah areas (quadrivalent polysaccharide within the last three years or the quadrivalent conjugate vaccines within the last five years).

Since 2018, routine immunisation with the MenACWY vaccine for Hajj and Umrah pilgrims, as well as military personnel, has been in place in Turkiye. This is also the case in Bahrain, where it is recommended that pilgrims travelling for the Hajj should receive a MenACWY dose, followed by a booster dose every 5 years. Equally, in Oman, pilgrims planning to travel for Hajj and Umrah are required to be vaccinated with MenACWY vaccine at least 10 days prior to departure.

The MenACWY vaccine is recommended in Qatar for children > 2 years, high-risk persons, and travellers to endemic areas. However, the epidemiology of IMD in Qatar does not mandate adding meningococcal vaccination to the NIP. The MenACWY polysaccharide vaccine was introduced in Kuwait in 1994 and was replaced with the conjugate MenACWY vaccine in 2019, with the age for immunisation being lowered to those > 1 year.

#### Update on the new Gulf CDC: a regional hub for disease prevention and control

To support countries across the region with IMD surveillance and control efforts, the new collaboration between the six Gulf Cooperation Council (GCC) countries has resulted in establishing the Gulf CDC. The GCC member states include UAE, Bahrain, KSA, Qatar, Oman and Kuwait. Although not fully established, the GCC envisages that the Gulf CDC will be a regional public health technical agency aimed at strengthening public health coordination, capacity building, knowledge exchange, and evidence generation across the six member states of the GCC and Yemen.<sup>33</sup> Governed by the Gulf Health Council, the Gulf CDC will be a semi-autonomous body and established through a staged approach.

The strategic objectives of the Gulf CDC are to: support the development of collaborative public health programmes, policies, and practices; strengthen regional public health training and capability building; enable the collection, integration, and utilisation of public health data across key indicators through surveillance and research; enhance preparedness, early detection and rapid response to health hazards in the Gulf region. However, the Gulf CDC will not be a replacement for public health capacity within each member state, but a critical resource in the establishment of public health capacity and expertise across the region. Nor will it be an organisation with a significant physical footprint (e.g., owning and operating major laboratories) and will instead leverage existing infrastructure and resources from member states and/or partners.

When considering public health emergency preparation, the Gulf CDC will monitor hazards and threats to the region and provide early

notifications and routine insights. The centre will also provide a confidential forum for Gulf countries to exchange information, expertise, and best practices on emergencies and will facilitate the development and implementation of joint activities.

From a response perspective, the Gulf CDC will act as an emergency operating centre for response coordination between the Gulf countries during a public health emergency, mainly for cross-border public health threats. It will also support in activating and deploying a regional rapid response team for support in the investigation and/or containment of public health events of regional concern.

The first CDC standard operating procedure (SOP) has been developed, based on best practices shown by the European Centre for Disease Prevention and Control, the World Health Organization, the UK Health Security Agency, and other organisations. The SOP includes details of procedures and instruments for decision-making. The Gulf CDC is actively liaising with laboratories to assess capacity and notify others of specific testing capabilities if required.

The Gulf CDC are also in ongoing discussions with WHO to help implement a regional framework for defeating meningitis; however, these discussions are in the early stages. The public health surveillance in the Gulf CDC would be in a better place to enhance this in the future.

### Advocacy and the role of meningitis charities

In November 2020, the World Health Assembly approved a new global road map to defeat meningitis by 2030.<sup>34</sup> The road map goals are to (i) eliminate epidemics of bacterial meningitis; (ii) reduce cases of vaccine preventable bacterial meningitis by 50% and deaths by 70%; (iii) reduce disability and improve quality of life after meningitis of any cause. To achieve these visionary goals, there are a number of strategic activities across five key pillars: prevention and epidemic control; diagnosis and treatment; disease surveillance; support and care for people affected by meningitis, and advocacy and engagement.

For the latter pillar, advocacy efforts should be geared towards raising awareness around the disease, and in establishing a commitment to equal access to treatment and support. These advocacy efforts should help foster an environment where populations are aware of the signs and symptoms and would seek appropriate medical care, as well as know how to access vaccination and other preventative measures. Ultimately, advocacy may help to ensure that the road map is integrated into country plans at all levels.

Meningitis charities play a central role in these advocacy efforts, with the international charity the Meningitis Research Foundation (MRF) being one such example. MRF and its member arm, the Confederation of Meningitis Organizations (CoMO), support scientific research, coordinate World Meningitis Day, an annual event to raise disease awareness globally, and support local activism across the globe. CoMO currently has over 120 members in 50 countries, but only one country in the Middle East is currently part of the organisation.

To better understand the priorities, barriers, and networks of organisations that advocate on behalf of patients with meningitis, CoMO conducted a survey in January 2020. Seventy groups in 22 countries within the Middle East were canvassed as part of the survey, with both English and Arabic translations available for the survey questions. The charities' interests included: social development, disability, meningitis, visual impairments, hearing impairments, neurological conditions, and many others.

Information was organised by country and focus area, where applicable, to allow categorisation and filtering. Pre-determined and sector-accepted categorisations were also applied.

In terms of respondents, only five groups responded to the survey. The majority of responding groups were registered charities and had been operating for a long time, an average of 23 years. Groups had at least one full-time member of staff, with some form of

'membership' model, and most operated on less than \$20,000 per year. The average number of members was 50. Most groups provide information and support, and most work to improve diagnosis and treatment of illnesses and target their advocacy efforts to civil society and patient groups. All groups work on public awareness raising and most work on research. Funding and political environment were highlighted as the main barriers by the majority of respondents.

In terms of strategic focus: 3/5 of respondents reported that meningitis is very or extremely important to their organisation's goals; 3/5 reported that sepsis/septicaemia is very or extremely important to their organisation's goals. 2/5 reported that their main advocacy focus is on meningitis or septicaemia.

The most common target audiences for advocacy efforts were civil society/patient groups (targeted by 4 of the 5 groups) and service delivery professionals (targeted by 3/5). Specific priorities for organisations captured in the survey were: "Awareness and training"; "Health, education, cash for work, involving youth in development"; "Maintaining the health of people with special needs"; "Continuing to provide services to persons with disabilities, with an emphasis on prevention, early detection and protection programmes in light of the comprehensive development approach."

### The role of WHO collaborating centres (WHOCC)

The WHOCC are playing an important role in supporting Middle Eastern countries in disease surveillance. There are three WHOCC for meningitis: CDC, Atlanta, GA, USA; the Norwegian Institute of Public Health, Oslo, Norway; Institut Pasteur, Paris, France.

The key activities of these centres are three-fold: (i) To provide support to WHO in meningitis surveillance and outbreak investigations; (ii) to strengthen countries' laboratory capacity for meningitis diagnosis; (iii) to provide identification and molecular characterisation of *N. meningitidis* isolates.

Surveillance is typically performed through an initial diagnosis at a hospital in the country of origin using bacteriological techniques. Confirmatory testing and further typing would be conducted at a regional reference laboratory and a WHOCC. Within this established system, there remain a number of potential gaps in diagnostics, including poor infrastructure, issues with sample transportation, information sharing, and case definitions based on meningitis and not IMD.

To address these gaps, there remains a need to train a critical mass of health personnel in lumbar puncture, as well as establish effective systems for CSF transportation. There also needs to be a strengthening of coordination between meningitis laboratories and surveillance teams. Laboratories also need to be regularly monitored for ongoing performance.

When considering some of the aforementioned issues in the Middle East (i.e. lack of epidemiological data; policies predominantly focused on pilgrimages), WHOCC can support in addressing these needs. In particular, these centres could support in: establishing a standardised case definition for IMD; generate access to laboratory capacity for the diagnosis of IMD and characterisation of *N. meningitidis*; and help advocate for the use of conjugate vaccines.

### Conclusion

With bacterial meningitis being used consistently as a case definition for IMD, the actual burden of the disease may remain poorly understood across the Middle East, with other clinical manifestations likely being missed. Notwithstanding this ongoing concern, reported IMD cases remain low across the region, with MenB and MenW being prevalent in different countries.

Equally, case confirmation methodologies vary across the region, with PCR only being used in a small number of countries. This may

be owing to constraints on sample storage, transportation, expertise, laboratory capacity, or expenditure. Emerging diagnostic tools, such as the LAMP assay, may help to alleviate some of this pressure in offering low-cost, practical, and rapid specimen testing.

Alternatively, in working closer with WHOcc, countries may foster closer research links. These WHOcc may receive meningococcal isolates from a country for molecular characterisation, serogrouping, strain tracking etc. Equally, these centres have supported regions with reagents and specialised laboratory training.

### Declaration of Competing Interest

Xilian Bai performs contract research on behalf of UKHSA for GSK, PATH, Pfizer and Sanofi Pasteur. Ray Borrow performs contract research on behalf of UKHSA for GSK, PATH, Pfizer and Sanofi Pasteur. Ener Cagri Dinleyici performs contract work for the Eskisehir Osmangazi University funded by GSK, Sanofi Pasteur and Pfizer. Jay Lucidarne performs contract research on behalf of UKHSA for GSK, PATH, Pfizer and Sanofi Pasteur. Marco A. P. Sáfadi reports research grants and personal fees for advisory boards from GSK, Pfizer, and Sanofi. Vinny Smith and Claire Wright work for the MRF that receives grants and/or sponsorship from GSK, PATH, Pfizer, Sanofi, Bill and Melinda Gates Foundation, and Serum Institute of India. M.K. Taha performs contract work for the Institut Pasteur funded by GSK, Pfizer and Sanofi Pasteur. M.K. Taha and A.E. Deghmane has a patent NZ630133A Patent with GSK “Vaccines for serogroup X meningococcus” issued. J.A. Vázquez performs contract work for the Institute of Health Carlos III funded by GSK and Pfizer and he has received personal fees from Pfizer and Sanofi Pasteur.

### Acknowledgements

Medical writing support for the development of this manuscript, under the direction of the authors, was provided by Matthew Gunther of Ashfield MedComms, an Inizio company. Medical writing support was funded by Sanofi Vaccines. The authors would like to thank Naif K. Alharbi and Pasi Penttinen from the Gulf Centres for Disease Prevention and Control for their contributions to the GMI meeting and their insights. All authors discussed and agreed to the objectives of this manuscript and contributed throughout its production. All authors read and approved the final manuscript.

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