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MAJOR ARTICLE

Epidemiological and Clinical Characteristics of Melioidosis Caused by Gentamicin-Susceptible *Burkholderia pseudomallei* in Sarawak, Malaysia

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Background. *Burkholderia pseudomallei*, the causative agent of melioidosis, is intrinsically resistant to a broad range of antibiotics, including aminoglycosides. In Sarawak, Malaysia, a high proportion of melioidosis cases are caused by gentamicin-susceptible isolates. There are limited epidemiological and clinical data on these infections.

Methods. We conducted a retrospective study of culture-confirmed melioidosis among adults admitted to Bintulu Hospital in Sarawak, Malaysia, from January 2011 until December 2016.

Results. One hundred forty-eight adults with culture-confirmed melioidosis were identified. Of 129 (87%) tested, 84 (65%) had gentamicin-susceptible *B pseudomallei*. The average annual incidence of melioidosis was 12.3 per 100 000 population, with marked variation between districts ranging from 5.8 to 29.3 per 100 000 population. Rural districts had higher incidences of melioidosis and overwhelmingly larger proportions of gentamicin-susceptible *B pseudomallei* infection. Significantly more patients with gentamicin-susceptible infection had no identified risk factors, with diabetes less frequently present in this group. Ninety-eight percent had acute presentations. Pneumonia, reported in 71%, was the most common presentation. Splenic abscesses were found in 54% of those imaged. Bacteremia was present in 88%; septic shock occurred in 47%. Forty-five (35%) patients died. No differences in clinical, laboratory, or outcome characteristics were noted between gentamicin-susceptible and gentamicin-resistant infections.

Conclusions. Gentamicin-susceptible *B pseudomallei* infections are common in Sarawak and dominate in the high-incidence rural interior regions. Clinical manifestations and outcomes are the same as for gentamicin-resistant *B pseudomallei* infections. Further studies are required to determine if all gentamicin-susceptible *B pseudomallei* infections in Sarawak are clonal and to ascertain their environmental drivers and niches.

Keywords. melioidosis; *Burkholderia pseudomallei*; gentamicin-susceptible; clinical characteristics; Sarawak.

Melioidosis is an important cause of infectious disease mortality in the Western Pacific region and in Southeast Asia (SEA) [1, 2]. Although historically known to be endemic to SEA and northern Australia, cases are now increasingly being reported worldwide [3, 4]. Melioidosis is caused by the environmental saprophyte *Burkholderia pseudomallei* (*Bp*), a gram-negative bacillus that is intrinsically resistant to a broad range of antibiotics, including aminoglycosides [5].

In 2014, we reported the presence of rare gentamicin-susceptible *Bp* among a large proportion of clinical isolates from central Sarawak, Malaysian Borneo [6]. Interestingly, all gentamicin-susceptible isolates examined were genetically typed as either multilocus sequence type (ST) 881 or its single-locus variant ST997. The mechanism of the susceptibility to gentamicin was ascertained to be a novel mutation within the gene *amrB*, which encodes an essential component of the AmrAB-OprA multidrug efflux pump, with the mutation resulting in prevention of the efflux of gentamicin and macrolides that occurs in wild-type *Bp*.

Limited data are available on the disease burden and the epidemiological and clinical characteristics of melioidosis among adults in Sarawak. Importantly, the epidemiological and clinical characteristics of infection caused by gentamicin-susceptible

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