

Considerations in designing and interpreting prevalence studies for Behçet syndrome

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Prevalence studies are important for identifying the disease burden and planning health care needs for a condition, for determining the changes in disease prevalence in a country or a certain population over time, and for making comparisons across different populations, which helps estimate how the results of a study in a certain country may be applicable to other countries indicating the generalizability of the results. Moreover, such epidemiology studies may provide clues for pathogenesis by pointing to the role of certain genetic or environmental factors. The key issue in conducting good prevalence studies is the choice of the right sample, right methodology, and right analysis.¹ Several prevalence studies have been conducted for Behçet syndrome (BS) in different parts of the world, with different approaches regarding each of these points. Differences such as community-based versus hospital-based studies, differences in the criteria used for defining patients with BS, such as the International Study Group (ISG) criteria or the International Criteria for Behçet's Disease (ICBD) criteria, and the use of prevalence rates or prevalence odds ratios may render the interpretation and comparison of these studies difficult.²

BS is more prevalent along the ancient Silk Route where the prevalence of HLA-B51 is high. The highest prevalence is in Turkey (420 per 100 000), followed by Iran (80 per 100 000), Iraq (17 per 100 000), Japan (7–13.5 per 100 000), and China (2.6 per 100 000). The estimated prevalence of BS varies across European countries, ranging between 0.3 and 27 per 100 000 and is higher in the southern parts.³ It was thought that immigration may be a cause of increased BS prevalence in European countries. In a study from Germany that elaborates on this issue, the prevalence of BS was 1.47 per 100 000 among Germans and 77 per 100 000 among Turks living in Germany.⁴ Similarly, 2 other studies from Sweden (13.6 vs 2.0 per 100 000)⁵ and France (6.2–36.4 vs 2 per 100 000)⁶ found higher

prevalence rates among immigrants compared with native Europeans.

In the October 2017 issue of the *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Kanecki et al⁷ reported the first study from Poland on the incidence and prevalence of BS. This is actually the first prevalence study of BS from Eastern Europe, to the best of our knowledge. The authors report an incidence rate of 0.5 per 1 000 000 per year (95% CI, 0.35–0.61) and a point prevalence of 0.34 per 100 000, which is the second lowest prevalence rate reported from Europe after Scotland.⁸ The low immigration rate from countries with high prevalence of BS to Poland may be a contributing factor to this low prevalence, but it is still lower than that in native European populations reported in studies which give separate prevalence rates for natives and immigrants in that country.^{4–6}

A recent meta-analysis emphasized that caution is needed when interpreting and comparing the results of prevalence studies for BS.² The authors estimated a 22-fold higher pooled prevalence for sample surveys (also called field or population surveys), compared with census surveys. This may be explained by the fact that BS has a variable disease course. This is especially true for the severity and frequency of the symptoms. Moreover, some symptoms such as oral aphthous and papulopustular lesions are not rare in the general population, and all manifestations tend to ameliorate with aging.⁹ Thus, mild cases and especially those without major organ involvement may be underrepresented in census surveys. This may be even more pronounced in surveys based on hospitalization records. In the current study, which is also based on hospitalizations, the authors explain that systemic vasculitides with multiorgan involvement such as BS are usually hospitalized since treatment, and advanced diagnostic procedures that can be done in inpatient settings may be required. However, this may still be a source of bias for underreporting.

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Another source of bias in prevalence studies is the criteria or definition used for identifying the disease population. In the current study, due to retrospective data collection it is not clear whether any criteria sets were used for identifying patients with BS. The ICB criteria are favored over the ISG criteria by the authors which may mean that the ICB criteria were used. If so, this may be another source of bias towards underreporting, since the low specificity of the ICB criteria may be problematic in areas with low prevalence. A recent example to this is the Birmingham study where the specificity was 69.1% with the ISG and 19.1% with the ICB criteria.¹⁰ On the other hand, BS may be misdiagnosed in countries with low prevalence. For instance, gastrointestinal involvement of BS may be misclassified as Crohn disease.¹¹

An interesting finding in this study is the relatively older age at diagnosis. The authors suggest that this may be related to differences in genetic and environmental factors. Another explanation could be that the more serious complications of BS such as arterial, nervous system, and gastrointestinal involvement that are more likely to cause hospitalization, occur at a later age in patients with BS.¹² This may have caused the patients in this study to be hospitalized for the first time at a mean age of 42 years, even though their disease had started at an earlier age. However, female predominance among the hospitalized patients cannot be explained by this, since women are expected to have a less severe disease course at this age.¹² Knowing the reasons for hospitalization of BS patients would be more informative to make a conclusion. Additionally, standardized incidence and prevalence rates would be more appropriate for conditions that show variability according to age such as BS.

Another interesting finding is that this study showed no difference regarding the prevalence of BS between urban and rural regions of Poland. In surveys from Turkey, there were some differences between studies from rural and urban areas regarding the prevalence of BS, frequency of eye involvement, and pathergy positivity among patients with BS.³ A possible explanation for this would be differences in environmental factors that are thought to play a role in the pathogenesis of BS. Infections are considered to be especially important in this regard. Although there was no difference regarding BS prevalence between urban and rural parts of Poland, it would be interesting to know whether differences exist in demographic factors or the types of organ involvement.

Such studies are interesting and important for our understanding of BS as well as informing health care providers and policymakers. In this regard, it is important to standardize the methodology for studying and reporting incidence and prevalence of BS across countries.

NOTE The opinions expressed by the author are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

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