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International comparisons of social differences in inflammatory markers: different patterns, same drivers?

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In a paper recently published in *Brain Behavior and Immunity*, Maharani reports differences in C-reactive protein (CRP) by social position in an English population but no association in an equivalent Indonesian population (Maharani 2019). In the majority of studies that have examined them, it is apparent that there are social differences in a number of disease outcomes including heart disease and psychiatric morbidity such that more advantaged groups have lower levels of disease than less advantaged groups (Lorant et al., 2003). However the mechanisms that mediate these associations are unclear. Behavioral researchers suggest chronic, low-grade inflammation as a pathway through which social and behavioral variables exert long-term effects on health. Inflammatory markers are socially patterned (Berger et al., 2019) such that a more advantaged social position, measured by greater educational attainment (Davillas et al., 2017) and higher occupational position (Gimeno et al., 2007) is associated with lower levels of markers that reflect inflammatory load such as C-Reactive protein. There are number of mechanisms that may drive social differences in inflammatory markers; embodiment of adversity (Slopen et al., 2012), adverse health behaviors (Hamer 2014; Loprinzi 2016), and stress (Rohleder 2014). Identifying these drivers might provide important insights for policymakers to militate against social differences in health.

However, the majority of studies are conducted in high income countries with a paucity of information from low or middle income countries (LMIC). It is important to understand the drivers of disease in LMIC as 87% of premature deaths due to noncommunicable diseases occur in low- and middle-income countries (WHO). In a joint analysis comparing social differences in CRP in England and Indonesia, Maharani replicates a finding of CRP differences using two measures of social position in her analysis, with both educational attainment and wealth associated with CRP in England (Maharani 2019). However, the pattern evident in Indonesia was in the opposite direction and this association was no longer present following adjustment for body mass index, smoking and physical activity. These findings suggest that the social patterning of inflammatory markers that appear ubiquitous in high income countries are not universal. The pattern of association of health behaviors and inflammatory markers with social position in the two countries provide important insight into the pathways that may mediate social inequalities in health.

These data indicate that while drivers of health may be universal, they are patterned differently in LMIC than in high income countries. For example, in very low income countries obesity is positively associated with social position but negatively associated in higher income countries (Monteiro et al., 2004). Leveraging comparison and using concordant or discordant findings across the countries may provide insight into mechanisms that mediate social differences in health. To this end, Maharani demonstrates that many of the drivers of raised inflammatory markers are patterned by social position. Thus health behaviors, adiposity measured by BMI and physical activity are associated with social position with greater adverse health behaviors in disadvantaged groups in England but in advantaged groups in Indonesia. Interestingly there is no social patterning of smoking behavior in Indonesia. This differing pattern of health behaviors highlights the social and cultural determinants of health; provides insights into their role in the development of health and also the processes that drive inequalities in health and potentially provides guidance on where policy should be directed. In particular, the role of physical activity appears important to help understand the differences in patterns between the two countries.

In the English but not in the Indonesian population, social differences in CRP remain apparent independently of health behaviors. Maharani proposes occupational stress as a factor that may gain importance in high income countries. This provides an interesting avenue for research. A previous study in the UK of social differences in inflammatory markers across the adult age range describes the emergence of these differences in populations aged late 20s and early 30s and also proposed a role for occupational stressors in the social patterning of inflammatory markers (Davillas et al., 2017). Indeed evidence suggests that poor quality jobs may themselves result in poor health behaviors, with stressful jobs associated with lower levels of physical activity (Lin et al., 2014). Maharani investigated leisure time physical activities only but occupational activity and conditions may also have played a role. Thus, LIMC occupations may have a higher proportion of agricultural or manual workers and high income countries with a higher proportion of sedentary low quality non manual jobs, which may serve to explain the differences in patterns in inflammation apparent in the paper.

Overall Maharani's observation of opposing patterns of social differences in inflammatory markers illuminates the common drivers of inflammation and identifies these as physical activity and obesity and possibly occupational stress. Further, the context specific patterns of these factors in social differences in inflammation emphasizes identification of upstream policy levers for intervention. A number of national programs have been initiated for prevention of noncommunicable diseases in many LIMC countries. As LIMC such as Indonesia continue to develop, these programs need to consider the interaction of structural factors such as occupational conditions with individual drivers of health.

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