Gut environment and socioeconomic status: a study of children in urban area of Makassar

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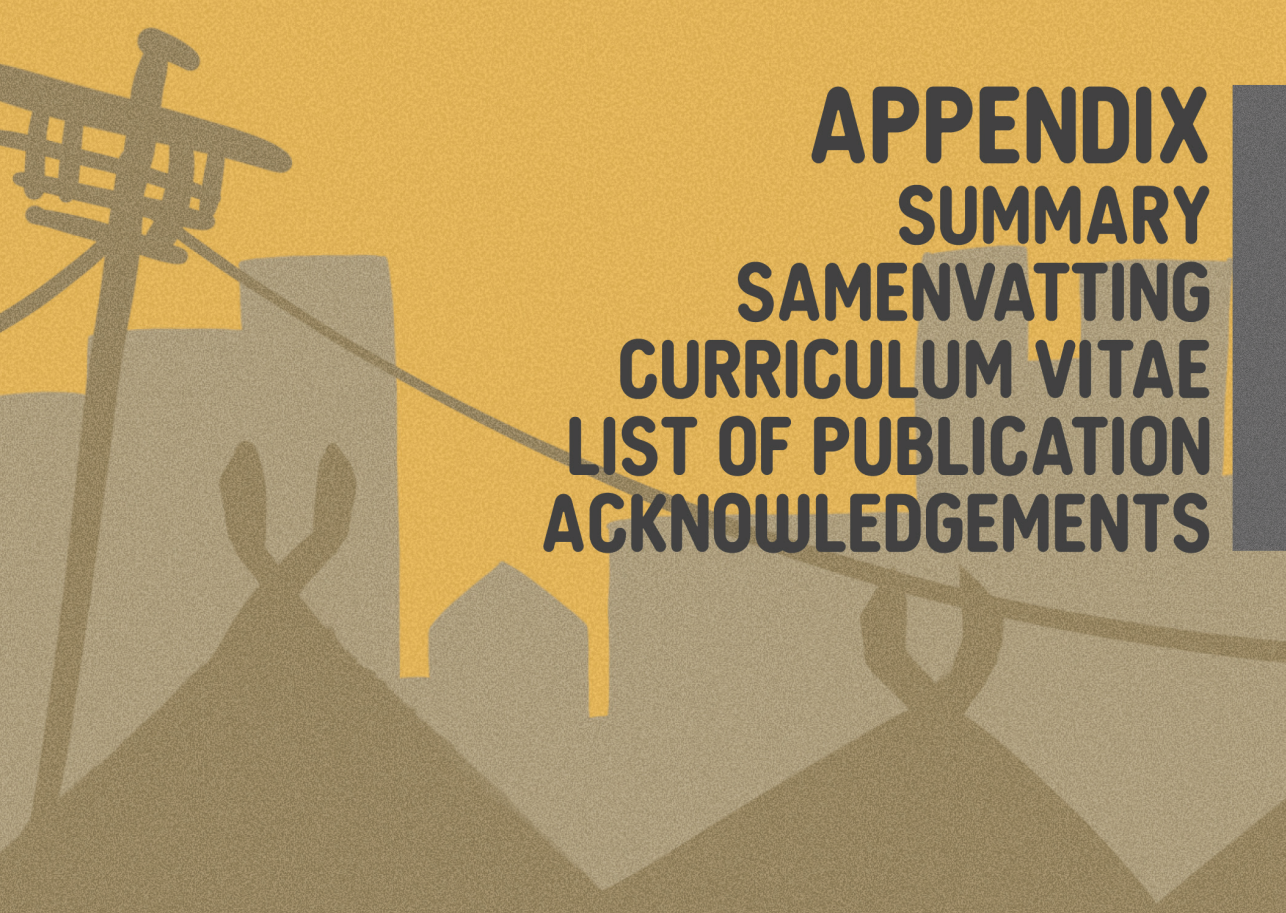

APPENDIX

SUMMARY

SAMENVATTING

CURRICULUM VITAE

LIST OF PUBLICATION

ACKNOWLEDGEMENTS

SUMMARY

Although urbanization has long been associated with human development and progress, recent research has revealed that urban environments can also result in significant inequalities in many areas including health. In particular, urban areas in low and middle income countries (LMIC), often see a widening gap in economic growth which contributes to health disparities between wealthy and underprivileged children. Several studies have established the association between socioeconomic status (SES) and child health, showing that children of low-income parents had poorer health status. The rise of non-communicable diseases, the persistence of communicable disease, and the challenge of re-emerging diseases are currently a burden in developing countries. Given the rapid increases of urbanization and urban poverty in several developing countries including Indonesia, it is important to elaborate to what extent SES affects child health. We have done so, in relation to outcome of BCG vaccination, atopic sensitization, and intestinal barrier function. We have also investigated the interaction between intestinal parasitic infections and bacterial gut microbiota in order to be able to delineate the contribution of this interaction on the function of intestinal barrier.

Chapter One, provides a general introduction to the research topics in the thesis including the background to why we perform the studies described in this thesis. This chapter also covers the study area, study population, and the scope of the thesis

Chapter Two establishes the association between the size of BCG scar, which indicates the degree of response to the vaccine, and SES. We included maternal helminth infection status and nutritional status of the newborn to assess their roles in the development of BCG scar in infants. We observed that children from the low-SES have smaller BCG scar size and total IgE (a marker of exposure to helminth infection) moderately contributes to reducing the size of the scar. At the same time, high-SES children have larger size of BCG scar, and leptin levels, a hormone that is released by fat cells, contributed to this association. This finding suggests that SES is the major determinant of BCG scar size and that leptin levels at birth together with total IgE can contribute to the development of BCG scar in Indonesian infants.

In **Chapter Three**, we reported for the first time Hymenoptera venom sensitizations in Indonesian schoolchildren. Higher prevalence of skin prick test reactivity (SPT), a measure of functional sensitization, was observed in high-SES compared to the low-SES children; in contrast, sIgE-positivity, a measure of allergen exposure that causes sensitization, was more prevalent in the low SES than the high SES. These sensitizations appear to have poor clinical relevance as they rarely translated into clinical symptoms. The finding that there is a discordance between SPT and sIgE in our study, suggests the presence of IgE (high levels of sIgE) with poor biologic activity (low SPT). We also found a considerable number of subjects positive for skin reactivity but negative for sIgE, indicating a non-IgE dependent reaction to venom allergen. Further studies are needed to determine the true sensitization of Indonesian children by using component-resolved diagnostic (CRD) methods. The CRD method has been widely used in affluent countries, but less used in low middle income countries. This method allows the detection of specific IgE against individual purified native or recombinant allergens, instead of against allergen extracts comprised of mixtures of allergenic and non-allergenic components, which are commonly used in SPT and conventional specific allergy testing.

In **Chapter Four**, we profiled fecal bacterial microbiota of Indonesian children to elucidate the characteristics of bacterial microbiota. The core microbiota of the children consisted of *Bifidobacterium, Collinsella*, and multiple members of the *Lachnospiraceae* and *Ruminicoccaceae* families. Here we show that bacterial gut microbiota was predominantly driven by children's SES. Bacterial diversity was higher in the low-SES and among others, *Prevotella* and *Escherichia-Shigella*, were more abundant, while in the high-SES, bacterial diversity was lower and we observed higher relative abundance *Bifidobacterium* and *Lactobacillus.* These differences might be associated with different diet and lifestyle which are distinct between high- and low-SES, however, we can not discern this association between gut microbiota composition and diet as food intake was not surveyed. To delineate the association between helminth infections and gut microbiota, in **Chapter five**, the alteration of the gut microbiota was assessed 4 weeks after albendazole administration and no changes in gut microbiota diversity were observed, however, the alteration of bacterial microbiota composition was more SES-related and not associated with helminth infections as the changes observed was found in the uninfected group only.

In **Chapter Five**, we assessed the intestinal barrier function of Indonesian schoolchildren living in the same urban area but distinct in SES. Low-SES children exhibited higher LMR, indicating increased intestinal permeability and higher I-FABP, a marker of epithelial damage. This indicates that the intestinal barrier function and integrity might be compromised in low- compared to the high-SES children. The high LMR in the low-SES is not due to higher prevalence of intestinal parasitic infections in the low-SES as the changes in the level of LMR after albendazole treatment were only altered in the uninfected children. In the future, placebo should also be used, to be able to discern whether the changes are albendazole related or time-related.

Chapter Six summarizes and discusses the main findings of this thesis together with previous studies on the relationship between child health and SES. We highlighted the effect of SES on BCG scar development in young infants. In addition, we also discussed the impact of SES on venom sensitization, bacterial gut microbiota and intestinal permeability function in schoolchildren. In the end, this thesis sparks some directions for future research and to this end how our findings might affect policies for child health especially in Indonesia where there are wide socioeconomic disparities.