Commentary: What is the role of co-morbidity in child mortality?

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Childhood infectious diseases remain the leading cause of morbidity and mortality among children under 5 years of age around the world. More than half of all child deaths can be attributed to the three most lethal communicable diseases: pneumonia (including sepsis in neonates), diarrhoea and malaria. Prevention and treatment of these infectious diseases should be the greatest public health priorities to improve the survival of children living in communities characterized by extreme poverty, poor health systems and environmental contamination. Children...
in these settings may be more susceptible to infection as a consequence of weakened immune function and nutritional deficiencies, or perhaps because of previous or other concurrent infections. There is limited information from prospective studies to quantify the prevalence of infectious disease co-morbidities among young children. Several studies have found that the rate of diarrhoea and pneumonia occurring together is greater than that of chance alone. However, in these analyses the authors were not able to differentiate between simultaneous or sequential infections or were they able to explain the relationship of the infections as either due to shared risk factors or because one infection increased the risk of the other.

The paper by Schmidt and his colleagues describes a series of time-to-event analyses conducted to assess the role of diarrhoea as a risk factor for subsequent acute lower respiratory tract infections (ALRI). There are few published studies designed to observe a relationship between sequential infectious co-morbidities among children under 5 years of age, and these primarily involve measles and subsequent diarrhoea or pneumonia. This study provides important quantitative evidence to support this relationship among serious infectious diseases. The prospective studies included in this analysis are from two large vitamin A studies conducted in the early 1990s among poor communities in Ghana and Northeastern Brazil. In both studies children were monitored on a routine basis, weekly in Ghana and three times per week in Brazil. With this design, daily diarrhoea prevalence could be measured, enabling the authors to consider the correlation between days of illness and subsequent ALRI infection rather than simply diarrhoea incidence. The use of prevalence provides a better measure of diarrhoea disease burden than incidence. The authors report an increased risk of ALRI for every additional day of diarrhoea among the Ghanaian children (1.08, 95% CI: 1.004–1.15) in the 14 days leading up to the reported ALRI episode. The relationship between increased days with diarrhoea and risk of ALRI was also observed 28 days prior to the index ALRI episode, suggesting that the full recovery from a diarrhoea episode requires >2 weeks and close monitoring for subsequent illness should be part of follow-up care and caregiver education. The relationship between diarrhoea prevalence and ALRI was not observed in Brazil. This might be explained by the relative affluence of this population compared with the study community in Ghana or may simply be a failure to replicate the association. There are several possible mechanisms that might explain the observed effect. Diarrhoea results in an increased loss of zinc in the stools and the subsequent deficiency may increase the child’s susceptibility to subsequent infections, including ALRI. In addition, diarrhoea can cause dehydration and an electrolyte imbalance, which may also increase the risk for ALRI. 

Because the association of most interest is the relationship between co-morbidity and a possible increased risk for mortality, additional information is needed. Thus far there has been only one community-based study that has assessed the correlation between diarrhoea and pneumonia occurring together and child mortality. Though this analysis did not show a synergistic effect of co-morbidity on overall mortality, the original study had not been designed to address this question, thus it lacked the power to detect an epidemiologically important effect. The Ghana data presented here come from the same study population as used in the Fenn et al. analysis.

Recognizing the fact that children who die in low-income countries commonly have multiple infectious diseases, including diarrhoea and pneumonia, at the time of death, it is critical that we continue to increase our understanding of the role of co-morbidity and the risk of mortality. The categorical attribution of child deaths to a single cause (one death, one cause) in tabulations such as the Global Burden of Disease obscures the potential importance of multi-disease causation and may lead to incorrect estimates of the possible effects of interventions on child mortality. In Schmidt et al., 68% of all ALRI episodes were preceded by a diarrhoea episode in the 2 weeks prior, suggesting a potential role for diarrhoea prevention and treatment interventions for reducing ALRI morbidity and possibly mortality. Though this paper focused on one chronological association between two common infectious diseases, the findings beg the reader to consider the many infectious disease relationships that may be intertwined in high-mortality settings. Additional analyses are greatly needed to further expand understanding of how simultaneous and sequential infections affect a child’s risk for the most serious outcomes.

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References


