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Neonatal meningitis and sepsis: what happens to survivors?

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Meeting Sustainable Development Goal (SDG) 3.2 for child survival is increasingly dependent on neonatal deaths, which now account for 47% of under-five mortality worldwide. Survivors of neonatal infections, especially meningitis, are at high risk of neurodevelopmental impairment (NDI), yet there has been limited attention to this burden. The "Defeating Meningitis Roadmap" has four pillars, one of which is identification and care for meningitis survivors.

We have <u>previously estimated</u> 2.2 million (uncertainty range: 1.1-2.4 million) cases of neonatal sepsis/pneumonia, and 200,000 (21,000-350,000) cases of neonatal meningitis annually in Low and middle income countries (LMIC). Our systematic review found that amongst neonatal meningitis survivors 23% (95% CI: 19-26% (2,700-35,000)) had moderate to severe NDI, by 18-32 months of age. This estimate was based on 8 studies from High income countries (HIC). For comparison the survivors of neonatal tetanus had an NDI risk of16% (6-27%). No meta-analyses were possible for NDI amongst non-preterm survivors of neonatal sepsis. Regarding aetiology-specific estimates, our <u>recent reviews</u> for Group B Streptococcus (GBS) identified 18 studies following up survivors of GBS meningitis, but only to 18 months and all from HIC. There was a 32% (95% CI, 25%-38%) prevalence of any NDI, including 18% (95% CI, 13%-22%) with moderate to severe NDI.

Whilst data are limited, there is a consistently high risk after neonatal meningitis with at least 1 in 4 severely affected, such as with cerebral palsy and/or cognitive impairment. However, there were major data gaps. Firstly geographically, with no data from LMIC which carry the majority of the burden. Secondly longer term follow-up is required to more accurately identify hearing or visual deficits and subtler developmental delays, behavioural conditions and educational consequences. Identifying modifiable co-morbidities (e.g. epilepsy, under-nutrition) is also important. Finally, data regarding NDI amongst survivors of neonatal sepsis is a black hole, and given the high incidence of this exposure, even minor NDI would be of major public health importance.

To help close this data gap, we are now undertaking five GBS cohort re-enrolment studies (Argentina, India, Kenya, Mozambique, South Africa) and two national e-Cohorts (Denmark, Netherlands). Longer term follow-up and measuring the consequences for families, including economic impact, are crucial to inform full value case proposition analyses for GBS vaccines being undertaken by LSHTM and WHO.

The care gap is even greater than the data gap. Improved case management, and support for children with NDI, as well as their families, are all important strategies, yet currently receive limited investment. Primary prevention would be the most effective strategy to reduce burden and also the major life-long consequences for families.