Commentary

Maternal childhood and lifetime traumatic life events and infant bronchiolitis

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Associations between childhood maltreatment (abuse or neglect) and poor adult health have been shown in numerous prospective studies.[1,2] Potential causal pathways include disruption of the hypothalamic pituitary axis and stress responses,[1] mediation through adolescent and adult life styles associated with cardiometabolic disease,[2] or as a risk factor potentiating genetic markers predisposing to mental health disorders.[3,4] Evidence for associations between maternal-reported child maltreatment and outcomes of pregnancy are more contentious. A recent study of 4,181 primiparous women found no association between maternal reports of various forms of child maltreatment and preterm birth, except

for sexual abuse by physical force by a non-parent or care giver.[5] Few studies have gone beyond delivery outcomes in pregnant women and compared health outcomes in children born to mothers with and without a history of child maltreatment.

The study in this issue of Paediatric and Perinatal Epidemiology, Adgent and colleagues' study adds to an emerging literature on associations between traumatic, maternal prenatal events and outcomes in her infant.[6] The study focuses on infant bronchiolitis, building on studies showing variable evidence for associations between maternal prenatal stress and allergy or respiratory disease in her child.[7] The present study followed mother-infant dyads from a low income urban population in Memphis who were enrolled prenatally (2006-2011) in a prospective cohort study, called CANDLE.[6] The cohort of 639 women were predominantly African-American (85%), and most were enrolled with Medicaid (59%). Inclusion was restricted to consenting, resident, white or African-American women, recruited at 16-28 weeks of gestation, who had no chronic conditions or pregnancy complications. How previous births were dealt with is unclear. The cohort was further restricted based on infant outcomes including delivery at term, birthweight $\geq$2500 g, no complications, congenital or respiratory or cardiac anomaly or disease or receipt of RSV prophylaxis, and with survival and continuous infant enrolment in Medicaid to 12 months of age.

Adgent et al.[6] measured recall of traumatic life events (TLE) using mothers' responses to a self-report questionnaire during the third trimester study visit. Yes/no answers to questions about 20 types of traumatic life events (TLE) at any time in their life course, including accidents, violence abuse, or death or illness of a loved one, were summed to create a score

of 0-20: 92% of mothers reported at least one of these TLEs and 63% reported three or more. Three questions asked about childhood TLEs in childhood related to family violence, physical abuse or sexual abuse while growing up or before her 13th birthday: 45% reported events in one or more of these categories and 3% reported events in all three categories. The correlation between TLE at any time and childhood TLE was not reported. The study found no significant association between the number of TLEs at any time and infant bronchiolitis recorded in hospital admission, emergency room or clinic visits. However, the authors found an increased risk of bronchiolitis for infants born to the 3% (n=20) of mothers who reported childhood TLEs in all three categories compared with the 55% of mothers reporting no childhood TLEs. Analyses were adjusted for ethnic group, maternal age, education level, access to people able to offer support, smoking in pregnancy, and birthweight. Findings did not change appreciably in sensitivity analyses that excluded smoking and birthweight or analyses that imputed missing data. The E–value, which quantifies the effect of unmeasured confounding required to nullify the observed association, was substantial with a lower 95% confidence interval of 2.26.

Do these findings provide evidence of enduring maternal stress from childhood TLEs affecting respiratory health in their infants?

Not yet! The high point estimate of the risk ratio for 3 childhood TLEs compared to none (2.65, 95% confidence interval [CI] 1.45, 4.85) is similar to the excess risk of respiratory infection admissions among children with severe and chronic heart or lung conditions.[8] There are several reasons why this high risk ratio may have been observed, and why caution is required pending further studies. First, the association between maternal childhood TLEs and infant bronchiolitis was based on few infants with bronchiolitis (9/20 of dyads with

childhood TLEs in all three categories). Much larger studies are needed. Second, the timing of TLEs was not defined, apart from specifying categories of trauma occurring while growing up. Maternal TLEs could have occurred at any time, including after birth, and could have affected maternal capacity and responses to infant illness.

Third, self-reported childhood maltreatment is unreliable.[4] A recent systematic review showed that half of individuals with prospectively recorded child maltreatment did not retrospectively report child maltreatment.[4] Conversely, half of those retrospectively reporting child maltreatment had no prospective record of maltreatment events. Recall has been associated with psychopathology,[4] and with adverse pregnancy events.[5] Misclassification of the exposure of childhood TLE is therefore likely. Fourth, stress or maternal mental health, neither of which were measured in the study by Adgent et al,[6] could confound the association between maternal recall of childhood TLE and infant bronchiolitis. Stress in pregnancy could also mediate associations with childhood respiratory disease through biological mechanisms affecting fetal growth and development or through social mechanisms affecting maternal responses to infant symptoms, mixing with other young children, or use of healthcare.

Fifth, unmeasured environmental and social influences could confound the relationship between maternal recall of childhood TLE, and the risk of infant bronchiolitis seen by healthcare services. Both contact with older siblings and deprivation, are strongly associated with earlier age of bronchiolitis and with hospitalisation.[9] The study by Adgent et al,[6] did not account for parity, other children in the household or involvement of other care givers with children, relative deprivation, or environmental risk factors for childhood respiratory

disease. Prenatal exposure to air pollution and poor housing conditions is also associated with childhood respiratory disease and may be more common in women living in more stressful situations linked to recall of TLE.

Lastly, the analyses introduced selection bias by excluding infants born preterm, low birthweight, with cardiac or respiratory complications, or without continuous follow-up through Medicaid. Associations between maternal recall of TLE and these excluded infant characteristics would most likely bias observed associations in favour of underestimating associations between maternal recall of TLE and infant bronchiolitis.[10]

What are the implications for further research?

Potential associations between maternal TLE and fetal and infant outcomes warrant further investigation in large studies, using prospectively recorded and timed indicators of traumatic events across the life course. Self-reported TLEs and measures of maternal stress captured in cohort studies (including biological measures) provide a key resource, but so do externally recorded TLEs in health or child protection administrative data. Increasing availability of record linkage between cohort studies and longitudinal administrative health data can reduce attrition in cohort studies, which disproportionately affects the more vulnerable, and enable follow up of mothers from their childhood to index pregnancy and delivery through to the maternal postnatal life course and that of her child. Understanding of socio-biological mechanisms will be enhanced by detailed mental health data and biological measures but need to be combined with whole population data that measure modifiable risk factors related to disadvantage, neighbourhood or ethnic mix and indices of social support that could potentially mediate the effects of TLE on adverse outcomes in

mothers and their children. The study by Adgent and colleagues[6] provides a thoughtful examination of an important problem that we need to approach through the lens of prevention.

About the authors

Ruth Gilbert is Professor of Clinical Epidemiology and Pia Hardelid is Lecturer in Epidemiology and Statistics. Both have leading roles in the Children and Families Policy Research Unit, which is funded by and works closely with the Department of Health and Social Care for England. Hardelid leads research on respiratory infections in children and Gilbert leads research on child maltreatment and other sources of adversity within families. Both make extensive use of linked administrative data in the UK and are part of Health Data Research UK.

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