Reviewer's report

Title: Maternal and perinatal factors associated with hospitalised infectious mononucleosis in children, adolescents and young adults: record linkage study

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Reviewer: dorothy crawford

Reviewer's report:

This manuscript is well written and the results are clearly presented. The study looks at maternal and perinatal factors in relation to severe infectious mononucleosis (IM) in children, and is well designed and executed. To my knowledge a study of this type has not been attempted before and could provide interesting pointers to the associations between IM and Hodgkin's lymphoma (HL) and multiple sclerosis (MS). Unfortunately few positive associations were found and the authors find those that were identified difficult to explain. In the field of my expertise (IM, EBV and HD), there are some omissions and mis-referencing and these have restricted the discussion.

Essential revisions:

- The working hypothesis should be stated ie why was the study undertaken and what did the authors expect to find?

- The IM/EBV references used are old and in many cases have been superseded. For example, reference 1 is used to show a 50% IM rate from late infections, but the incidence of IM is changing and the paper quoted is a hypothesis from the US published in 1982. The most recent and largest study was carried out in the UK and showed a 25% rate of IM from delayed primary EBV infections. This study generated several papers including Crawford et al JID 186: 731-6. 2002, Crawford et al CID 43: 276-82. 2006, Higgins et al JID 195: 474-82. 2007, Macsween et al CID 50: 699-706. 2010. Also, our knowledge of the epidemiology of HD and its association with EBV has moved on since reference 5 was published in 1980. More recent work by RF Jarrett and others would be worth quoting.

- The reference Lindberg 1991 is in the text but not the reference list.

- Page 7, Results, para 1, the authors state that the age profile of IM contrasts with that of primary EBV infection, but IM is a form of primary EBV infection - this needs rewording.

- Page 9, Discussion, it is important to know how the IM was diagnosed in the hospitalised patients - were IgM anti VCA levels always measured?

- The discussion should be more wide ranging including information on the biology of EBV, HD and MS, for example the recent findings that the risk of development of both IM and HD is related to genetic factors that influence the immune response to EBV during primary infection. Twin studies on HD would
also be worth a exploring. The inclusion of these studies may suggest possible explanations for the results found in the present study.
- The conclusion in the abstract is very negative. Once the risk factors for IM and HD are explored in more depth this could perhaps be revised.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.