Reviewer’s report

Title: Laboratory Testing for Cytomegalovirus among Pregnant Women in the United States: a Retrospective Study using Administrative Claims Data

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Reviewer: Klaus Hamprecht

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To the authors

Leung, Cannon, Grosse and Bialek submitted a paper entitled

Laboratory testing for Cytomegalovirus among pregnant women in the US: a retrospective study using administrative claims data

To BMC Infectious Diseases.

The authors identified nearly 80,000 pregnant women in the USA of whom 1700 (2%) had a claim for CMV specific testing. The data were derived from a commercial 2009 software (MarketScan®/Reuters) using ICD-9-CM codes and Current Procedural Terminology (CPT) codes.

44 women were identified using a diagnostic code for mononucleosis of whom 14% had CMV specific testing.

M Cannon and his coworkers contributed a large amount of knowledge to the epidemiology of congenital CMV infection during the last years.

In the actual manuscript however remain some open questions for the conclusive understanding of the interested reader.

1.) Commercial database.

Is the database using Marketscan® really representative for the american society respectively health assurance system or does it produce a bias?

To my knowledge in the US health assurance is not obligatory and ethinical minorities are not included adequately. We know that the highest rates of cCMV were reported from black cohorts in Birmingham/Alabama (Stagno/Pass/Fowler)

Is there a bias by the kind of software which may be different using another software from an other company?

2.) Statistical analysis/Code for CMV disease

Why the authors computed frequencies of pregnant women with a code for “CMV disease” and CMV testing.

Diagnosis of CMV primary infection is just by accident, because in 75% of all cases the CMV primary or recurrent infection during pregnancy is without any
symptom or with very unspecific symptoms.

3.) The quality of the disease parameter “CMV mononucleosis”
In Table 1 is shown, that >96% of all pregnant women are older than 20 years and 56% older than 30 years. Reflecting that “Mononucleosis” is an infection of the adolescence in most part of people below 20 years, only 4 % of data of the study would fit with it (Table 1, Age group 15-19).

4.) Type of CMV testing
The authors refer to Dollard et al, 2011 for diagnosis of CMV primary infection in pregnancy in context of the absence of CMV IgG avidity testing in the USA. (page 3). The adequate diagnosis of CMV primary infection in pregnancy is based on serology (Lazzarotto et al, 2011; Revello et al, 2004). But without IgG avidity its impossible to differentiate between CMV primary infection or recurrent infection. Thus all different test shown in Table 2 lack the most important tool for diagnosis of recent infection: the low avidity detection. IgM titers may persist over months, IgM titers may differ strongly using tests from different companies. The only option using only CMV IgG/IgM data would be to check reducing IgM indices, which has need for sequential examinations. And these are mostly not done.

PCR does not help for routine diagnosis, because CMV shedding into urine is detectable during every period of CMV primary infection and viral DNAemia has a small window of about 2 weeks around primary infection (Lazzarotto et al., 2011):

Virus culture, DFA, as shown in Table 2 do they have a real diagnostic value?

5.) The role of table 4 remains quite unclear.

Taken together, this paper seems to reflect the actual situation of diagnosis for primary or recurrent CMV infection during pregnancy in the USA- if the database does not create a bias. The key message could be: change diagnostic behaviours to an optimized diagnosis strategy for CMV primary or recurrent infection in the USA.

Please do not misunderstand: we have exactly the same problems in Germany to propagate adaequate CMV diagnosis methods to obstetricians and gynaecologists. However, in the last years CMV IgG avidity seems to be an accepted tool for CMV diagnosis in pregnancy in nearly all private and university labs.

Without the IgG avidity or gB absence and the restricted role of PCR, DFA, virus culture, a relevant differentiation between actual primary infection and recurrent CMV infection with persisting IgM cannot be done. And therefore this paper may contribute important details using the administrative claims data sets.

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Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

No interfering interests.