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Review

Consequences of brucellosis infection during pregnancy: A systematic review of the literature

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ABSTRACT

Background: The aim was to establish the incidence of adverse outcomes with brucellosis infection during pregnancy.
Methods: Ovid Medline (1946-), Ovid Embase (1974-), and Web of Science (Clarivate Analytics) (1900-), the World Health Organization website and Google were searched September 27, 2017 for (i) outcomes with brucellosis diagnosed during pregnancy and (ii) studies with retrospective diagnosis of maternal brucellosis following adverse pregnancy outcomes.
Results: Sixty studies met inclusion criteria. In 65 pregnancies from 28 case reports and 9 small case series (<10 women), there were 20 spontaneous abortions (SAs) (31%), 2 intra-uterine fetal deaths (IUFDs) (3%) and 11 cases of congenital brucellosis (17%). In 14 larger case series there were 181 SAs in 679 pregnancies (27%), 19 IUFDs in 458 pregnancies (4%), and 44 preterm infants (12%) plus 6 infants with congenital brucellosis (2%) in 362 pregnancies. SA, IUFD and preterm delivery incidence were increased with meta-analysis of the 5 case series with controls. Nine studies described brucellosis seroprevalence with adverse pregnancy outcomes with no increased seroprevalence in the two studies with controls.
Conclusions: Brucellosis almost certainly causes SA with increasing evidence that it also leads to IUFD and prematurity. Congenital brucellosis occurs in approximately 2% of infants exposed in-utero.

Contents

Introduction

Brucellosis is a zoonosis that can be acquired in most countries (Pappas et al., 2006). Human infection stems from direct contact with infected animals, inhalation of contaminated animal feces or consumption of infected animal products. Human-to-human transmission via blood transfusion, bone marrow transplantation, sex, transplacental or perinatal exposure, and breast milk have been documented (Tuon et al., 2017a).

Brucellosis in pregnancy is of special interest as it remains controversial whether it is a precipitant of poor outcomes beyond congenital brucellosis. This is the first systematic review with meta-analysis analyzing whether brucellosis increases the incidence of other adverse pregnancy outcomes.

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Search strategy, selection criteria and data collection

For this systematic review with meta-analysis, the databases Ovid Medline (1946-), Ovid Embase (1974-), and Web of Science (Clarivate Analytics) (1900-) were searched for concepts related to brucellosis and pregnancy (excluding studies in animal populations) on September 27, 2017 (Appendix A). The World Health Organization website and Google were searched for relevant reports. No language or date range restrictions were applied and all study designs were considered. Results were exported into EndNote X7 and duplicates removed. Reference lists of previous reviews were hand-searched. Cases or case series were included if one or more women had brucellosis detected during pregnancy and the incidence of at least one of the following outcomes was reported for all cases in the series: spontaneous abortion (SA), intra-uterine fetal death (IUFD), preterm or term live born infant, and/or congenital brucellosis. Cases were excluded if maternal brucellosis was recognized only after an infant was diagnosed with congenital brucellosis. Case series from endemic countries retrospectively seeking evidence of brucellosis in women with adverse pregnancy outcomes were also included if they described testing for minimum ten women.

Data recorded for the case reports and case series included country and outcome(s). The assumption was made that the terms "normal delivery" or "uncomplicated delivery" implied that the infant was term. Case series with ≥ 10 women were reported separately as larger series would be less subject to reporting bias; the diagnostic criteria for brucellosis and any outcome data from a control group were also recorded for these studies. Meta-analysis was limited to case series with women with brucellosis and their controls; results of all applicable studies were combined and incidence rates compared in cases and controls with a Chi-squared test. A p value of 0.05 was considered to be significant.

For case series looking for evidence of brucellosis with adverse pregnancy outcomes, the population studied and the seroprevalence of brucellosis were recorded.

To assess the risk of bias, the Newcastle-Ottawa Quality Assessment Scale was applied to studies that included a control group (http://ohri.ca/programs/clinical_epidemiology/nosgen.pdf). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (**PRISMA**) guidelines (http://www.prisma-statement.org/Default.aspx) were followed for reporting the results. This systematic review was registered with PROSPERO (CRD42017072061). Support for this study was provided by the Alberta SPOR SUPPORT Unit Knowledge Translation Platform.

Results

The search yielded 544 records of which 60 met the inclusion criteria (Figure 1). Other titles were excluded after full text review as maternal brucellosis was diagnosed after congenital brucellosis (n = 14), the article was not relevant (n = 7), they were review articles or a book chapter (n = 6), there was no pregnancy outcome data (n = 4), this was a conference abstract for a subsequently published study (n = 2), the article could not be translated (n = 1), remote and recent pregnancy outcomes were combined (n = 1) or the diagnosis of maternal brucellosis was presumptive (n = 1).

There were 28 case reports and nine small case series (<10 women) (Table 1) with outcomes reported for 65 pregnancies complicated by brucellosis leading to 20 SAs (31%), one therapeutic abortion (2%), 2 IUFDs (3%), 11 preterm infants (17%), and 31 term deliveries (48% – includes one set of twins) (De Carles, 1931;

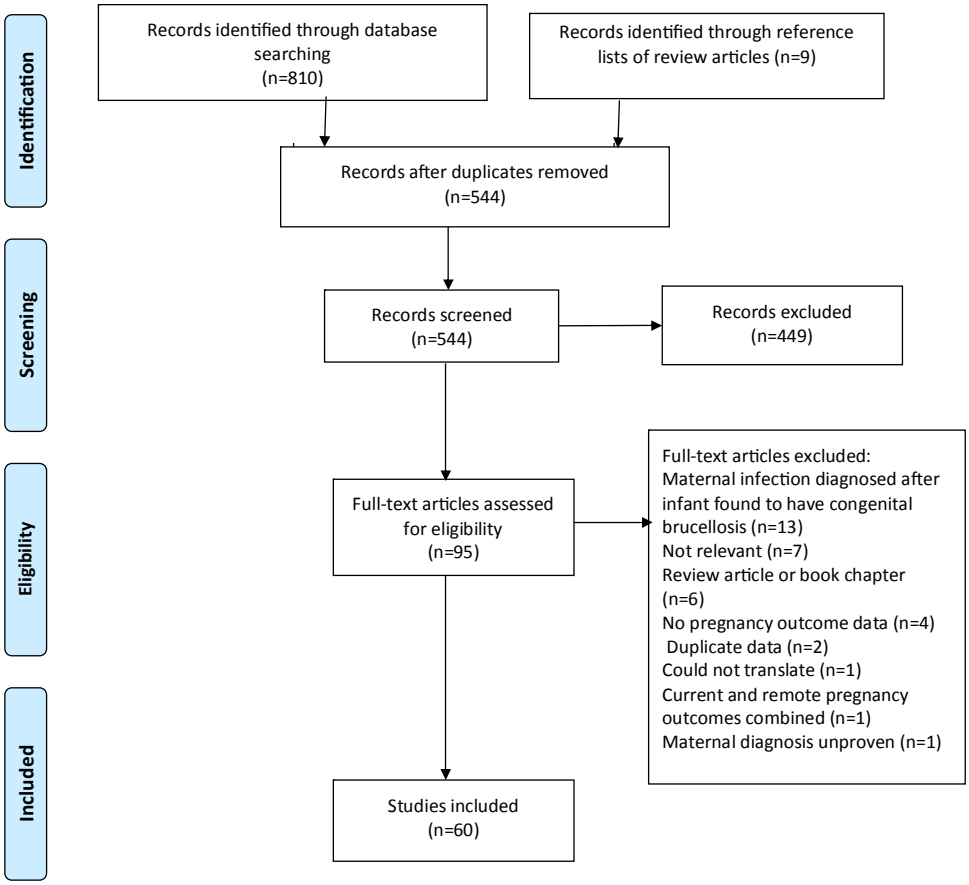

Figure 1. Flow diagram for systematic review.