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Universal gestational screening for *Streptococcus agalactiae* colonization and neonatal infection — A systematic review and meta-analysis

Hiberson D. da Silva, Lizziane Kretli Winkelströter*

Health Sciences Faculty, University of Western Sao Paulo, 700, Jose Bongiovani St., Presidente Prudente, Sao Paulo, Brazil

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ABSTRACT

The review aimed to analyze the evidence of the correlation between universal screening for *Streptococcus agalactiae* colonization in pregnant women and early onset Group B neonatal infection. The research followed the descriptors "screening", "pregnancy", "*Streptococcus agalactiae*" and "neonatal infections" on the Pubmed, scielo and LILACS databases, for studies published in English between January 1st, 2008 and April 24th, 2018. A total of 200 articles were found, of which 198 were excluded. The present review presented some limiting factors, including the low number of studies selected, the difference of patients included, the risk profile of the populations and the results of the isolated studies, expressed in a significant difference between them. The statistical calculations were performed using secondary data. The meta-analysis revealed a Risk Ratio of 0.37 with a 95% of Confidence Interval, indicating a positive factor for the questioning of this review. However, should be understood as a trend, since a small amount of studies were found. More structured clinical studies are recommended to assess the impact of gestational screening for GBS and neonatal infection to better inform public health measures in gestational and neonatal health.

Introduction

Streptococcus agalactiae or Group B Streptococcus (GBS) is a gram-positive bacterium that can colonize the human gastrointestinal and genitourinary tract asymptomatically. However, it can also behave pathogenically in different populations, culminating in relevant infections [1].

Among the most common colonizers of the genitourinary tract in the gestational period, the GBS plays a relevant role, with an average worldwide incidence of 17,9%. This microorganism has an important pathogenic potential in the newborn, and can usually result in sepsis or meningitis. Initial manifestations have a higher mortality rate up to 10%, while late manifestations have significant sequelae indexes [2–4].

In the gestational period, GBS infection is a common cause of cystitis, pyelonephritis and asymptomatic bacteriuria, related to a large colonization of the genital tract. Such colonization raises the risk of endometritis, chorioamnionitis and premature births [5].

However, its major relevance in the neonatal period, for in this age group the infection is more common as a cause of important illness, besides the maturational immune deficiency of the newborn. Commonly, transmission occurs from maternal infection and contamination in the intrauterine period, when there is rupture of the ovular membranes or when the neonate passes through the vaginal canal. Vertical transmission during the intrapartum has high incidence rates, reaching approximately 50% of cases of GBS colonization during gestation [6–10].

In view of the relevance and risks pertinent to the topic, and the divergence of positions taken regarding the procedure for screening and early identification of possible cases, the present research aimed to analyze the evidence of the correlation between universal screening for *S. agalactiae* infection in pregnant women and neonatal infection.

Material and methods

This systematic review and meta-analysis is based on the Cochrane Organization guideliness. The research followed for original articles, randomized clinical trials or cohort studies, on PubMed, LILACS and Scielo platforms, published in English between

* Corresponding author.
E-mail address: lizziane@unoeste.br (L. Kretli Winkelströter).

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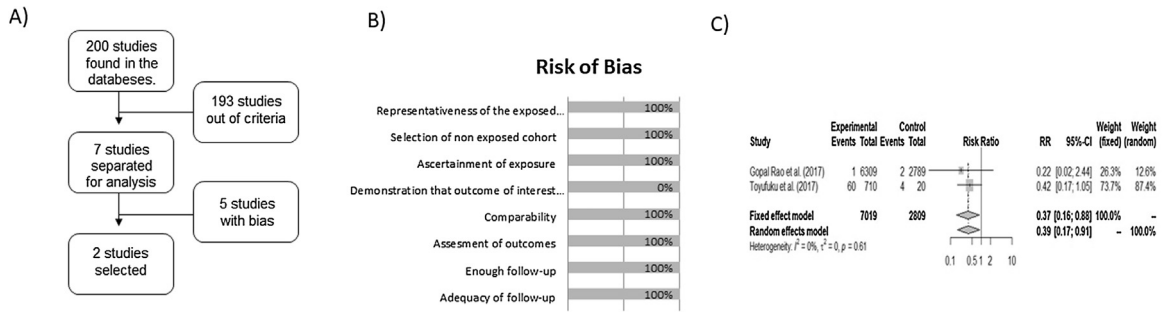

Fig. 1. Parameters and results found for systematic review and meta-analysis on universal gestational screening for *Streptococcus agalactiae* infection and neontal infection: (A) study selection flowchart (B) bias risk graph (C) forest plot of the studies included in the research.

Table 1
Studies included in the research.

Study	Design of study	Type of approach on universal screening of GBS	Limitations
Gopal Rao et al. (2017)	Retrospective cohort	secondary	Lower number of neonatal infections
Toyufuku et al. (2017)	Prospective cohort	secondary	Lower number of women not screened for GBS

January 1st, 2008 and April 25th, 2018. The descriptors used were: "Screening", "Pregnancy", "*Streptococcus agalactiae*" and "Neonatal Infections", in addition to the publication type, language and date filters.

Among the inclusion criteria were: being an original article, randomized clinical or cohort type, with study in human population, with publication within the stipulated period and that accumulated data about a gestational population submitted to the screening of infection by *S. agalactiae* according to the recommendations of the CDC and a group in which the screening was not performed, being the main questioning of the study or secondary data. The CDC recommendations include the sample collect with swab of the anorectal and vaginal region between the 35–37 weeks of gestation, and however it's recommended the enrichment broth, it's not compulsory. The identification of colonization is made by the isolation of GBS in blood agar and the CAMP test or serologic tests. Any studies that did not follow these design study, were not related to the subject, were previous systematic reviews or had bias that diminished the quality of the work were excluded. The bias risk analysis followed the Newcastle–Ottawa scale model [11].

After the selection of the studies, and analyzing the possible repetition of them in the different databases, the evaluation of potential bias risks was initiated through personal interpretation of the authors. This analysis took into consideration the population selection, ruling out any study in which it presented some characteristic that was not representative and mirror of the general population. The method was also taken into account, since it would be necessary to apply the criteria obeyed by WHO for diagnosis of GBS colonization in pregnant women. The information of the results should be expressed in order to demonstrate both the hypothesis group and the control group, not omitting information about any of them and that could obtain data directly or indirectly.

The analysis was made using the statistical package RStudio®, the summary measure was calculated with a 95% Confidence Interval (CI), the forest plot was obtained and the heterogeneity between the studies was evaluated. The Mantel–Haenszel statistical method and the fixed effects model were used, since the differences observed in both studies are due to epidemiological characteristics and sample number and not in the methodology applied, also combined with the low rate of heterogeneity.

Results and discussion

The survey resulted in 200 different studies. Of these, 193 were excluded for not fitting the established criteria of article type or language of publication, 4 were excluded for presenting population selection bias and 1 for information bias (Fig. 1A).

Two studies were selected, with a minimized risk of bias (Fig. 1B), whose data on gestational screening for GBS infection was consistent with secondary data (Table 1).

According to the study lead by Gopal Rao et al. [12], in a total of 9098 pregnant women, 6309 were screened for GBS infection (69%), while 2789 were not tested (31%). The screening was performed following the WHO recommendations of cultures between the 35–37 weeks of gestation and the study informed that was possible the self-collection of the anorectal and vaginal sample. Among the infected infants, 2 were born of untested mothers (0.07%), while 1 was of mother who had been tested (0.01%). The Odds Ratio (OR) of the association between gestational screening and neonatal infection in this study was 0.22 and the Risk Ratio (RR) was also 0.22, the Confidence Interval (CI) ranged from 0.02 to 2.44.

In the study lead by Toyufuku et al. [13] out of a total of 730 newborns, 710 were born to mothers who were screened for GBS, 60 of which were infected (8.4%) and 20 were not screened, of whom 4 were infected (20%). The gestational screening followed the WHO indications cultures collected between the 35–37 weeks of gestation, however there was not information about the methodology used in this cultures. The OR of the association between gestational screening and neonatal infection in this study was 0.37 and RR of 0.42; with HF between 0.17 and 1.05. Between the combined studies, the RR was 0.37 (CI = 0.15: 0.88), and p = 0.0244. The heterogeneity test performed showed Q of 0.26, with p = 0.6104 and the hypothesis of homogeneity between the studies was not rejected (Fig. 1C).

Despite the dimensions of the problem, there was a shortage of recent clinical studies that had as fundamental question the association between the universal screening of pregnant women for GBS infection and the reduction of neonatal infection rates, and therefore, it was used studies in which such data were secondary. Part of this fact is due to the fact that the guidelines are established in several countries, with a decrease in the morbidity and mortality rate [14].

The implantation of IAP also has a positive impact on mortality reduction, once the potential risk of vertical transmission is detected, intrapartum antibiotic therapy reduces the chances of infection of the newborn, as well as classic and low-cost antimicrobials, such as benzylpenicillin, are the first choice [15]. Significant differences were observed in the incidence rates of neonatal GBS infection and RR between the two studies included in this systematic review.

Among the explanations, we can mention the difference in sample number and study development period, which can corroborate for different results. Another reason for these ranges is that colonization rates may vary by location and population, as demonstrated by other studies [16].

Both studies, separately, present an RR lower than 1, thus denotes a tendency of protection to the intervention group in relation to the control one. The meta-analysis revealed a RR of 0.37, that is, a 63% lower risk of neonates born to women who were screened for GBS infection to acquire infection by this microorganism due to vertical transmission, either in the intrauterine or intrapartum period. Such data, however, should be understood as a trend, since a small amount of studies were found.

However, in comparison with a cohort study developed by Chang et al. [17], there is corroboration between the results, since this study demonstrates the benefits of the implementation of the universal screening of GBS colonization in pregnant women in Taiwan, demonstrated by the high correlation between neonatal infection by such microorganisms and the suspicion of maternal colonization (89.9%).

Many techniques have been tested in order to validate a fast and efficient method of GBS screening to replace the culture. Nowadays, molecular biology based assays, such as PCR (polymerase chain reaction) tests, have become the focus of investigation of detection of GBS colonization in pregnant women [18,19]. Paris et al. [18] demonstrated that PCR technique yielded 71 (26.99%) positive results. Sensitivity and specificity for PCR were 100% and 86.88%, respectively. Silveira et al. [19] demonstraded that PCR based test presented a higher prevalence of positive results (35.9% versus 22.5%) in comparison to standard method. Thus, comparison of a PCR assay to culture standard method for the screening of Group B *Streptococcus* in pregnant women, providing a diagnostic tool for GBS detection, allowing effective treatment to be initiated in shorter time to prevent newborn infection.

Therefore, more structured clinical studies are recommended to assess the impact of gestational screening for GBS and neonatal infection to better inform public health measures in gestational and neonatal health.

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Competing interests

None declared.

Ethical approval

Not required.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jiph.2019.03.004.

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