Maternal and Neonatal Group B Streptococcus Colonization: Systematic Review and Meta-Analysis of Matched-Pair Studies

Running Title: Group B Streptococcus colonization in parturient and newborns

Kai Wei Lee, Sook Fan Yap, Sudaxshina Murdan, Zurina Zainudin, Habibah Abdul Hamid, Mohsen Emamjomeh, Mohd Nasir Mohd Desa, Narcisse Mary Sither Joseph, Mohammad Noor Azmai Amal, Syafinaz Amin-Nordin*

Name, Email, Affiliation

Kai Wei Lee, Email: lee_kai_wei@yahoo.com
[1]Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Sook Fan Yap, Email: yapsf@utar.edu.my
[2]Department of Pre-Clinical Sciences, Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, 43000, Kajang, Selangor, Malaysia.
[3]Centre for Research on Communicable Diseases, Universiti Tunku Abdul Rahman, Kajang, Malaysia

Sudaxshina Murdan, Email: s.murdan@ucl.ac.uk
[4]Department of Pharmaceutics, UCL School of Pharmacy, University College London, 29-39 Brunswick Square, London WC1N 1AX, UK

Zurina Zainudin, Email: zaizurina@upm.edu.my
[5]Department of Paediatrics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Habibah Abdul Hamid, Email: habib@upm.edu.my
[6]Department of Obstetric and Gynaecology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Mohsen Emamjomeh, Email: mohsen.emamjomeh94@gmail.com
[1]Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Mohd Nasir Mohd Desa, Email: mnasir@upm.edu.my
[7]Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Narcisse Mary Sither Joseph, Email: narcissems@upm.edu.my
[1]Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Mohammad Noor Azmai Amal, Email: mnamal@upm.edu.my
[8]Department of Biology, Faculty of Science, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

Syafinaz Amin-Nordin, Email: syafinaz@upm.edu.my
[1]Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia
[9]Hospital Sultan Abdul Aziz Shah, Universiti Putra Malaysia, Persiaran MARDI-UPM, 43400, Serdang, Selangor, Malaysia
[10]Institute of Bioscience, Universiti Putra Malaysia, 43400, Serdang, Selangor, Malaysia

*Corresponding Author
Syafinaz Amin-Nordin,
(MBChB, MPath, MHEd)
Department of Medical Microbiology,
Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia,
43400, Serdang, Selangor, Malaysia
Email: syafinaz@upm.edu.my

Maternal and Neonatal Group B Streptococcus Colonization: Systematic Review and Meta-Analysis of Matched-Pair Studies

ABSTRACT

Aim: To determine the prevalence of group B streptococcus (GBS) carriage among parturient women and neonates, and relative risk of vertical transmission, the relative risk of early and late-onset GBS and the pooled incidence of early-late-onset GBS infection.
Methods: A systematic search of relevant cohort studies from three electronic databases to identify all relevant studies published up to 7 November 2022. The review was conducted in accordance to PRISMA guidelines. Estimates were pooled using random-effects meta-analyses.
Results: A total of 54 articles with 355,787 matched pairs of parturient women and neonates from 30 countries were included in the analysis. The pooled prevalence of GBS colonisation was 17.1% among the pregnant women and 1.0 % among neonates. The pooled prevalence of vertical transmission of GBS was 4.5% and the pooled relative risk of GBS colonisation of neonates born to mothers with GBS was 9.9.
Conclusion: We support the implementation of targeted intrapartum antibiotic prophylaxis for all women who are positive for GBS as well as women with risks factors for early onset GBS in their infants regardless of their GBS colonisation status.

PROTOCOL REGISTRATION NUMBER: CRD42022364943

Keywords: Group B streptococcus; delivery; newborn; colonization; intrapartum antibiotic prophylaxis; early onset; late onset;

Keynotes:

- This is the first review to provide pooled estimates of maternal GBS, the risk of vertical transmission, and the neonatal incidence of early and late onset GBS infection.
- The pooled prevalence of maternal and neonatal GBS colonization was 17.1% and 1.0%, respectively, and prevalence of vertical GBS transmission was 4.5%, with a relative risk of 9.9.
- This review affirms the need for intrapartum antibiotic prophylaxis.

1. INTRODUCTION

Group B Streptococcus (GBS), also known as *Streptococcus agalactiae*, a bacterium commonly found in the gastrointestinal and genital tracts of men and women is quite harmless in healthy individuals. However, it can cause serious infection in those at risk such as the elderly, people with chronic illnesses and/or impaired immunity, and in neonates. About one out of every four healthy women have GBS as part of the normal flora and in whom the presence of the bacteria may be continuous, transient or intermittent. The significance of GBS colonisation among women is the possible risk of pregnant women transmitting the bacteria to their neonate with subsequent possibility of infection and complication. Indeed, pregnant women have higher odds of contracting GBS infection than non-pregnant women. The adjusted pooled prevalence of recto-vaginal GBS colonization among pregnant women was reported to be 18% (95% CI, 17%–19%) worldwide (1) while that among healthy non-pregnant women was estimated to be 11.7% in a recent systematic review and meta-analysis (2). In pregnant women, GBS can infect the urinary tract, uterus, placenta and amniotic fluid, the latter via intact or ruptured membranes. However, in many cases the infection remains asymptomatic.

Neonatal infections can be acquired through foetal aspiration or ingestion of infected amniotic fluid, or during passage of the neonate through the birth canal in vaginal deliveries. The reported proportion of vertical transmission of GBS based on individual reports across the globe spans quite a wide range varying from 0.9% to 14.1% in china (3, 4) through 35.5% to ~~40.3~~41% in Kuwait (5, 6) and 40% in Bangladesh (7), 59.1% in Ethiopia (8) and 41.8% in USA (9). According to the Guidance for the clinician in rendering paediatric care for the management of infants at risk for GBS, the incidence of early-onset GBS (EOGBS) in the United States ranged from 0.23 to 1.8 cases per 1000 live births between the years of 1990 to 2015, while the average incidence for late-onset GBS (LOGBS) was 0.31 per 1000 live births between 2006 to 2015 (10). Based on incidence or prevalence data and using a compartmental model, the authors came up with global estimates of 205000 infants with EOGBS and 114000 with LOGBS for 2015. In addition, it was estimated that there is a minimum of 7000 cases of GBS related neonatal encephalopathy and at least 10000 children with disability (11).

Infected neonates present with fever or temperature instability, listlessness or irritability, poor feeding and breathing difficulties; complications include sepsis, pneumonia, respiratory distress and even meningitis (12). The Centers for Disease Control and Prevention recommends that the intrapartum antibiotic prophylaxis be given to GBS carrier mothers to prevent the occurrence of EOGBS infection in the neonates (13). However, there appears to be no effective approach for preventing LOGBS infection (10). The importance of and need for effective treatment is highlighted by an extensive study in 2017 on the worldwide burden of GBS disease among pregnant/postpartum women and affected infants (11).

Till date, information on the association between maternal GBS and adverse neonatal outcomes based on systematic review and meta-analysis is relatively scarce; this calls for more extensive studies and analysis of the said relationship. Therefore, the primary objectives of this systematic review and meta-analysis were to estimate the pooled prevalence of GBS carriage among parturient women (colonized antenatally or during labour) and neonates (colonized before and/or during labour), and the pooled relative risk of vertical transmission. With this data, the secondary objectives, which were to estimate (i) the relative risk of early and late-onset GBS infection and (ii) the pooled incidence of early and late-onset GBS infection, can then be determined. Additionally, we can also consider other GBS-related adverse neonatal complications and outcomes among the available cohort studies.

2. METHODS

2.1 Study design and protocol registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (**Appendix S1**) (14, 15) and registered with PROSPERO (Registration number: CRD42022364943).

2.2 Literature Search

Three databases (Medline, CINAHL, and PubMed) were searched for studies that were published from the inception to 7 November 2022, by two investigators (KWL and SAN) independently. The search strategy consisted of several terms which were: ((neonates AND pregnancy complications AND pregnancy AND Group B streptococcus) NOT (review OR intervention)) with limiters of ENGLISH and HUMAN (**Appendix S2**). Papers that were published beyond the end-date were not considered for this review.

2.3 Data Handling

All relevant articles identified through the databases were imported into the Endnote Programme version X5, and any duplicate was then removed. The relevance of articles to the topic was next reviewed carefully by checking the titles and abstracts of articles (those missing either maternal or neonatal information related to GBS in the title or abstract were excluded) before proceeding to full-text assessment. The aforementioned process was conducted independently by KWL and SAN. Discrepancies between the investigators were resolved through discussion with a third investigator (SFY) before final consensus for quantitative analysis was reached.

2.4 Selection Criteria

Any observational studies were eligible for inclusion; however, we did not consider case-control studies, case reports, and case series as these study designs did not carry the statistics required for prevalence calculation; thus, they were not eligible for the first objective of this review. To calculate the pooled relative risk of vertical transmission of GBS infection and GBS-infection related complications or outcomes (e.g., sepsis, meningitis, pneumonia and death), we need data on the probability of an event occurring for the exposed group (parturient women with GBS) divided by the probability of that event occurring for the control group (parturient women without GBS); for this reason, studies with any one of the following characteristics were excluded:

(1) The study has data on GBS status in parturient women but the adverse outcomes in neonates were due to a composite of bacteria whereby data on GBS was inseparable from that of other pathogens
(2) The study has data on GBS status in parturient women but the adverse outcomes of neonates were not clearly associated with GBS
(3) Bacterial infections in parturient women and/or neonates were not specifically due to GBS
(4) Missing information regarding GBS in parturient women
(5) Maternal information was absent
(6) Neonatal information was absent
(7) Parturient women and their neonates could not be matched up
(8) The study did not include parturient women without GBS
(9) The study did not include neonates without GBS

In addition, we also excluded studies in which the full-text was not available, or was not in English, or was presented only as conference proceedings, and repeated samples cohort (multiple studies published from same cohort).

2.5 PICO

"Participants" referred to pregnant women screened for GBS colonization. Exposure referred to exposure of the baby to a mother with GBS colonization. The comparator in the current review referred to babies born to a mother without GBS colonization. The main outcomes of this review were an estimate of the pooled prevalence of GBS colonization in parturient women and in neonates, and the prevalence of GBS vertical transmission. The secondary outcome was to determine the relative risk of GBS vertical transmission and GBS-infection related complications or outcomes in neonates.

2.6 Data Extraction

The information extracted from included manuscripts were basic characteristics of the studies (Author, year, and country of participants), timing of screening for GBS, screening methods, the types of sample (from both parturient women and neonates) used for screening, and the extent of intrapartum antibiotic prophylaxis use in GBS positive and negative parturient women, the total number of matched pairs of parturient women-neonates, number of parturient women and neonates with GBS, number of neonates with GBS born to parturient women with and without GBS.

2.7 Quality Assessment

The quality of the papers, evaluated using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) to assess the quality of observational studies (16), are as shown in **Appendix S3**. The quality of the articles was graded as “good” if STROBE score was ≥14/22; or graded as “poor” if STROBE score < 14/22.

2.8 Data Syntheses

Meta-analyses were performed with Open Meta (Analyst) (17) using a random-effect model (DerSimonian and Laird method) to produce the pooled prevalence of GBS colonization in parturient women, neonates, and vertical transmission. We also estimated the pooled relative risk of vertical transmission of GBS. Additionally, mortality and adverse neonatal complications such as GBS-related sepsis, pneumonia and meningitis, and infant mortality were also considered in the analyses if the data was sufficient (at least two studies per analysis). Heterogeneity was assessed using I^2, and a p-value of less than 0.05 was considered to be significant. A sensitivity analysis was conducted using a leave-one-out meta-analysis to examine how the exclusion of each individual study affects the overall estimate.

3. RESULTS

3.1 Search Results

As depicted in the PRISMA flow diagram (**Appendix S4**), our search strategy initially produced 1121 unique articles. We conducted title/abstract screening and full-text assessment, scrutinizing adherence to selection criteria and eligibility for meta-analyses. In the end, 54 articles were deemed suitable and included in this review (3-9, 18-64).

3.2 Description of Included Studies

The main characteristics of the 54 articles are summarized in **Table 1**. A total of 355,787 matched pairs of parturient women and neonates from 30 countries spanning Asia, Europe, Africa and North America were included in the analysis. Twenty-two studies from 13 Asian countries included 4 each from China and Japan, 3 from India, 2 each from Bangladesh and Kuwait, and one each from South Korea, Taiwan, Pakistan, Israel, Turkey, Iran and Lebanon. Sixteen studies were from European countries including 3 from Italy, 2 each from Germany, Spain, the United Kingdom and Sweden, and 1 each from France, Spain, Greece, Denmark, Lithuania and Hungary. Seven studies from Africa comprised 2 each from Gambia and Nigeria and 1 each from Ethiopia, Egypt and South Africa. Of the remaining 9 studies from North America, 8 were from the USA and 1 from Canada.

North America and European countries were classified as high-income countries as per World Bank classification (except Lithuania and Hungary which were middle income countries). Of the 13 Asian countries, 5 were considered to be middle income, 1 as low income and the remaining as high-income countries. Lastly, 2 of the 5 African countries were classified as middle and 2 as low-income countries.

1

Table 1: Characteristics of included studies and its participants.

	Author	Year	Country	Continents	Economy	Major religion	Exclusion criteria	Sample collection Timing	Identification method	Parturients samples	Neonatal samples	Antibiotic use among GBS (+) parturients, %	Intrapartum antibiotic prophylaxis use among GBS (-) parturients, %
1	Ali et al., (8)	2019	Ethiopia	Africa	Low	Non-Islamic	Use of antibiotics for last 3 weeks, pregnant women with Cesarean section delivery	During labour	Bacteriological culture methods, Serotyping	Lower vaginal and rectal swabs	Swabs of external ear, nasal area, throat and umbilical area	NA	NA
2	Allardice et al.,(18)	1982	Canada	Latin America	High	Non-Islamic	Women with history of penicillin hypersensitivty, booked for elective cesarean section	During labour	Bacteriological culture methods	Vaginal swabs	Ear and umbilicus swabs	17.0	1.1
3	Al-Sweih et al.,(5)	2005	Kuwait	Asia	High	Islamic	NA	During labour	Bacteriological culture methods, Serotyping	Vaginal and anorectal swabs and urine sample	Ear and umbilical swabs	NA	NA
4	Barcaite et al.,(19)	2012	Lithuania	Europe	Middle	Non-Islamic	Use of antibiotics for last 2 weeks, heavy vaginal bleeding	Prenatal, during labour	Bacteriological culture methods, Serotyping	Lower vaginal and rectal swabs	ear canal and throat swabs	21.6	NA
5	Berardi et al., (58)	2016	Italy	Europe	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	NA	NA	87	NA
6	Boyer et al., (20)	1983	USA	Latin America	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	Vaginal and rectum swabs	Swabs of throat, umbilicus, rectum, external ear, and nasogastric aspirate	NA	NA
7	Cassidy et al.,(21)	2016	USA	Latin America	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	Vaginal and preanal swabs	Stool sample	75	29

8	Chan et al., (7)	2013	Bangladesh	Asia	Middle	Islamic	Women who presented with obstructed labor, hemorrhage, severe pre-eclampsia or fetal distress, were excluded, and who used antibiotics or steroids within 2 weeks of labor also were excluded	During labour	Bacteriological culture methods	Vaginal and rectal swabs	Umbilical swabs	NA	NA
9	Chaudhry et al., (59)	2010	Pakistan	Asia	Low	Islamic	Pregnant females with systemic diseases, on antibiotics, and those with obstetrical problems, PROM were excluded from the study	During labour	Bacteriological culture methods	Lower vaginal swabs	Swabs of skin of abdomen and ear canals	NA	NA
10	Chen et al., (BMC)(22)	2018	China	Asia	High	Non-Islamic	All twins or multiple birth were excluded	Prenatal, during labour	Bacteriological culture methods	Rectovaginal swabs	Nasopharyngeal, ear canal, and umbilical swabs	0	0
11	Chen et al., (JP)(4)	2018	China	Asia	High	Non-Islamic	Multiple pregnancies	During labour	Bacteriological culture methods	Lower vaginal swabs	Swabs of ear canal, throat, and umbilical samples	NA	NA
12	Christensen et al., (23)	1981	Sweden	Europe	High	Non-Islamic	Multiple pregnancies	During labour	Bacteriological culture methods	Urethra and cervix swabs	Swabs of external auditory canal, throat and umbilicus	NA	NA
13	De Cueto et al., (60)	1995	Spain	Europe	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	Vaginal swabs	Blood, urine and mucocutaneous swabs	44.3	NA
14	Easmon et al.,(24)	1983	UK	Europe	High	Non-Islamic	NA	Antenatal, during labour	Bacteriological culture methods, Serotyping	Anorectal and vaginal swabs	Rectal and umbilical swabs, external eear, anterior nares, anorectal area.	0	0
15	Elbaradie et al., (25)	2009	Egypt	Africa	Middle	Islamic	NA	Antenatal	Genotyping	Vaginorectal swabs	Swabs of exteral auditory canals	0	0

16	Elikwu et al., (26)	2016	Nigeria	Europe	Middle	Non-Islamic	who had received antibiotics within two weeks of presenting at the antenatal clinic were excluded from the study	Antenatal, during labour	Bacteriological culture methods	Vaginorectal swabs	Swabs of mouths, ears and umbilical stumps	NA	NA
17	Eren et al., (27)	2005	Turkey	Asia	Middle	Islamic	NA	During labour	Bacteriological culture methods, Serotyping	Vaginal and rectal swabs	Swabs of throat and umbilicus	NA	NA
18	Faro et al., (28)	2010	USA	Latin America	High	Non-Islamic	NA	During labour	Bacteriological culture methods	Vaginal, perineum and external anal sphincter swabs	NA	94.7	23.8
19	Gurudas et al., (61)	2022	India	Asia	Middle	Non-Islamic	Those posted for elective lower segment caesarian section for rupture of membranes	Antenatal	Bacteriological culture methods	Lower vagina and rectum swabs	NA	100	100
20	Hakansson et al., (29)	2008	Sweden	Europe	High	Non-Islamic	NA	During labour	Bacteriological culture methods, Genotyping	Vaginal and rectum swabs	Cheek, umbilicus and groin swabs	NA	NA
21	Hamedi et al., (30)	2012	Iran	Asia	Middle	Islamic	NA	During labour	Bacteriological culture methods	Vaginal and rectum swabs	Ear swabs and umbilical cord samples	NA	NA
22	Hammoud et al.,(6)	2003	Kuwait	Asia	High	Islamic	NA	During labour	Bacteriological culture methods	Lower vaginal-anorectal swabs	Skin swab	NA	NA
23	Hickman et al., (9)	1999	USA	Latin America	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	Lower vaginal or rectal swabs	Throat, umbilicus, rectum	22.8	12.7
24	Horvath et al., (31)	2013	Hungary	Europe	Middle	Non-Islamic	NA	Antenatal	Bacteriological culture methods	Distal vaginal and rectum swabs	NA	NA	NA
25	Ji et al., (32)	2019	China	Asia	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods, Genotyping	Lower vaginal and rectum swabs	Throat and ears swabs	74.4	0

26	Kunze et al., (EJP)(34)	2015	Germany	Europe	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods, Serotyping	Lower vaginal, rectum swabs	Throats, ear canals swabs	89.3	NA
27	Kunze et al., (JPM)(33)	2011	Germany	Europe	High	Non-Islamic	preterm delivery secondary to fetal or maternal indications	Antenatal	Bacteriological culture methods	Vaginal-rectal swabs	Ear swabs	39	NA
28	Le Doare et al., (35)	2016	Gambia	Africa	Low	Islamic	Mothers were excluded if they were not planning to breastfeed	During labour	Bacteriological culture methods, Genotyping	Retrovaginal swabs and cord blood	Nasopharyngeal and rectal swabs	21	19.9
29	Li et al., (36)	2018	Taiwan	Asia	High	Non-Islamic	NA	NA	NA	NA	NA	100	NA
30	Lijoi et al., (37)	2007	Italy	Europe	High	Non-Islamic	Exclude those with length of membrane rupture >18 h, had delivery before 37 completed weeks of gestatio, had intrapartum fever (temperature >38°) or previous delivery of an infant with invasive GBS disease.	Antenatal, during labour	Bacteriological culture methods	Vaginal-rectal swabs, urine.	Auricular and nasopharyngeal	93	NA
31	Madzivhandila et al.,(38)	2011	South Africa	Africa	Middle	Non-Islamic	NA	Prenatal	Bacteriological culture methods, Serotyping, Genotyping	Vaginal swabs	Swabs of ears, nose and umbilicus	NA	NA
32	Matorras et al., (39)	1989	Spain	Europe	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods	Low vaginal and rectal swabs	Swabs of Pharynx, nasal cavity, conjunctiva, umbilicus and external auditory duct	NA	NA
33	Medugu et al., (40)	2017	Nigeria	Europe	Middle	Non-Islamic	Multifetal gestation, placenta previa or elective caesarean sections	NA	Bacteriological culture methods	Vaginal and rectal swabs	External auditory meatus	0	0

34	Mirsky et al.,(41)	2020	USA	Latin America	High	Non-Islamic	delivery at <22-week gestation, multiple gestations	Antenatal	Bacteriological culture methods	Vaginal and rectal swabs	Blood and/ or cerebrospinal fluids	NA	NA
35	Miyata et al.,(42)	2012	Japan	Asia	High	Non-Islamic	Preterm delivery, elective caesarean section, stillbirth	Antenatal	Bacteriological culture methods	Vaginal introitus and perianal lesions	Swabs of Nasal and auricularis	100	NA
36	Pasnick et al., (43)	1980	USA	Latin America	High	Non-Islamic	NA	Prenatal	Bacteriological culture methods	Vaginal swabs	NA	NA	NA
37	Petersen et al., (44)	2014	Denmark	Europe	High	Non-Islamic	NA	NA	Bacteriological culture methods	Vaginal swabs and urine	Blood, cerebrospinal fluid, swabs from the trachea	NA	NA
38	Reid et al., (45)	1975	Scotland	Europe	High	Non-Islamic	NA	Prenanatal	Bacteriological culture methods	High vaginal swabs	Swabs of Eyes, ears, throats, nose, umbilicus, blood and cerebrospinal fluid	NA	NA
39	Saha et al., (46)	2017	Banglade sh	Asia	Middle	Islamic	Stillbirth	Antenatal, during labour	Bacteriological culture methods, Serotyping	Retrovagina l swabs	Swabs of ear, umbilicus, and nasal	1.2	1.1
40	Santhanam et al., (47)	2017	India	Asia	Middle	Non-Islamic	NA	Antenatal	Bacteriological culture methods	Lower vaginal and rectum swabs	Surface swabs	73.9	NA
41	Scheftelowitz et al.,(62)	2021	Isreal	Asia	High	Non-Islamic	Multiple pregnancies, gestational week <27 or >42	Antenatal	Bacteriological culture methods, Serotyping	Vaginal swabs	NA	NA	NA
42	Schrag et al., (48)	2002	USA	Latin America	High	Non-Islamic	Excluded all women with risk factors and adequate time for prophylaxis who did not receive antibiotics	Prenatal	NA	NA	NA	NA	NA
43	Sensini et al.,(49)	1997	Italy	Europe	High	Non-Islamic	NA	During labour	Bacteriological culture methods, Serotyping	Lower vaginal swabs	Auricular, pharyngeal swabs and gastric aspirate	NA	NA
44	Seoud et al., (50)	2010	Lebanon	Asia	Middle	Islamic	NA	During labour	Bacteriological culture	Lower vaginal and rectal swabs	Swabs of ear, pharynx and rectum.	2.1	2.1

									methods, Serotyping				
45	Shibata et al.,(51)	2021	Japan	Asia	High	Non-Islamic	Stillbirth	Antenatal	Bacteriological culture methods, Genotyping	Retrovaginal swabs	Nasopharyngeal and rectal swabs	96.5	NA
46	Suara et al., (52)	1994	Gambia	Africa	Low	Islamic	NA	Antenatal	Bacteriological culture methods	Vaginal and rectal swabs	Swabs of throat, umbilical, rectal.	NA	NA
47	Takahashi et al., (53)	2021	Japan	Asia	High	Non-Islamic	NA	During labour	Bacteriological culture methods	Rectovaginal and umbilical swabs	Umbilical swabs	NA	NA
48	Toyofuku et al., (54)	2017	Japan	Asia	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods, Genotyping	NA	Nasopharyngeal and rectal swabs	94.3	32.5
49	Tsolia et al., (55)	2003	Greece	Europe	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods, Serotyping	Vaginal and rectal swabs	Swabs of ear canal, throat, and umbilicus	NA	NA
50	Uh et al., (63)	1997	South Korea	Asia	High	Non-Islamic	NA	During labour	Bacteriological culture methods, Serotyping	Swabs of Vaginal, urethral meatus, anorectal areas	Swabs of ear canal and umbilicus	NA	NA
51	Volumenie et al., (56)	2001	France	Europe	High	Non-Islamic	Preterm	Antenatal	Bacteriological culture methods	Vaginal swabs	Swabs of ear, gastric aspirate and anal margin	93	0
52	Warrier et al., (64)	2022	India	Asia	Middle	Non-Islamic	Recurrent vaginal trush, Preterm premature rupture of the membranes	Antenatal	Bacteriological culture methods	Retrovaginal swabs	Throat and rectal swabs	100	100
53	Yow et al.,(57)	1980	USA	Latin America	High	Non-Islamic	NA	Antenatal	Bacteriological culture methods, Serotyping	Swabs of throat, vagina	Swabs of ear, throat, umbilicus and rectum	NA	NA
54	Zhu et al., (3)	2019	China	Asia	High	Non-Islamic	Habitual abortion, use of antibiotics and fetal malfomation	Antenatal	Bacteriological culture methods	Vaginal swabs	Tracheal secretions, gastric fluid, and blood	97.5	NA

1
2

3.3 Prevalence of GBS among matched pairs of parturient women and neonates, and prevalence of vertical transmission

The summary of results is shown in **Table 2**. Based on the data gathered from 54 articles, the pooled prevalence of GBS among the pregnant women was 17.1% (95% CI 14.6%, 19.6%, I^2 = 99.8%) (**Figure 1**) and 1.0 % (95% CI 0.9%, 1.1%, I^2 = 98.6%) among neonates (**Figure 2**). The pooled prevalence of vertical transmission of GBS (i.e., GBS colonized neonates born to GBS colonized mothers) was 4.5% (95% CI 4.1%, 4.9%, I^2 = 98.6%) (**Figure 3**). We also performed subgroup analysis to determine any correlation between the coverage of intrapartum antibiotic prophylaxis in GBS colonized mothers and vertical transmission rate. **Figure 4** shows that 27 out of 54 articles reported on the coverage of intrapartum antibiotic prophylaxis among GBS colonized mothers, of which 12 had ≤50% antibiotic prophylaxis coverage (ranging from 0% to 44.3%) while the remaining 15 studies had >50% antibiotic prophylaxis coverage (ranging from 73.9% to 100%). The pooled prevalence of vertical transmission was only 1.4% (95% CI 0.9%, 2.0%) among studies with >50% antibiotic prophylaxis coverage compared to 34% (95% CI 22.6%, 45.3%) in studies with ≤50% antibiotic prophylaxis coverage.

Table 2: Summary of Pooled Prevalence of GBS and vertical transmission among matched pair of parturient and neonates.

Analyses	Category	No. of studies	PP/RR	95% CI	I^2	Leave-one-Out meta-analysis	Figure
Prevalence of GBS in parturient	Overall	54	17.1	14.6, 19.6	99.82	16.2-17.2	1
Prevalence of GBS in neonates	Overall	54	1.0	0.9, 1.1	98.58	0.9-2.5	2
Prevalence of GBS vertical transmission	Overall	54	4.5	4.1, 4.9	98.62	3.7-14.8	3
	IAP ≤ 50	12	34.0	22.6, 45.3	97.53	NA	
	IAP > 50	15	1.4	0.9, 2.0	94.20	NA	
	NA	27	19.9	18.1, 21.7	98.83	NA	
Relative risk of GBS vertical transmission	Overall	54	9.933	7.530, 13.103	87.15	9.496-10.310	4
	IAP ≤ 50	12	13.766	8.230, 23.026	87.23	NA	
	IAP > 50	15	5.011	2.986, 8.410	80.07	NA	
	NA	27	11.874	7.932, 17.776	87.26	NA	
Relative risk of early onset GBS infection	Overall	17	7.642	4.015, 14.546	79.28	6.569-8.845	5
	IAP > 50	8	11.172	3.163, 39.463	75.14	NA	
	NA	9	5.648	2.976, 10.720	72.74	NA	
Incidence of early onset GBS per 1000 live birth	Overall	25	2	1, 2	97.17	NA	6
Incidence of Late onset GBS per 1000 live birth	Overall	3	81	37, 124	92.99	NA	7

Note:
PP=Pooled Prevalence;
RR=Relative risk
I^2=Unit of Heterogeneity
IAP=Intrapartum antibiotic prophylaxis coverage
NA=Not available

3.4 Pooled Relative Risk of Vertical GBS Transmission, Infections, Complications and Mortality

As shown in **Figure 4**, the overall pooled relative risk of GBS colonisation in neonates born to GBS-positive mothers was 9.940 (95% CI 7.533, 13.114, I^2 = 87.17%); this implies that the risk of GBS

colonization in neonates is 9.940 times greater if they were born to GBS colonized mothers compared to those who had seen born to GBS-negative mothers. In the subgroup analysis by intrapartum antibiotic prophylaxis, it was noted that the relative risk was 5.011 (95% CI 2.986, 8.410, I^2=80.07%) in the subgroup with >50% antibiotic prophylaxis coverage, which is almost 3 times lower than in those in the ≤50% antibiotic prophylaxis coverage subgroup, in whom the relative risk was 13.766 (95% CI 8.230, 23.026, I^2=87.23%).

Out of 54 studies, only 17 have data on EOGBS infection in neonates. As shown in **Figure 5**, the overall pooled relative risk of EOGBS infection in neonates born to GBS colonized mothers was higher at 7.642 (95% CI 4.015, 14.546, I^2=79.28) compared to neonates born to GBS negative mothers. As shown in **Figure 6** and **Figure 7**, the pooled incidence of early-onset and late onset GBS infection is 2 (95% CI=1.0, 2.0) per 1000 live birth and 81 (95% CI=37, 124) per 1000 live birth, respectively. Meta-analysis was not performed for GBS-induced sepsis (n=2), GBS-induced pneumonia (n=1), GBS-induced meningitis (n=1), and GBS-induced mortality (n=1), due to insufficient number of studies to give meaningful results.

4. DISCUSSION

GBS colonization in pregnant women is common and the neonatal complications due to GBS infection can be reduced by giving intrapartum antibiotic prophylaxis. In view of this, quite a number of cohort studies have been conducted to determine the association between maternal GBS status and adverse neonatal outcomes. However, there is a relative lack of reviews with meta-analysis that address the relative risk of neonatal colonization born to mothers with or without GBS. Therefore, the objectives of this initiative were to systematically review and conduct meta-analysis using data of cohort studies to determine the pooled prevalence of GBS colonization in pregnant women and neonates (matched pairs), the relative risk of vertical transmission, early and late-onset GBS infection, and pooled incidence of early and late-onset GBS infection per 1000 live births.

4.1 Prevalence of GBS colonization in pregnant women

In the current review, the overall pooled prevalence of GBS colonization in pregnant women from the meta-analysis was 17.1% (95% CI=14.6, 19.6, I^2=99.8). This result was derived from studies spanning 1975 to 2022 and involving 355,787 parturient women across 30 countries covering 4 continents. A brief summary of other reviews on the prevalence of GBS colonisation is given in **Table 3**. Of these, the review by Russell (1) is comparable to the current review in terms of the time frame (1977-2017) and the geographical coverage (all continents inclusive of Australia and New Zealand). The worldwide pooled prevalence reported by Russell et. al. was 15.2 % and the prevalence adjusted for less-sensitive sampling or microbiological methods was 18.0%. The study by Kwatra (65) reported a pooled prevalence of 17.9%, which is very close to our result although this analysis was more limited in terms of the period covered (1997-2015), the number of pregnant women included for analysis (n=73791) and the number of countries covered (n=37). Another study which was focused on comparing the prevalence between Islamic and non-Islamic countries reported an overall prevalence of 15.5% (Abbasalizadeh et al., 2021). Nevertheless, the authors did a sub-analysis based on the state of development of the countries covered and found that the pooled prevalence of pregnant women from developed countries (n=55288) was 17.7% and that of women from less developed countries (n=60392) was 14.9%, highlighting the need to relate reported pooled prevalence of GBS infection among pregnant women to the particular population studied. Two other reviews included in the **Table 3** were from restricted geographical areas; the one from China covering 10 studies gave a rather low pooled prevalence of 10%

(66) while that from Sub-Saharan Africa which also covered 10 studies gave a relatively high prevalence of 21.8% further highlighting the importance of geographical area. Overall, the pooled prevalence of maternal GBS carriage ranges from 15.5% to 17.9% based on previous systematic reviews referred to above (1, 65) which is quite a narrow range, and within which our result also fall.

In terms of regional distribution, a relatively high pooled prevalence was reported from African countries ranging from 19% (67) to 20.4% (65) and 21.8% (68). In the present review, we noted a pooled prevalence of 23.7% for the African region, the highest yet reported. Multiple factors contributing to the high percentage of GBS-colonized pregnant women in Africa have been proposed. They include low levels of health literacy (lack of knowledge, lack of information, and communicative problems), financial constraints (poverty, unemployment and high transportation costs), and barriers in accessing healthcare systems (lack of insurance coverage and transportation facilities) (69). Indeed, it has further been suggested that the prevalence of GBS colonization is likely to be underestimated due to lack of screening and testing facilities (68) and a less well-established healthcare infrastructure system.

In contrast, as shown in Table 3, the pooled prevalence is much lower in Asia. A prevalence 11.1% in South East Asia (65), 12.9% in Asia (67) and 10% in China (66). We found a prevalence of 11.8% for Asia, which included countries from East, South and West Asia concurring with findings from previous reviews. Data from the Americas and Europe demonstrate a pooled prevalence that is intermediate; in the Americas, it ranged from 18.6% (67) to 19.7% (65); in Europe, from 16.4% (67) to 19.0% (65). Results from our analysis show a similar trend; the pooled prevalence is 22.6% for the Americas and 19.7% for Europe.

Table 3. Summary of findings of reviews on pooled prevalence of maternal GBS colonization.

Studies	Year of studies included in meta-analysis	No. of pregnant women	No. of Countries	Overall %	Asia	Americas	Europe	Africa	Oceania	Others meaningful comparisons
Kwatra et al., (65)	1997-2015	73791	37	17.9	11.1	19.7	19.0	20.4	13.3	NA
Huang et al., (66)	2000-2016	52837	10	10	7				19	NA
Abbasalizadeh et al., (67)	1973-2019	115680	NA	15.5	12.9	18.6	16.4	19	22.5	• Islamic countries (14%) versus non-Islamic countries (16.3%). • Developed countries (17.7%) versus less developed countries (14.9%).
Sinha et al., (68)	1990-2014	11204	10	21.8	NA	NA	NA	21.8	NA	NA
Russel et al., (1)	1977-2016	299924	85	18	11.0	18.3	15.2 - 20.8	18.2	19.0	Developed region (18.4%)
Current review	1975-2022	355,787	30	17.1	11.8	22.6	19.7	23.7	NA	• Low income countries (21.9%), middle income countries (15.3%) and high income (17.3%). • Islamic countries (15.4%) versus Non-Islamic countries (17.5%)

The higher prevalence among the largely developed countries in America and Europe compared to Asian countries, which are generally less-developed, could be related to greater screening and reporting due to better healthcare facilities. The factors underlying this argument include sampling sites, screening/isolation methods for GBS (conventional biochemical methods or PCR tests), and cultivation methods (enrichment or no enrichment). In addition, several obstetric variables such as parity, premature rupture of membranes, history of GBS in past pregnancy have been shown to be associated with higher risk of GBS colonization. However, without access to individual-level data, this aspect was difficult to explore and compare.

4.2 Prevalence of GBS colonization in neonates and vertical transmission

In the current review, the pooled prevalence of GBS colonization in neonates was 1.0% (95% CI=0.9, 1.1%) and the prevalence of vertical transmission was 4.5% (95% CI=4.1, 4.9%). New-borns of mothers with colonization had a 9.9 (95% CI=7.53, 13.10) times higher risk of GBS colonization than neonates of non-colonized mothers. The relative risk of EOGBS infection was 7.6 (95% CI=4.0, 14.5) in neonates born to GBS colonized mothers compared to neonates born to non-colonized mothers. The pooled incidence of early onset and late onset GBS infection were 2 (95% CI=1.0, 2.0) per 1000 live birth and 81 (95% CI=37, 124) per 1000 live birth, respectively.

A review by Chan (70) reported that the pooled odds ratio of vertical transmission from GBS colonized mothers to their new-borns was 28.6 (95% CI=13.2, 62.1). The results of the current review, reported as pooled relative risk is 9.9 (95% CI=7.5, 13.1) which is equivalent to a pooled odds ratio of 14.5 (95% CI=10.3, 20.5), half of that reported by Chan et.al. This could be due to differences in the sample size and design of the studies included for the respective reviews. The review by Chan et. al., included 19 case-control or cohort studies with a total sample size of 10, 369 neonates; in comparison our review included 54 cohort studies with a total sample size of 298, 037 neonates for the estimation of vertical transmission. A comparison of the risk for early-onset GBS infection between our analysis and that of Chan et. al. showed that these results are quite similar. Our estimated pooled relative risk for early-onset GBS infection was 7.6 (95% CI=4.0, 14.5) which is equivalent to a pooled odds ratio of 8.3 (95% CI=4.3, 16.1), while that reported by Chan et.al. was 9.4 (95% CI 3.1, 28.5).

A review on Sub-Saharan countries (68) reported a pooled incidence of EOGBS infection of 1.3 cases (95% CI=0.8, 1.9) per 1000 live births; and late onset GBS infection of 0.73 (95% CI=0.48, 1.0) per 1000 live births. In the present review, the incidence is 2.0 cases early-onset GBS infection per 1000 live births, which is not too different from that of Sinha et.al. However, the incidence of late onset is 81 cases per 1000 live birth (95% CI=37, 124) in our review, which is very much higher comparatively. The possible explanation for such a great difference could be the difference in sample size for early-onset and late-onset GBS infection in neonates between the review by Sinha et al., and the current review. The total number of neonates included in the analysis of pooled incidence of early onset was fairly similar in both reviews, being 330746 neonates in the current review and 203986 neonates in the review by Sinha et. al. However, for the estimation of pooled incidence of the LOGBS infection, the total number of neonates in the current review is relatively few at 3533 compared to 175562 in the review by Sinha et, al. Hence, the very high incidence of LOGBS incidence in the present study need to be viewed with caution.

4.3 Benefit of Intrapartum antibiotics prophylaxis

Use of intrapartum antibiotic prophylaxis had been shown to be effective in reducing the risk of neonatal colonization. It had been reported that the relative risk of neonatal GBS among newborns of GBS-colonised mothers who received intrapartum antibiotics prophylaxis compared to those who did not was significantly lower (71). Intrapartum antibiotic prophylaxis involves administering antibiotics to women in labour who are at increased risk of transmitting Group B Streptococcus (GBS) to their newborns. This has been shown to be an effective method of preventing neonatal colonization, as well as reducing the risk of early-onset GBS disease in newborns. This intervention has been widely adopted in clinical practice and has been proven to be safe and effective in reducing the incidence of GBS in newborns. However, it is important to note that the use of intrapartum antibiotics should be done in accordance with guidelines and under the supervision of a healthcare provider to minimize the risk of antibiotic resistance.

This finding is corroborated by the present review, albeit indirectly. The pooled prevalence of vertical transmission among the group of colonised mothers with >50% intrapartum antibiotics prophylaxis coverage is 1.4% whereas that in the group with <50% coverage is very much higher at 34%. Likewise, the relative risk among the former group is 5.0 (95% CI=2.9, 8.4) compared to 13.8 (95% CI=8.2, 23.0) among the latter. Hence, we conclude that antibiotic prophylaxis is necessary to mitigate the risk of vertical transmission of GBS and thus neonatal infection.

We note that studies that report a very high intrapartum antibiotics prophylaxis (95% to 100%) for colonised pregnant women, such as that from India (61, 64), China (3), Taiwan (36), Japan (42) and USA (28) also report very low prevalence of neonatal colonisation (less than 0.2%), further lending support to the argument for prophylaxis.

4.4 Heterogeneity across studies

To address the high degree of heterogeneity across the 54 studies, leave-one-out meta-analysis was performed. The results indicated that each of these studies actually had substantial effect (p-value <0.001) on the overall estimate from the rest of the studies. Further, our results showed that the difference in regional, economical, religious as background, IAP coverage, and quality of study (as defined according to STROBE scores) did not explain the high heterogeneity (>90%) across studies. We note, however, that there is a vast difference in the size of the studies which ranged from 31 (39) to 154,088 parturient women (36), which could account for, at least in part, the observed heterogeneity. On top of that, the heterogeneity could also associated to screening methods (i.e bacteriological culture method and genotyping). PCR is the most widely used molecular technique and most accurate, precise and rapid method of identifying pathogens (72, 73). Having said that, genotyping method was not widely used in the postnatal setting based on the observation seen in current review, whereby bacteriological culture methods are the most commonly used, follow by 14 studies used serotyping and only seven studies used genotyping technique in GBS screening.

4.5 Strength and Limitations

The analysis in this review was performed on 355, 787 matched pairs of parturient and neonates from 30 countries, and is believed to be the first of its kind to estimate prevalence of GBS in mothers and neonates, and the relative risk of vertical transmission, early of and late-onset of GBS infection. The large number of paired samples is expected to lend support to the reliability of our results. We note also the differences in various aspects across the range of studies reviewed, which could be considered a plus in that the results are reflective of the situations across different circumstances, or a minus, as

such variations could have negative effect on the results. Further, the strict inclusion criteria on the selection of matched pairs of parturient women and neonates necessitated the exclusion of many studies that only reported the prevalence of GBS in pregnant mothers, or the prevalence of GBS in neonates, underscoring the discrepancies between our results and those in the literature.

5. CONCLUSION

This review provides an estimation of the pooled prevalence of maternal GBS colonization (17.1%), neonatal GBS colonization (1.0%), the relative risk of vertical transmission (RR=9.933) and of early-onset GBS infection (RR=7.642), the pooled incidence of EOGBS (2 cases per 1000 lives birth) and LOGBS (81 cases per 1000 live birth) infection. It is important to offer intrapartum antibiotic prophylaxis, to reduce the risk of infection to neonates.

List of Abbreviations

- CI – Confidence Interval
- EOGBS – Early onset GBS
- GBS - Group B streptococcus
- LOGBS – Late onset GBS
- PRISM - Preferred Reporting Items for Systematic Reviews and Meta-analyses
- STROBE - Strengthening the Reporting of Observational Studies in Epidemiology

Declarations

- Authors contribution: Kai Wei Lee – Conceptualized the review; searched databases and selected articles and performed data extraction and analysis; took the lead in writing the review; critically revised the first and final draft manuscript; Sook Fan Yap – Conceptualized the review; searched databases and selected articles and performed data extraction and analysis; took the lead in writing the review; critically revised the first and final draft manuscript; Sudaxshina Murdan - Conceptualized the review; critically revised the first and final draft manuscript; Zurina Zainudin - Conceptualized the review; searched databases and selected articles and performed data extraction and analysis; critically revised the first and final draft manuscript; Habibah Abdul Hamid - Conceptualized the review; searched databases and selected articles and performed data extraction and analysis; critically revised the first and final draft manuscript; Mohsen Emamjomeh - performed data extraction and analysis; Mohd Nasir Mohd Desa - revised several draft versions of the manuscript; Narcisse Mary Sither Joseph - revised several draft versions of the manuscript; Mohammad Noor Amal Azmai - revised several draft versions of the manuscript; Syafinaz Amin-Nordin – Conceptualized the review; searched databases and selected articles and performed data extraction and analysis; All authors read and approved the submission of the final version of the manuscript.
- Funding statement: This work was supported by Ministry of Higher Education under Fundamental Research Grant Scheme (FRGS/1/2023/WAB04/UPM/01/4)
- Acknowledgement: Not applicable
- Ethical statement with approval date: This study was registered with PROSPERO (Registration number: CRD42022364943) and approved on 15 October 2022.

- Data Availability Statements - The data underlying this article are available in the article and in its online supplementary material.
- Conflict of Interest - The authors declare that they have no competing interests.

REFERENCES

1. Russell NJ, Seale AC, O'Driscoll M, O'Sullivan C, Bianchi-Jassir F, Gonzalez-Guarin J, et al. Maternal colonization with group B Streptococcus and serotype distribution worldwide: systematic review and meta-analyses. Clinical infectious diseases. 2017;65(suppl_2):S100-S11.
2. van Kassel MN, Janssen SW, Kofman S, Brouwer MC, van de Beek D, Bijlsma MW. Prevalence of group B streptococcal colonization in the healthy non-pregnant population: a systematic review and meta-analysis. Clinical Microbiology and Infection. 2021;27(7):968-80.
3. Zhu Y, Huang J, Lin XZ, Chen C. Group B Streptococcus Colonization in Late Pregnancy and Invasive Infection in Neonates in China: A Population-Based 3-Year Study. Neonatology. 2019;115(4):301-9.
4. Chen Z, Wu Ca, Cao X, Wen G, Guo D, Yao Z, et al. Risk factors for neonatal group B streptococcus vertical transmission: a prospective cohort study of 1815 mother-baby pairs. Journal of Perinatology. 2018;38(10):1309-17.
5. Al-Sweih N, Hammoud M, Al-Shimmiri M, Jamal M, Neil L, Rotimi V. Serotype distribution and mother-to-baby transmission rate of Streptococcus agalactiae among expectant mothers in Kuwait. Archives of gynecology and obstetrics. 2005;272(2):131-5.
6. Hammoud MS, Al-Shemmari M, Thalib L, Al-Sweih N, Rashwan N, Devarajan LV, et al. Comparison between different types of surveillance samples for the detection of GBS colonization in both parturient mothers and their infants. Gynecologic and obstetric investigation. 2003;56(4):225-30.
7. Chan GJ, Modak JK, Mahmud AA, Baqui AH, Black RE, Saha SK. Maternal and neonatal colonization in Bangladesh: prevalences, etiologies and risk factors. Journal of Perinatology. 2013;33(12):971-6.
8. Ali MM, Woldeamanuel Y, Woldetsadik DA, Chaka TE, Fenta DA, Dinberu MT, et al. Prevalence of group B streptococcus among pregnant women and newborns at Hawassa University comprehensive specialized hospital, Hawassa, Ethiopia. BMC infectious diseases. 2019;19(1):325.
9. Hickman ME, Rench MA, Ferrieri P, Baker CJ. Changing epidemiology of group B streptococcal colonization. Pediatrics. 1999;104(2):203-9.
10. Puopolo KM, Lynfield R, Cummings JJ, Hand I, Adams-Chapman I, Poindexter B, et al. Management of infants at risk for group B streptococcal disease. Pediatrics. 2019;144(2).
11. Seale AC, Bianchi-Jassir F, Russell NJ, Kohli-Lynch M, Tann CJ, Hall J, et al. Estimates of the burden of group B streptococcal disease worldwide for pregnant women, stillbirths, and children. Clinical infectious diseases. 2017;65(suppl_2):S200-S19.
12. Curcio AM, Shekhawat P, Reynolds AS, Thakur KT. Neurologic infections during pregnancy. Handbook of Clinical Neurology. 2020;172:79-104.
13. Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC, 2010. Department of Health and Human Services, Centers for Disease Control and …; 2010.
14. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Systematic reviews. 2015;4(1):1-9.
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic reviews. 2021;10(1):1-11.

16. Vandenbroucke JP, Elm Ev, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. Annals of internal medicine. 2007;147(8):W-163-W-94.
17. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the gap between methodologists and end-users: R as a computational back-end. Journal of statistical software. 2012;49:1-15.
18. Allardice JG, Baskett TF, Seshia MM, Bowman N, Malazdrewicz R. Perinatal group B streptococcal colonization and infection. American journal of obstetrics and gynecology. 1982;142(6 Pt 1):617-20.
19. Barcaite E, Bartusevicius A, Tameliene R, Maleckiene L, Vitkauskiene A, Nadisauskiene R. Group B streptococcus and Escherichia coli colonization in pregnant women and neonates in Lithuania. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2012;117(1):69-73.
20. Boyer KM, Gadzala CA, Kelly PD, Burd LI, Gotoff SP. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. II. Predictive value of prenatal cultures. The Journal of infectious diseases. 1983;148(5):802-9.
21. Cassidy-Bushrow AE, Sitarik A, Levin AM, Lynch SV, Havstad S, Ownby DR, et al. Maternal group B Streptococcus and the infant gut microbiota. Journal of developmental origins of health and disease. 2016;7(1):45-53.
22. Chen J, Fu J, Du W, Liu X, Rongkavilit C, Huang X, et al. Group B streptococcal colonization in mothers and infants in western China: prevalences and risk factors. BMC infectious diseases. 2018;18(1):291.
23. Christensen KK, Dahlander K, Eskström A, Svenningsen N, Christensen P. Colonization of newborns with group B streptococci: relation to maternal urogenital carriage. Scandinavian journal of infectious diseases. 1981;13(1):23-7.
24. Easmon CS, Hastings MJ, Blowers A, Bloxham B, Deeley J, Marwood R, et al. Epidemiology of group B streptococci: one year's experience in an obstetric and special care baby unit. British journal of obstetrics and gynaecology. 1983;90(3):241-6.
25. Elbaradie SMY, Mahmoud M, Farid M. Maternal and neonatal screening for Group B streptococci by SCP B gene based PCR: a preliminary study. Indian journal of medical microbiology. 2009;27(1):17-21.
26. Elikwu CJ, Oduyebo O, Ogunsola FT, Anorlu RI, Okoromah CN, König B. High group B streptococcus carriage rates in pregnant women in a tertiary institution in Nigeria. The Pan African medical journal. 2016;25:249.
27. Eren A, Küçükercan M, Oğuzoğlu N, Unal N, Karateke A. The carriage of group B streptococci in Turkish pregnant women and its transmission rate in newborns and serotype distribution. The Turkish journal of pediatrics. 2005;47(1):28-33.
28. Faro S, Brehm B, Smith F, Mouzoon M, Greisinger A, Wehmanen O, et al. Screening for group B streptococcus: a private hospital's experience. Infectious diseases in obstetrics and gynecology. 2010;2010.
29. Håkansson S, Axemo P, Bremme K, Bryngelsson A-L, Wallin MC, Ekström C-M, et al. Group B streptococcal carriage in Sweden: a national study on risk factors for mother and infant colonisation. Acta obstetricia et gynecologica Scandinavica. 2008;87(1):50-8.
30. Hamedi A, Akhlaghi F, Seyedi SJ, Kharazmi A. Evaluation of group B Streptococci colonization rate in pregnant women and their newborn. Acta medica Iranica. 2012;50(12):805-8.
31. Horváth B, Grasselly M, Bödecs T, Boncz I, Bódis J. Screening pregnant women for group B streptococcus infection between 30 and 32 weeks of pregnancy in a population at high risk for premature birth. International Journal of Gynecology & Obstetrics. 2013;122(1):9-12.
32. Ji Y, Zhao C, Ma X-X, Peppelenbosch MP, Ma Z, Pan Q. Outcome of a screening program for the prevention of neonatal early-onset group B Streptococcus infection: a population-based cohort study in Inner Mongolia, China. Journal of medical microbiology. 2019;68(5):803-11.

33. Kunze M, Ziegler A, Fluegge K, Hentschel R, Proempeler H, Berner R. Colonization, serotypes and transmission rates of group B streptococci in pregnant women and their infants born at a single University Center in Germany. Journal of perinatal medicine. 2011;39(4):417-22.
34. Kunze M, Zumstein K, Markfeld-Erol F, Elling R, Lander F, Prömpeler H, et al. Comparison of pre- and intrapartum screening of group B streptococci and adherence to screening guidelines: a cohort study. European journal of pediatrics. 2015;174(6):827-35.
35. Le Doare K, Jarju S, Darboe S, Warburton F, Gorringe A, Heath PT, et al. Risk factors for Group B Streptococcus colonisation and disease in Gambian women and their infants. Journal of Infection. 2016;72(3):283-94.
36. Li-Chen H, Pei-Tseng K, Tsan-Hung C, Hsun-Pi S, Ming H, Hui-Fen K, et al. Risk factors for neonatal early-onset group B streptococcus-related diseases after the implementation of a universal screening program in Taiwan. BMC public health. 2018;18(1):1-9.
37. Lijoi D, Di Capua E, Ferrero S, Mistrangelo E, Giannattasio A, Morano S, et al. The efficacy of 2002 CDC guidelines in preventing perinatal group B Streptococcal vertical transmission: a prospective study. Archives of gynecology and obstetrics. 2007;275(5):373-9.
38. Madzivhandila M, Adrian PV, Cutland CL, Kuwanda L, Schrag SJ, Madhi SA. Serotype distribution and invasive potential of group B streptococcus isolates causing disease in infants and colonizing maternal-newborn dyads. PloS one. 2011;6(3):e17861.
39. Matorras R, Garcia-Perea A, Usandizaga JA, Omeñaca F. Natural transmission of group B Streptococcus during delivery. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 1989;30(2):99-103.
40. Medugu N, Iregbu KC, Parker RE, Plemmons J, Singh P, Audu LI, et al. Group B streptococcal colonization and transmission dynamics in pregnant women and their newborns in Nigeria: implications for prevention strategies. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2017;23(9):673.e9-.e16.
41. Mirsky R, Carpenter DM, Postlethwaite DA, Regenstein AC. Preventing early-onset group B streptococcal sepsis: is there a role for rescreening near term? Journal of Maternal-Fetal & Neonatal Medicine. 2020;33(22):3791-7.
42. Miyata A, Takahashi H, Kubo T, Watanabe N, Tsukamoto K, Ito Y, et al. Early-onset group B streptococcal disease following culture-based screening in Japan: a single center study. The journal of obstetrics and gynaecology research. 2012;38(8):1052-6.
43. Pasnick M, Mead PB, Philip AG. Selective maternal culturing to identify group B streptococal infection. American journal of obstetrics and gynecology. 1980;138(5):480-4.
44. Petersen KB, Johansen HK, Rosthøj S, Krebs L, Pinborg A, Hedegaard M. Increasing prevalence of group B streptococcal infection among pregnant women. Danish medical journal. 2014;61(9):A4908.
45. Reid TM. Emergence of group B streptococci in obstetric and perinatal infections. British medical journal. 1975;2(5970):533-5.
46. Saha SK, Ahmed ZB, Modak JK, Naziat H, Saha S, Uddin MA, et al. Group B Streptococcus among Pregnant Women and Newborns in Mirzapur, Bangladesh: Colonization, Vertical Transmission, and Serotype Distribution. Journal of clinical microbiology. 2017;55(8):2406-12.
47. Santhanam S, Jose R, Sahni RD, Thomas N, Beck MM. Prevalence of group B Streptococcal colonization among pregnant women and neonates in a tertiary hospital in India. Journal of the Turkish-German Gynecological Association. 2017;18(4):181-4.
48. Schrag SJ, Zell ER, Lynfield R, Roome A, Arnold KE, Craig AS, et al. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. The New England journal of medicine. 2002;347(4):233-9.
49. Sensini A, Tissi L, Verducci N, Orofino M, von Hunolstein C, Brunelli B, et al. Carriage of group B Streptococcus in pregnant women and newborns: a 2-year study at Perugia General Hospital. Clin Microbiol Infect. 1997;3(3):324-8.

50. Seoud M, Nassar AH, Zalloua P, Boghossian N, Ezeddine J, Fakhoury H, et al. Prenatal and neonatal Group B Streptococcus screening and serotyping in Lebanon: incidence and implications. Acta obstetricia et gynecologica Scandinavica. 2010;89(3):399-403.
51. Shibata M, Morozumi M, Maeda N, Komiyama O, Shiro H, Iwata S, et al. Relationship between intrapartum antibiotic prophylaxis and group B streptococcal colonization dynamics in Japanese mother-neonate pairs. Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy. 2021;27(7):977-83.
52. Suara RO, Adegbola RA, Baker CJ, Secka O, Mulholland EK, Greenwood BM. Carriage of group B Streptococci in pregnant Gambian mothers and their infants. The Journal of infectious diseases. 1994;170(5):1316-9.
53. Takahashi K, Sato Y, Ikeda K. Group B streptococcus neonatal umbilical colonization managed by dry cord care in nurseries: A retrospective cohort study. Pediatrics and neonatology. 2021;62(5):506-11.
54. Toyofuku M, Morozumi M, Hida M, Satoh Y, Sakata H, Shiro H, et al. Effects of Intrapartum Antibiotic Prophylaxis on Neonatal Acquisition of Group B Streptococci. The Journal of pediatrics. 2017;190:169.
55. Tsolia M, Psoma M, Gavrili S, Petrochilou V, Michalas S, Legakis N, et al. Group B streptococcus colonization of Greek pregnant women and neonates: prevalence, risk factors and serotypes. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2003;9(8):832-8.
56. Voluménie JL, Fernandez H, Vial M, Lebrun L, Frydman R. Neonatal group B streptococcal infection. Results of 33 months of universal maternal screening and antibioprophylaxis. European journal of obstetrics, gynecology, and reproductive biology. 2001;94(1):79-85.
57. Yow MD, Leeds LJ, Thompson PK, Jr.Mason EO, Clark DJ, Beachler CW, et al. The natural history of group B streptococcal colonization in the pregnant woman and her offspring. I. Colonization studies. American Journal of Obstetrics & Gynecology. 1980;137(1):34-8.
58. Berardi A, Buffagni AM, Rossi C, Vaccina E, Cattelani C, Gambini L, et al. Serial physical examinations, a simple and reliable tool for managing neonates at risk for early-onset sepsis. World J Clin Pediatr. 2016;5(4):358-64.
59. Chaudhry BY, Akhtar N, Balouch AH. Vaginal carriage rate of group B Streptococcus in pregnant women and its transmission to neonates. Journal of Ayub Medical College, Abbottabad : JAMC. 2010;22(4):167-70.
60. de Cueto M, Sánchez MJ, Moltó L, Miranda JA, Herruzo AJ, Ruiz-Bravo A, et al. Efficacy of a universal screening program for the prevention of neonatal group B streptococcal disease. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 1995;14(9):810-2.
61. Gurudas G, Arjun R, Jain N, Ranganayaki V, Sasikumar C, Mohan V, et al. Prevalence of Group B Streptococcus in pregnant women in Kerala and relation to neonatal outcomes: a prospective cross-sectional study. Journal of tropical pediatrics. 2022;68(6).
62. Scheftelowitz Cohen R, Chodik G, Eisenberg VH. Re-evaluating Perinatal Group B Streptococcal screening in Israel - Is it time for a change in policy? Preventive medicine. 2021;153:106716.
63. Uh Y, Jang IH, Yoon KJ, Lee CH, Kwon JY, Kim MC. Colonization rates and serotypes of group B streptococci isolated from pregnant women in a Korean tertiary hospital. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 1997;16(10):753-6.
64. Warrier LM, Joy S, C RR, Bashir RA. Group B Streptococcal Colonization among Pregnant Women and Neonates in a Tertiary Care Hospital in South India. Indian J Pediatr. 2022;19:1-8.
65. Kwatra G, Cunnington MC, Merrall E, Adrian PV, Ip M, Klugman KP, et al. Prevalence of maternal colonisation with group B streptococcus: a systematic review and meta-analysis. The Lancet Infectious Diseases. 2016;16(9):1076-84.

66. Huang J, Li S, Li L, Wang X, Yao Z, Ye X. Alarming regional differences in prevalence and antimicrobial susceptibility of group B streptococci in pregnant women: A systematic review and meta-analysis. Journal of global antimicrobial resistance. 2016;7:169-77.
67. Abbasalizadeh F, Pourasghary S, Shirizadeh M, Mousavi S, Ghojazadeh M, Hoseinifard H, et al. Prevalence of group B streptococcus in vagina and rectum of pregnant women of Islamic & Non-Islamic countries: a systematic review and meta-analysis. Iranian Journal of Public Health. 2021;50(5):888.
68. Sinha A, Russell LB, Tomczyk S, Verani JR, Schrag SJ, Berkley JA, et al. Disease burden of group B Streptococcus among infants in sub-Saharan Africa: a systematic literature review and meta-analysis. The Pediatric infectious disease journal. 2016;35(9):933.
69. Matin BK, Williamson HJ, Karyani AK, Rezaei S, Soofi M, Soltani S. Barriers in access to healthcare for women with disabilities: a systematic review in qualitative studies. BMC women's health. 2021;21(1):1-23.
70. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE. Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis. PLoS medicine. 2013;10(8):e1001502.
71. Li S, Huang J, Chen Z, Guo D, Yao Z, Ye X. Antibiotic prevention for maternal group B streptococcal colonization on neonatal GBS-related adverse outcomes: a meta-analysis. Frontiers in microbiology. 2017;8:374.
72. Rudkjøbing VB, Thomsen TR, Xu Y, Melton-Kreft R, Ahmed A, Eickhardt S, et al. Comparing culture and molecular methods for the identification of microorganisms involved in necrotizing soft tissue infections. BMC infectious diseases. 2016;16(1):1-13.
73. Babalola OO. Molecular techniques: An overview of methods for the detection of bacteria. African journal of biotechnology. 2003;2(12):710-3.

Legends of figures

Figure 1: Pooled Prevalence of GBS colonization in parturient.

Figure 2: Pooled Prevalence of GBS colonization in neonates.

Figure 3: Pooled Prevalence of GBS vertical transmission.

Figure 4: Pooled Relative Risk of GBS Vertical Transmission.

Figure 5: Pooled Relative Risk of Early-onset GBS infection in neonates born to colonized mothers.

Figure 6. Incidence of Early-onset GBS infection per 1000 live birth.

Figure 7. Incidence of late-onset GBS infection per 1000 live birth.

Legends of Tables

Table 1: Characteristics of included studies and its participants.

Table 2: Summary of Pooled Prevalence of GBS and vertical transmission among matched pair of parturient and neonates.