Original Article

Neonatal Group B *Streptococcus* infection at a single center in Al-Madinah Al-Munawarah, Saudi Arabia

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ABSTRACT

الأهداف: يهدف هذا البحث إلى تحديد نسبة حدوث عدوى GBS عند حديثي الولادة وعوامل الخطر المرتبطة بها في المدينة المنورة، المملكة العربية السعودية.

المنهجية: أجريت دراسة مرجعية في مستشفى الولادة والأطفال بالمدينة المنورة، من عام 2017م إلى 2022م. وتم جمع بيانات مختبرية وسريرية لـ 64 من حديثي الولادة وتحليلها باستخدام برنامج GraphPad Prism 7.

النتائج: من بين 16,022من حديثي الولادة الذين تم إدخالهم إلى الحضانة، تم تشخيص إصابة 64 رضيعًا بعدوى المكورات العقدية 53.1% ذكور، 46.9% إناث، 15.6% خدج، و84.4% مكتملي النمو. وبلغت نسبة الولادات المهبلية 71.9%. كان متوسط عمر حدوث العدوى من 10±12.4 يومًا. كان 53.1% منهم يعانون من بداية مبكرة للمرض (0-6 أيام)، بينما كان 46.9% يعانون من مرض متأخر الظهور (7-90 يومًا). المولودين لأمهات غير مفحوصات للكشف المبكر عن المكورات العنقودية لديهم نسبة أعلى من الإصابة بالعدوى. بلغ معدل الوفيات 10.9% بينما خرج 89.1% من المستشفى.

الخلاصة: تنتشر عدوى المكورات العقدية عند الأطفال حديثي الولادة في المدينة المنورة، وقد تساهم العديد من عوامل الخطر في حدوث العدوى مثل الولادة المبكرة، وارتفاع درجة حرارة الجسم أثناء الولادة، وتمزق الأغشية المبكر لفترة طويلة لأكثر من 18 ساعة، والبيلة الجرثومية GBS. بالإضافة إلى ذلك، فإن عدم وجود فحص مناسب لإكتشاف البكتريا أثناء الحمل يزيد من قابلية الإصابة بالعدوى لدى المواليد.

Objectives: To determine the occurrence of Group B *Streptococcus* (GBS) infection in neonates and its associated risk factors in Al-Madinah Al-Munawarah, Saudi Arabia.

Methods: This retrospective study was carried out at the Maternity and Child Hospital in Al-Madinah Al-Munawarah, between 2017-2022. The laboratory and clinical data of 64 neonates were collected and analyzed using GraphPad Prism 7 software.

Results: Out of 16,022 neonates admitted to the nursery, 64 infants were diagnosed with GBS infection. Approximately 53.1% were male, 46.9% female, 15.6% were preterm, and 84.4% were full-term. Vaginal births accounted for 71.9%. The mean onset age was 10±12.4 days. Among the GBS patients, 53.1% had early-onset disease (EOD, 0-6 days), while 46.9% had late-onset disease (LOD, 7-90 days). Unexamined mothers had a higher incidence of GBS and EOD newborns (p=0.05). Meningitis was more common in LOD than EOD patients and correlated with illness onset (p=0.05). Early-onset disease patients had a higher incidence of sepsis. The mortality rate was 10.9%, while 89.1% were discharged from the hospital.

Conclusion: Neonatal GBS infection is prevalent in Al-Madinah Al-Munawarah. Several risk factors may contribute to the occurrence of GBS infection including preterm labor, higher body temperature during delivery, prolonged premature rupture of membranes for more than 18 hours, and GBS bacteriuria. We recommend that larger multi-centric studies are needed in Al-Madinah Al-Munawarah, to study the magnitude of neonatal GBS infection and risk factors to develop a screening protocol in maternity and children's hospital.

Keywords: neonatal infection, GBS, B *Streptococcus*, GBS Saudi Arabia

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Group B *Streptococcus* (GBS), represents the leading cause of perinatal infections globally. It contributes to invasive bacterial infections in newborns and infants, as well as pregnancy-associated complications. These complications include neonatal sepsis/infections, such as meningitis or pneumonia, and infections in pregnant women that may lead to preterm labor, abortion, and stillbirth.[1]

Based on the age at onset of GBS manifestations, it is categorized as either early, late, or ultra-late onset disease. Early onset GBS infection (EO-GBS) is defined as an infection during the first 6 days following delivery, with the majority of cases occurring within the first 24 hours. It is attributed to vertical transmission from colonized mothers during passage through the vagina during labor and delivery.[2] On the other hand, late-onset GBS (LO-GBS) occurs between 7-90 days, while ultra LO-GBS occurs within the next 3 months of age.[3] The global average prevalence of colonized women with GBS is 18% ranging from a high prevalence in the Caribbean of 35% to a much lower prevalence in Southern Asia at 13%, and Eastern Asia at 11%, while locally in Saudi Arabia the GBS colonization prevalence among pregnant women ranged from 2.1-32.8%.[4,5] So neonates are 29 times more likely to experience early-onset disease (EOD), although only 1-2% will experience invasive GBS infection. Risk factors for EOD include positive GBS colonization, preterm labor before the 37th week of gestation, prolonged premature rupture of membranes lasting more than 18 hours, and higher body temperature during delivery.[6]

Tremendous efforts have been carried out since the late 80s to prevent GBS-EOD. This includes implementing and improving intrapartum antibiotic prophylaxis, given to carrier GBS pregnant women during delivery, and developing vaccines for maternal immunization during pregnancy.[7-9]

Knowing the epidemiology and risk factors for GBS provides data that could be used to estimate disease distribution in certain groups and geographical areas in Saudi Arabia and plan the development of appropriate GBS screening programs. At the the Maternity and Child Hospital, Al-Madinah Al-Munawarah, Saudi Arabia, where the study was carried out, the screening for GBS was carried out for high risk cases.

These programs are essential as they offer information that may assist clinicians in their practice and in understanding the disease behavior. Therefore, this study aimed to determine the prevalence of neonatal GBS infection in Al-Madinah Al-Munawarah and identify the related risk factors.

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Methods. A retrospective review of medical data at the Maternity and Child Hospital, Al-Madinah Al-Munawarah, Saudi Arabia, 64 neonatal samples with GBS infection of neonates born between 2017-2022.

Cases were divided into EOD and late-onset (LOD) categories. Only those who met the inclusion requirements of having a GBS-positive culture from a sterile site were included. Cases collected from Maternity and Child Hospital Medinah which have laboratories that carried out such tests. The main categories used to classify the cases were sepsis (GBS grown only from blood) or meningitis (defined as GBS isolated from cerebrospinal fluid [CSF] only or from both CSF and blood). Antimicrobial susceptibility testing data were collected using the disc diffusion technique, as determined by the National Committee for Clinical Laboratory Standards.[10]

King Salman bin Abdulaziz Medical City's institutional review board in Al-Madinah Al-Munawarah, reviewed and approved the research protocol (national registr. no.: NCBE, H-03-M-11). The study was carried out according to principles of Helsinki Declaration.

Statistical analysis. Graphpad Prism 7 software (GraphPad Software, CA, USA) was used for data collection and its statistical analysis. For quantitative variables, the mean along with the standard deviation (SD) were used, and for qualitative variables, frequency and percentage were used. The Chi-square test was employed to identify relationships between variables. A significance threshold of 0.05 was used for this study.

Results. Out of a total of 16,022 neonates admitted to the nursery during the course of the study's 5-year period, 64 (0.40%) were found to have GBS infection. The study collected data on the incidence of neonatal GBS cases and the total number of neonates admitted to the nursery of the Maternity and Children Hospital for each year. A significant decrease in neonatal GBS cases was observed in the final year of the study. The study period yielded an overall incidence rate of 0.40 per 16,022 neonates in the nursery, corresponding to a rate of 6.4 per 1,000 neonates (Appedix 1).

The number of male cases accounted for 53.1% (n=34), while the number of female cases comprised 46.9% (n=30). Among the newborns, 84.4% (n=54) were delivered after full-term pregnancies, while 15.6%

(n=10) were born prematurely. The term "mode of delivery" refers to the choice between vaginal delivery or cesarean section (C-section); the majority of infants were delivered vaginally (71.9%, n=46), while 28.1% (n=18) were born via C-section. The average birth weight was 2.4±0.73 kg, with 54.6% (n=35) ranging from 2.1-3.5 kg and 45.4% (n=29) ranging from 600 g to 1.2 kg. The age at the time of diagnosis varied widely, ranging from 0-28 days, with a mean of 10±2.4 days and a median of one day. Among those identified with GBS, 53.1% (n=34) exhibited symptoms of EOD (0-6 days), while 46.9% (n=30) showed symptoms of LOD (7-90 days). However, 7.8% of the infected neonates had leukopenia (white blood cells [WBCs] of <3,000/mm^3, Table 1)

The mothers of the newborns had an average age of 20 years. Among them, 39.1% (n=25) had some predisposing risk factors for infection transmission. These risk factors are described as follows: I) during their respective pregnancies, 40% (n=10) of the women experienced preterm labor; II) 44% (n=11) of the women had a high temperature at the time of delivery; III) 36% (n=9) of the women experienced prolonged premature rupture of the membrane lasting more than 18 hours; and IV) 16% (n=4) of the women had GBS bacteriuria. Chorioamnionitis was not observed in any of the examined pregnancies (Table 2).

As our study center lack of routine GBS screening we found that most neonate who develop GBS infection their mothers were not screened.

Among the mothers, 87.5% (n=56) were not screened for GBS during their respective pregnancies, and 91.2% (n=31) gave birth to neonates with EOD. Meningitis showed a statistically significant association with the onset of the illness (p<0.05), being more common in LOD patients than EOD patients. On the other hand, sepsis was more common in EOD patients. A total of 7 neonates did not survive, with 2 having EOD, and the remaining 5 having LOD. The overall mortality rate for the disease was 10.9%. The majority of the included participants (89.1%, n=57) survived and were discharged.

Table 3 illustrates the associations between the onset of GBS illness and the increased risks of infection, complications, and mortality.

Table 1 - Study participants' demographics.

Characteristics	n (%)
Sample size	64 (100)
Gender	
Female	30 (46.9)
Male	34 (53.1)
Gestational age	
Preterm	10 (15.6)
Term	54 (84.4)
Mode of delivery	
Vaginal	46 (71.9)
Cesarean section	18 (28.1)
Birthweight, mean±SD	2.4±0.73 kg
2.1-3.5 kg	35 (54.6)
1.2 kg - 600 g	29 (45.4)
Age at diagnosis, mean±SD	10±12.4 days
Temperature (fever)	
Yes (>36.5)	10 (15.6)
No (≤36.5)	54 (84.4)
CBC results:	
RBC (5.1-5.3 million/mm^3)	4.9±1.5 million/mm^3
WBC (9,000-30,000/mm^3)*	10,000±1000/mm^3
PLT (150×10^3 - 450×10^3/mcL)	300×10^3±100.6/mcL
Cardiorespiratory instability	
Ventilated	20 (31.3)
Shocked	15 (23.4)
No need	29 (45.3)
Participants categories	
EOD	34 (53.1)
LOD	30 (46.9)

Values are presented as numbers and precentages (%) or mean ± standard deviation (SD). *Approximately 7.8% of infected neonatal had leukopenia (WBCs of <3,000/mm^3) wherase, 59 (92.2%) pateintes had normal WBCs level. RBC: red blood cells, WBC: white blood cells, PLT: platelets, EOD: early-onset disease at 0-6 days, LOD: late-onset disease at 7-90 days

Table 2 - Group B *Streptococcus* screening and the pregnancy record of the mother.

Characteristics	n (%)
Total sample size	64 (100)
Screens for GBS	
Positive	4 (6.2)
Negative	4 (6.2)
None	56 (87.5)
Predisposing risk factors among the mothers of newborns (n=25)	
Sample size	25 (39.1)
Age (years)	20±5.4 years
Gestational age	
Preterm	10 (40.0)
Term	15 (60.0)
Mode of delivery	
Vaginal	15 (60.0)
Cesarean section	10 (40.0)
Fever at the time of labor	11 (44.0)
Prolonged premature rupture of the membrane	9 (36.0)
Screens for GBS in 25 mothers	
Positive	4 (16.0)
Negative	4 (16.0)
None	17 (68.0)

Values are presented as numbers and precentages or mean ± standard deviation (SD). GBS: Group B *Streptococcus*

Table 3 - The associations between risk factors for Group B *Streptococcus* infection and the onset of Group B *Streptococcus*.

Characteristics	Total	EOD	LOD
Sample size	64 (100)	34 (53.1)	30 (46.9)
Gender			
Female	30 (46.9)	15 (44.1)	15 (50.0)
Male	34 (53.1)	19 (55.9)	15 (50.0)
Gestational age			
Preterm	10 (15.6)	7 (20.6)	3 (10.0)*
Term	54 (84.4)	27 (79.4)	27 (90.0)
Mode of delivery			
Vaginal	46 (71.9)	24 (70.6)	22 (73.3)
Cesarean section	18 (28.1)	7 (13.3)	8 (26.7)
Prolonged rupture of membranes of >18 hours	11 (17.2)	9 (26.5)*	2 (6.0)
Intrapartum fever	14 (21.9)	10 (29.4)*	4 (13.3)
Birthweight			
2.1-3.5 kg	35 (54.6)	13 (38.2)	22 (73.3)
1.2 kg - 600 g	29 (45.4)	21 (61.8)*	8 (26.7)
Age at diagnosis, mean±SD	10±12.4 days	5±1.4 days	9±2.2 days
Diagnosis			
Sepsis	50 (78.1)	32 (94.1)*	18 (60.0)
Meningitis	10 (15.6)	1 (2.9)	9 (30.0)*
Pneumonia	4 (6.3)	1 (2.9)	3 (10.0)
GBS screening (for mothers)			
Yes	8 (12.5)	3 (8.8)	5 (16.7)
No	56 (87.5)	31 (91.2)*	25 (83.3)
Outcomes			
Alive	57 (89.1)	32 (94.1)	25 (83.3)
Dead	7 (10.9)	2 (5.9)	5 (16.7)*

Values are presented as numbers and precentages or mean ± standard deviation (SD). **P*-value of ≤0.05 (*P*-values obtained from Chi-squared test). EOD: early-onset disease at 0-6 days, LOD: late-onset disease at 7-90 days, GBS: Group B *Streptococcus*

Discussion. In this retrospective study of 64 infants with GBS, we observed that the majroity (84.4%) were full-term infants, while only 15.6% were premature. Vaginal delivery was more common than C-section. We identified several risk factors for neonatal GBS infection, with the most common being preterm labor, followed by higher body temperature during delivery, prolonged premature rupture of membranes lasting more than 18 hours, and GBS bacteriuria. In our result we found that most neonate who develop GBS infection their mothers were not screened.

Meningitis was more prevalent in LOD neonates compared to those with EOD. The mortality rate in our study population was estimated at 10.9%.

Group B *Streptococcus* colonization in the mother's vagina, rectum, and urine increases the risk of neonatal infections.[11] High mortality and severe morbidity, including sepsis and meningitis, are common among neonates infected with GBS in both developed and developing countries.[12]

Locally, it was also observed that GBS colonization prevalence was higher among women in the cities Riyadh (27.6%) and Jeddah (31.6%), Saudi Arabia.[5] Studies have reported varying rates of maternal GBS colonization in Saudi Arabia, ranging from 13.4-31%.[13-15] However, a study by Ahmad et al[16] reported a prevalence of 2.1% for maternal GBS colonization. The incidence of neonatal GBS infection/sepsis has also been reported in various studies from different countries, ranging from 4.9 per 1000 live births to 55 per 1000 live births.[17] Almudeer et al[18] reported an incidence of 21 per 1000 live births, while Almuneef et al[19] reported an incidence of 23 per 1000 live births. Most of these infections were EO-GBS. A significant decrease in neonatal GBS cases was observed in our study in last year as shown in **Appendix 1** during 2022 which need more internal investigation to know the possible cause.

The variations between studies may be attributed to differences in screening protocols, availability of data from medical records, and patient characteristics

such as age, parity, geographic distribution, and socio-econmic status, all of which can influence the incidence of neonatal GBS detected.[20]

Similar to our findings, Al Luhidan et al[19] in Riyadh, Saudi Arabia, reported that preterm labor (16.4%), fever at the onset of delivery (14.5%), prolonged premature rupture of membranes (12.7%), and GBS bacteriuria (5.5%) were risk factors associated with GBS infection to the neonate. Our study also observed that approximately 87.5% of the mothers of GBS-infected neonates were not screened for GBS during their pregnancy. This finding is consistent with other studies carried out in Saudi Arabia and emphasizes the importance of universal screening recommended by The American College of Obstetricians and Gynecologists and the American Society for Microbiology that recommends carrying out universal GBS screening between 36 (0/7) and 37 (6/7) weeks of gestation to detect GBS infection through vaginal and rectal culture testing.[21,22]

Regarding neonatal infection characteristics, our study showed that the rate of GBS infection is more common in term babies (84.4%) than in preterm babies (15.6%). Similar to our results, Al Luhidan et al[17] reported a significant association between the LOD and a higher risk of developing meningitis (p<0.008). They also reported no significant association between the disease onset and other clinical manifestations in newborns.

Mainly the GBS is transmitted during vaginal delivery, our study observed that approximately 28.1% of the infected neonates were delivered via C-section with no difference between EOD and LOD, but suggesting that other transmission routes may be possible, that were supported in a study to investigate cause of early onset sepsis (EOS) where the ceseran delivery account for 35% and other studies detecting GBS transmission to the neonate through breast milk, also a study found that nosocomial transmission has been known to occur for babies born to GBS negative mothers.[18,23,24]

In terms of hematological changes, leucopenia (WBCs of <3,000/mm^3) was evident in 7.8% of infected neonates. This finding is similar to results reported by Adane et al[25] and Diakité et al.[26]

The mortality rate in our study after GBS disease was 10.9%, with the LOD subgroup showing a higher rate. This is comparable to the globally reported rate of 10%,[27] but higher than the 3.6% rate reported in the Saudi study by Al Luhidan et al[17] which reported the death of one case for EOD and LOD subgroups. Almudeer et al[18] carried out a retrospective study in Jazan region, Saudi Arabia, reporting a mortality rate of 23% (29 infants) among 126 neonates diagnosed with EOS, with GBS being the second most commonly isolated organism (17%). Mortality rates were significantly associated with gestational age and birth weight, with infants who died within the first week having a higher incidence of gestational age below 37 weeks and extremely low or very low birth weight compared with the infants who survived. No significant relationship was found between survival and maternal age, parity, infant gender, premature rupture of membranes, or the mode of delivery.

Several risk factors for GBS neonatal infection were identified. We found that the majority (84.4%) were full-term infants, while only 15.6% were premature, which is consistent with the findings of Lin et al.[28] A meta-analysis by Karampatsas et al[29] also revealed that preterm and low birth weight infants were more prone to LO-GBS infection. However, they failed to find a significant association between LO-GBS and the premature ruptur of membrane.[29] Various factors can attributed to get invasive GBS infection among neonate such as immature neonatal immune response, poor antibody transport across the placenta, higher intestinal permeability, and the potential transmission of nosocomial organisms among hospitlized neonate. In addition, prematurity is characterised by abnormalities of the maternal microbiome that may prevent GBS from adapting to its newborn host environment, the excessive use of the antibiotics by mothers, the dependance on formula feeding as the main source, and the limited contact with mother microbiota.[30] More importantly, maternal age was thought to be an important risk factor. In a study by Parente et al,[31] maternal age was one of the most important predictors of EO-GBS. Many other studies have showed that mothers younger than 18 years old and of black race have a higher susceptibility to EO-GBS infection.[31-33] Early onset GBS infection is 3 times more prevalant in mothers less than 18 years old compared with mothers more than 35 years old. The role of age and race in GBS infection is still being investigated, as they have been linked to increased likelihood of GBS colonization, preterm labor, and missed prenatal screening.[34,35]

Study limitations. The small sample size and the single-center nature of our study may limit the interpretation and generalizability of our data across the wider Saudi population. Additionally, the lack of a prenatal GBS screening policy is a significant limitation.

In conclusion, neonatal GBS infection is prevalent in Al-Madinah Al-Munawarah. Several risk factors may contribute to the occurrence of GBS infection including preterm labor, higher body temperature during delivery,

prolonged premature rupture of membranes for more than 18 hours, and GBS bacteriuria. Moreover, the absence of adequate GBS screening during pregnancy may escalates the risk of GBS neonatal infection. We recommend larger multi-centric studies to be carried out in Al-Madinah Al-Munawarah to study the magnitude of neonatal GBS infection, the associated risk factors, and to develop a screening protocol in Al-Madinah Al-Munawarah region hospital.

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Appendix 1 - Number of infants admitted to the nursery and their incidence from 2017-2022.

Years	number of neonatal in nursery	number of cases	Incidence	Incidence/1000
2017	2711	10	0.37	1.0
2018	2262	15	0.66	1.5
2019	2541	11	0.43	1.1
2020	2786	11	0.39	1.1
2021	3092	11	0.36	1.1
2022	2630	6	0.23	0.6
Total	16022	64	0.41	6.4

Chi-square test was carried out at a significance level of $p \leq 0.05$.