The Impact of Group B Streptococcus Infection Random Screening during Pregnancy on Subsequent Neonatal Infection/Admission Rates

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Background: Screening pregnant women at 35 to 37 gestational weeks for group B streptococci (GBS) colonization and the usage of intrapartum penicillin as prophylactic antibiotic could reduce the incidence of GBS infection.

Objective: To evaluate random screening of pregnant women for GBS infection, the rate of neonatal GBS infection and neonatal admission.

Design: A Retrospective Cohort Study.

Setting: Bahrain Defence Force Hospital, Bahrain.

Method: Two thousand one hundred seventeen patients who delivered from April 2016 to September 2016 were included in the study. The patients were divided into two groups of GBS: screened and not screened. Age, nationality, mode of delivery, result of screening and bacteriuria, membrane status and treatment received prior to labor were documented. The presence of fever or chorioamnionitis, neonatal admission, and blood or cerebrospinal fluid (CSF) cultures were documented. The data were analyzed using StatsDirect software and a P-value of less than 0.05 was considered statistically significant.

Result: One thousand forty-seven were screened antenatally, a rate of 49.5%. Two hundred twenty-six (21.6%) were positive for Beta Hemolytic Streptococci (BHS). The screened group had more spontaneous rupture of membrane (SROM)/or artificial rupture of membrane (ARM) and was treated with antibiotics pre-delivery more than unscreened patients. There was no difference between the groups regarding positive blood and CSF culture at birth. There were more cases of intrauterine fetal death (IUFD) and admission to the neonatal intensive care unit (NICU) in the non-screened group. Five (0.24%) of the neonatal sepsis were colonized with GBS among both groups. Two cases were a product of screened pregnancy for GBS colonization and found to be positive, but did not receive the appropriate length of intrapartum antibiotics; the remaining three cases were a product of a non-screened mother who did not receive antibiotic.

Conclusion: Patients who had selective screening for GBS during pregnancy had no reduced incidence of neonatal sepsis and early neonatal admission; however, they had less admission to NICU and more late neonatal admissions.

Bahrain Med Bull 2019; 41(4): 241 - 245

Neonatal sepsis is a known serious complication, leading to serious morbidity and mortality in newborns^{1,2,3,4}. Early-onset GBS is defined as from birth to 6 days of life, late-onset GBS from 7 days to 89 days of life, and late late-onset GBS from >3 months of life. GBS infection is the most common cause of early-onset sepsis in neonates. It seems to be intermittent or transient rather than a chronic condition⁵. Colonization rates in the United States range from 10% to 30%, almost similar to Europe, where it ranges from 6.5% to 36%. The Middle East colonization rate is approximately 22%, which is similar to North Africa and Asia at 19%^{3,6,7,8}. Most cases of early-onset GBS disease occur within the first 24 hours of life; the risk of death is eight times higher in preterm births than in term births⁴. Furthermore, more than 99% of premature births in

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low-income and middle-income countries develop early-onset neonatal group B streptococcal (EOGBS)⁹.

The Centers for Disease Control and Prevention (CDC) suggested a universal screening of pregnant women at 35 to 37 weeks of gestation and intrapartum penicillin^{1,3,10}. The incidence of GBS had declined from 1.8 to 0.3 per 1000 live births^{1,11,12}. Several maternal obstetrical factors have been associated with an increased risk of developing EOGBS^{3,13}.

A GBS vaccination is an alternative way of preventing infection in pregnant women. It has completed its phase II trials¹⁴. The estimated prevention of neonatal GBS infection in the USA is 60-70%, whereas the prevention rate for preterm births is only 4%¹⁵. A study of the cost-effectiveness of routine GBS vaccination, screening and Intrapartum Antibiotic Prophylaxis (IAP) prevented 899 cases of GBS infection and 35 neonatal deaths. The cost of immunization was approximately \$100 per person¹⁶.

The aim of this study is to evaluate screening pregnant women for GBS infection, the rate of neonatal group B streptococcal infection and neonatal admission.

METHOD

Two thousand one hundred seventeen patients who delivered between April 2016 and September 2016 were included in the study. Maternal age, nationality, result of screening, previous history of BHS positive, bacteriuria, mode of delivery, treatment of BHS received during delivery, induction of labor, ARM/SROM, duration of ROM during delivery and presence of fever or chorioamnionitis were documented. Sex of baby, gestation at delivery, blood/CSF culture at birth, admission place, type of admission (early/late), blood/CSF culture on admission and length of admission were documented.

The patients were divided into two groups: GBS screened and not screened. A swab was collected from the cervix/vagina and was placed into blood agar or MacConkey agar at 35-37°C.

The patients were classified into three groups according to nationality: Gulf (Bahraini, Saudi, Kuwaiti, Emirati, Omani, Qatari, and Yemeni), Asian (Indian, Pakistani, Bangladeshi, Filipino, Sri Lankan and Thai), and others (Syrian, Jordanian, Iraqi, Egyptian, Sudanese, Somali, Kenyan, Russian, Moroccan, British, Seychellois and Bulgarian). In the screened group, the results were positive, negative or unknown. Urine bacteria were tested for beta-hemolytic streptococcus and classified into negative or positive cultures. We also checked if the patients received antibiotics or not.

Rupture of the membrane (ROM) could occur either ≥ 18 hours and < 18 hours. The duration of antibiotic usage prior to delivery was documented: < 4 hours, ≥ 4 hours and not received antibiotics. Intrapartum maternal pyrexia is defined as body temperature more than 38° C (100.4° F). Chorioamnionitis is known as an inflammation of the fetal membrane due to bacterial infection; this was confirmed by placental histopathology in suspected women. Peripheral blood cultures and cerebrospinal fluids were collected from infants where sepsis was suspected or if the mother had positive GBS. Collection was done either within 72 hours of life or during admission of the first year of life. The admission was classified into early admission (day 1 to day 7 of life) and late admission (day 8 to 1 year of life). Neonatal admission were either regular nursery, intermediate, intensive care unit or isolation.

Data were analyzed using StatsDirect statistical package (version: 3.0.141 Cheshire UK 2015). A two-sided unpaired T-test, Mann-Whitney U test, the Chi-square test, the Fisher-Freeman-Halton exact were used. P-values of less than 0.05 were considered statistically significant.

RESULT

One thousand forty-seven patients were screened during the antenatal period and 1,070 were not screened. Two hundred twenty-six (21.6%) of the screened group were positive. The screened group were younger, 27.8 years versus 29.2 years, P-value <0.0001. Six hundred ninety-four (66.3%) were from the Gulf area, P-value=0.003. Fifty-two (5%) of the screened

group had positive repeated screening during labor. The screened group had a higher incidence of previous positive screening; however, it was not statistically significant. There was no difference in the presence of positive Beta Hemolytic Streptococcus (BHS) in the urine between the two study groups, see table 1.

Table 1: Patient's Characteristics

	Screened N=1,047	Non Screened N=1,070	Total N=2,117	P-value
Maternal age	27.8±5.8	29.2±5.9		< 0.0001*
Nationality				
Gulf area	694 (66.3%)	778 (73%)	1,442 (68.1%)	
Asia area	120 (11.5%)	112 (10%)	232 (11%)	0.003***
Other	233 (22.2%)	180 (17%)	413 (19.5%)	
BHS screening res	ult			
Positive	226 (21.6%)		226 (10.7%)	
Negative	682 (65.1%)		682 (32.2%)	
Unknown	139 (13.3%)		139 (6.6%)	
Result of screening	g at labor time			
Positive	52 (5%)	66 (6.2%)	118 (5.6%)	. 0.73***
Negative	127 (12.1%)	174 (16.3%)	301(14.2%)	
Previous BHS +ve				
Positive	240 (22.9%)	182 (17%)	422 (19.9%)	0.08***
Negative	384 (36.7%)	359 (33.6%)	740 (35%)	
Urine bacteriuria				
BHS	8 (0.8%)	5 (0.5%)	13 (0.6%)	0.55***
Other organism	23 (2.2%)	27 (2.5%)	50 (2.4%)	
*unpaired t-test***	Chi-square test			

Regarding urine bacteriuria, we identified 13 (0.6%) cases of GBS infection and 50 (2.36%) cases of other organisms among the study groups. Three hundred sixteen (14.9%) had GBS colonization, of which, 10 cases had a positive culture in both High Vagina Swabs (HVS) and urine samples, whereas 31 cases had HVS positive culture antenatally and at the time of labor.

The screened group had a higher incidence of vaginal delivery, 805(76.9%) versus 242(22.6%), P-value <0.0001. Furthermore, the screened group had more antibiotic treatment during labor compared to the non-screened group, P-value<0.0001. The screened group had more induction of labor, P=0.002. There were more SROM/ARM in the screened group compared to the non-screened, P<0.0001. We did not find any difference between the groups with regards to duration of ROM or the presence of fever and chorioamnionitis, see table 2.

The screened group had a higher gestation delivery age, but a lower birth weight, P-value <0.0001 and 0.001, respectively. There was no difference between the groups with regards to positive blood and CSF culture at birth. There were more cases of IUFD and admission to NICU in the non-screened group, see table 3.

Table 2: Delivery Details

	Screened N = 1,047	Non Screened N=1,070	Total N=2,117	P-value	
MOD					
Cesarean	242(23.1%)	350 (33%)	592 (28%)	<0.0001***	
SVD	805 (76.9%)	720 (67%)	1525 (72%)		
Treatment during d	lelivery				
Not given	812 (77.5%)	925 (86.5%)	1737 (82.1%)		
\geq 4 hours	119 (11.4%)	81 (7.5%)	200 (9.4%)	<0.0001***	
<4 hours	116 (11.1%)	64 (6%)	180 (8.5%)		
Induction of Labor	199 (19%)	150 (14%)	349 (16.5%)	0.002***	
ARM/ SROM					
None	172 (16.4%)	282 (26.3%)	454 (21.4%)		
SROM	331 (31.6%)	342 (32%)	673 (31.8%)	< 0.0001***	
ARM	544 (52%)	446 (41.7%)	990 (46.8%)		
Duration ROM during delivery					
\geq 18 hours	51 (4.9%)	49 (4.6%)	100 (4.7%)	0.73***	
<18 hours	823 (78.6%)	737 (68.9%)	1560 (73.7%)		
Fever	5 (0.5%)	5 (0.5%)	10 (0.5%)	>0.999****	
Chorioamnionitis	12 (1.2%)	11 (1%)	23 (1.1%)	0.79***	

*** Chi-square test**** Fisher-Freeman-Halton exact

Table 3: Fetal Characteristics

	Screened N = 1,047	Non Screened N=1,070	Total N=2,117	P-value	
Gender					
Female	514 (49.1%)	543 (50.8%)	1057 (50%)	0.45***	
Male	533 (50.9%)	527 (49.2%)	1060 (50.1%)		
Gestation at delivery	39 (41-24)	38 (41-23)		<0.0001**	
Birth weight	3±0.5	3.1±0.6		0.001*	
Baby blood culture at	birth				
Positive	0 (0%)	1 (0.09%)	1 (0.04%)	> 0.99****	
Negative	215 (20.5%)	200 (18.7%)	415 (19.6%)		
CSF culture at birth				0.71****	
Negative	2 (0.19%)	3 (0.28%)	5 (0.2%)		
Admission place (at birth)					
Regular nursery	922 (88.1%)	903 (84.4%)	1825 (86.2%)	0.01***	
Intermediate	98 (9.3%)	114 (10.6%)	212 (10%)	0.32***	
NICU	24 (2.3%)	48 (4.5%)	72 (3.4%)	0.005***	
Isolation	1 (0.1%)	0 (0%)	1 (0.04%)	0.49****	
No admission (IUFD)	2 (0.2%)	5 (0.5%)	7 (0.3%)	0.45****	
* unpaired t-test ** Ma Halton exact	nn-Whitney U	test*** Chi-squ	are test**** Fis	her-Freeman-	

Thirty-two (1.5%) were cases of neonatal sepsis; no mortality was recorded in either group. Five (15.6%) were colonized with GBS while the rest with other pathogens. The neonatal sepsis caused by GBS was found in 5 (0.24%) and neonatal sepsis caused by other pathogens was found in 27 (1.27%). Two of the five affected neonates with GBS were products of a screened pregnancy for GBS colonization and found to be positive; they did not receive the appropriate length of intrapartum antibiotics. The mothers of the other three GBS affected infants were not screened during pregnancy and did not receive intrapartum antibiotics, see tables 3 and 4.

Table 4: Admission Details

	Screened N = 1,047	Non Screened N=1,070	Total N=2,117	P-value		
Early admission	24 (2.3%)	15 (1.4%)	39 (1.8%)	0.13***		
Blood culture in a	early admissio	n				
Positive	0 (0%)	0 (0%)	0 (0%)	0.33****		
Negative	11 (1.1%)	7 (0.7%)	18 (0.9%)			
CSF culture at ea	rly admission					
Negative	1 (0.1%)	0 (0%)	1 (0.04%)	0.49****		
Late admission	117 (11.2%)	78 (7.3%)	195 (9.2%)	0.002***		
Blood culture in late admission						
Positive	2 (0.19%)	2 (0.19 %)	4 (0.2%)	0.98****		
Negative	97 (9.3%)	66 (6.2%)	163 (7.7%)			
CSF culture at la	CSF culture at late admission					
Negative	6 (0.6%)	1 (0.1%)	7 (0.3%)	0.06****		
IUFD	2 (0.2%)	5 (0.5%)	7 (0.3%)	0.45****		
Length of early admission	2 (8-1)	2 (51-1)	4 (0.2%)	0.5**		
Length of late admission	3 (72-0)	4 (20-1)	7 (0.3%)	0.81**		
** Mann-Whitney Halton exact	y U test ***	Chi-square t	est**** Fishe	er-Freeman-		

Forty-eight (4.5%) were admitted to the NICU at birth among the non-screened mothers compared to 24 (2.3%) among the screened mothers. Conversely, the neonatal admission to the regular nursery at birth was higher among the screened group (P=0.01). One hundred seventeen (11.2%) were late neonatal admission among screened women compared to 78 (7.3%) among non-screened.. In early neonatal admission, the nonscreened group had two neonates with positive bacterial infection other than GBS. In the late neonatal admission, 14 neonates from screened mothers and 10 from non-screened mothers were infected with a pathogen other than GBS, see table 4.

DISCUSSION

Neonatal sepsis is considered a serious complication^{17,18}. GBS could lead to serious morbidity and mortality in newborns, with a case fatality rate of 50%¹⁹⁻²². In recent years, the case fatality rate improved by 4-10% due to neonatal care. Studies in Saudi Arabia, Bahrain, and Kuwait found that the most common maternal colonization organisms were Staphylococcus aureus, whereas GBS colonization was more common in the United Arab Emirates²³.

The case fatality ratio of GBS infection reached as low as 4-6% after the universal screening of 2002 was recommended^{3,4,10,24,25}. In our study, GBS colonization rate was 14.9%, which is similar to Kuwait (14.6%), Bangladesh (15%), and Germany $(16\%)^{23,26,27}$. Lower rates were reported in Greece (6.6%) and India (7.6%)^{28,29}. Our study rate was lower compared to Jeddah (31.6%), Riyadh (27.5%), United Arab Emirates (24%), North Africa (22%), United Kingdom (Oxford) (21.3%), Poland (19.7%), Taiwan (19.58%), Canada (19.5%) and Al-Khobar (18%)^{8,25,30-36}.

GBS neonatal colonization born from GBS colonized mothers in our study was in 7 out of 316 (2.2%). Our rate is lower than that reported in Al-Khobar $(5.7\%)^{36}$. A study found that 6% of GBS carriers were not detected during pregnancy if screening took place before 35 weeks³⁷.

In our study, 6.2% of non-screened mothers showed positive GBS with HVS screening during labor. However, those screened positive patients during labor did not receive intrapartum antibiotics prophylaxis due to our culture method which takes at least 48 hours for results to be available. Wollheim et al used polymerase chain reaction (PCR) assay to detect GBS colonization in labor, which takes approximately 3 hours^{38,39}. Similar studies highlighted the same outcome regarding the efficiency of the PCR in detecting GBS^{40,41}.

The presence of GBS infection in the urine specimen indicates heavy maternal colonization and a high risk of early-onset GBS infection⁴². Urine GBS infection bacteriuria rate in our study was 0.6% (n=13) from both screened and non-screened groups. GBS infection is a risk factor for preterm delivery⁴³. Oddie et al found that GBS is recognized at a higher rate in the premature babies than controls⁴³.

One limitation to our study was that our data were obtained retrospectively, which means some cases had to be excluded due to incomplete records. The other limitation was the selective screening at different gestational ages. Most studies focus on pre-delivery screening between 35 to 37 weeks. Our data contained patients who were screened before 35 weeks.

CONCLUSION

Patients who had selective screening for GBS during pregnancy had no reduced incidence of neonatal sepsis and early neonatal admission, however, they had less admission to NICU and more late neonatal admission.

Author Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 27 August 2019.

Ethical Approval: Approved by the Ethical Committee and Research Center, Bahrain Defence Force Hospital, Bahrain.

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