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Correlation between Preterm Birth and Group B Streptococcal Colonization in Pregnant Women in Egypt

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ABSTRACT

Background: Preterm birth (PTB) is a prevalent reason for fetal and neonatal mortality and morbidity, characterized by all births that occur prior to thirty-seven weeks of gestation.

Aim: This study aimed to examine the association between PTB and early-stage vaginal colonization with GBS, a significant reason for disease throughout pregnancy.

Patients and methods: This was retrospective cohort research that included 100 electronic health records from March 2022 to March 2023 retrieved from Damanhur Medical National Institute and used in a single center. Regardless of their symptoms, all pregnant females underwent vaginal sampling for culture and Gram staining during the initial stages of pregnancy

Results: The examination did not reveal any statistically significant correlation between Gestational age (GA) and GBS during the initial stages of pregnancy, overweight, maternal age, diabetes mellitus, thyroid disease, GDM, preterm PROM, term PROM, GA at delivery, birth weight, sex, Apgar score after 1 minute, Apgar score after five minutes, NICU admission and neonatal Group B Streptococcus (GBS) disease, while there has been a statistically significant correlation between nullipara and GBS during the initial stages of pregnancy (PTB below 34 weeks and PTB below 37 weeks, $p<0.05$).

Conclusion: This investigation demonstrated the association among PTB and group B streptococcal colonization in pregnant females and found that there was a significant correlation between PTB and GBS-positive during the initial stages of pregnancy, both PTB at less than thirty-four and at less than thirty-seven weeks of gestation. Also, there was a significant association between PTB and diabetes mellitus at less than thirty-seven weeks.

Keyword: PTB, Streptococcal colonization, Pregnant women.

INTRODUCTION

PTB is a prevalent reason for neonatal and fetal mortality and morbidity, defined as all births happening prior to thirty-seven weeks of gestation. Approximately fifteen million preterm deliveries occur globally per year, according to our estimates [1].

The most frequent reason for preterm delivery is infection. The transplacental route, ascending cervical route, and descending peritoneal tubal route are the routes through which viral and bacterial infections travel. The upper vagina or cervical canal are the most common entry routes for microorganisms, representing the ascending route of infection [2].

GBS and other Gram-positive bacteria have been related to numerous complications during pregnancy and potentially fatal infections in newborns. From fifteen percent to sixty percent, the rate of GBS colonization throughout pregnancy in the United States differs based on the research population [3].

GBS is linked to infections such as cystitis, endometritis, and pyelonephritis in pregnant females. Furthermore, it may be associated with the impairment of pregnancy's evolution, which may result in premature delivery, intrauterine fetal death, chorioamnionitis, early membrane rupture, and abortion [4].

The correlation among maternal GBS genital colonization and PTB remains ambiguous; however, preterm delivery is recognized as a risk factor for the early occurrence of newborn Group B Streptococcus illness (GBS-EOD) in women colonized by GBS [5].

Our goal was to examine the association among PTB and early-stage vaginal colonization with GBS, a significant reason for disease throughout pregnancy.

PATIENTS AND METHODS

This retrospective cohort research involved one hundred electronic health records from March 2022 to March 2023 that have been received from Damanhur Medical National Institute and utilized in a single center.

Inclusion criteria: Females that received vaginal cultures throughout their routine prenatal checkup at our hospital as quickly as possible throughout fourteen weeks of gestation.

Exclusion criteria: females with a history of spontaneous PTB (multiple pregnancies), uterine malformation, myoma uteri, or previous PTB or who may need PTB because of a medical indication (intrauterine fetal death, fetal malformation, fetal growth restriction, or preeclampsia).

METHODS

All cases were subjected to the following:

Sample collection

Regardless of their symptoms, all pregnant females underwent vaginal sampling for culture and Gram staining during the initial stages of pregnancy.

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A sterile cotton swab has been utilized to obtain a smear from the vagina following the sterile speculum insertion with water-based lubrication. After calculating the Gram stain-based Nugent score, the complete specimen has been incubated on Separated Sheep Blood Agar/Chocolate for twenty-four hours at a temperature of 35 degrees Celsius in five percent carbon dioxide. This was done in order to determine the Gram stain-based Nugent score.

This was done in line with the instructions provided by the manufacturer. An extra twenty-four hours were spent incubating the negative plates before they were subjected to a second round of inspection. The positive plates were put through a test utilizing the Street LA® GBS latex agglutination assay.

Procedure

A vaginal Group B Streptococcus identification in the early stages of PTB and pregnancy was the focus of the project, which attempted to investigate the relationship among both of them. According to the results of the vaginal culture, the cases were classified as either having a positive or negative GBS (Group B Streptococcus) result. Comorbidities and maternal age, including thyroid disorders, diabetes mellitus, and chronic hypertension, comprised the baseline maternal variables.

The term "nullipara" denotes a pregnancy that has never been delivered after twenty weeks of gestation. Overweight is determined as a BMI of twenty-five or greater, and thyroid diseases encompass both hypothyroidism and hyperthyroidism.

In accordance with the global consensus criteria established by the OGTT, the diagnosis of GDM is made when the fasting plasma glucose level is over ninety-two milligrams per deciliter, the level is over 180 mg/dL after an hour, or the level is above 153 milligrams per deciliter following two hours following 75 g of glucose loading. The delivery results have been defined as the gestational age (GA) at delivery, premature rupture of membranes, and birth weight, which are diagnosed through a case's physical examination and medical history. This procedure involves the detection of amniotic fluid pooling in the vaginal fornix or the use of the check PROM® to assess insulin growth factor binding protein-1 (IGFBP-1).

Ethical consideration

The GOTHI Research Centre approved the research protocol. According to the Caset’s condition, Prior to enrollment, written informed consent was gathered from individuals or their legal representatives in accordance with the individual's condition. The purpose of this study was to perform research on humans in compliance with the Declaration of Helsinki, the code of ethics of the World Medical Association.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using , mean, standard deviation, median and range (minimum and maximum). Significance of the obtained results was judged at the 5% level.The used tests were:- Chi-square test for categorical variables, to compare between different groups, Student t-test for normally distributed quantitative variables, to compare between two studied groups, Mann Whitney test for abnormally distributed quantitative variables, to compare between two studied groups and multivariable logistic regression analysis of the factors that are correlated with PTB.. P- value: level of significance, P>0.05: Non-significant (NS), P< 0.05: Significant (S) and P<0.01: Highly significant (HS).

RESULTS

This table demonstrates that there was insignificant distinction between the initial stages of pregnancy and the 3rd trimester in terms of Nugent score and abnormal bacterial colonization ($p > 0.05$), whereas there was statistically significant distinction regarding GA (Table 1).

Table 1: The occurrence of vaginal microorganisms in the initial stages of pregnancy compared to the third trimester.

	The initial stage of pregnancy	Third trimester	p-value
	Vagina n = 50	Rectum and vagina n = 50	
GA at the examination, week, median [range]	13.6 [10.9–18.1]	35 [33.0–37.0]	<0.001*
Nugent score			
0–3	43 (86)	44 (88)	0.94
4–6	5 (10)	4 (8)	
7–10 (Bacterial vaginosis)	2 (4)	2 (4)	
Abnormal bacterial colonization			
GBS			
Positive	4 (8)	6 (12)	0.51
Negative	46 (92)	44 (88)	
Candida albicans			
Positive	3 (6)	4 (8)	0.70
Negative	47 (94)	46 (92)	
Candida glabrata			
Positive	2 (4)	3 (6)	0.66
Negative	48 (96)	47 (94)	
Candida krusei			
Positive	1 (2)	2 (4)	0.56
Negative	49 (98)	48 (96)	
CNS			
Positive	1 (2)	4 (8)	0.17
Negative	49 (98)	46 (92)	
Staphylococcus aureus			
Positive	1 (2)	2 (4)	0.56
Negative	49 (98)	48 (96)	
Enterococcus species			
Positive	1 (2)	1 (2)	1
Negative	49 (98)	49 (98)	
Escherichia coli			
Positive	1 (2)	2 (4)	0.56
Negative	49 (98)	48 (96)	
MRSA			
Positive	0 (0.0)	1 (2)	0.31
Negative	50 (100)	49 (98)	
Others			
Positive	2 (4)	1 (2)	0.56
Negative	48 (96)	49 (98)	

Continuous variables are represented as median [range], while categorical variables are represented as n (%). GA: gestational age. GBD: Global Burden of Disease *: Significant. CNS: Coagulase-negative staphylococci, MRSA: Methicillin-resistant Staphylococcus aureus.

This table indicates that there was a statistically insignificant link among Group B Streptococcus in the first stage of pregnancy and the following variables: GA at the examination, weeks, Maternal age, Nullipara, Overweight (BMI ≥ 25), Diabetes mellitus, Thyroid disease, GDM, Preterm PROM, Term PROM, GA at delivery, weeks, PTB less than thirty-seven weeks, Sex, Birth weight, Apgar score after1 minute, Apgar score after 5 minutes, NICU admission and Neonatal GBS diseaseHowever, there was a statistically significant link among GBS in the nullipara and beginning stage of pregnancy, preterm delivery less than thirty-four weeks, and (Table 2).

Table 2: A baseline comparison of the characteristics of females in the early stages of pregnancy, categorized by vaginal flora

	Group B Streptococcus in the early stage of pregnancy		
	Positive (n = 6)	**Negative (n = 94)**	**p-value**
GA at the examination, weeks, median [range]	13.7 [13.6–16.4]	13.9 [11.3–17.9]	0.91
Maternal age, years, mean ± standard deviation	33.9 ± 4.1	33.1± 4.7	0.32
Nullipara			
Yes	4 (66.7)	53 (56.4)	0.64
No	2 (33.3)	41 (43.6)	
Overweight (BMI ≥ 25)			
Yes	1 (16.7)	11 (11.6)	0.72
No	5 (83.3)	83 (88.4)	
Diabetes mellitus			
Yes	1 (16.7)	8 (12.5)	0.50
No	5 (83.3)	86 (87.5)	
Thyroid disease			
Yes	1 (16.7)	9 (9.6)	0.57
No	5 (83.3)	85 (90.4)	
GDM			
Yes	1 (16.7)	13 (13.8)	0.85
No	5 (83.3)	81 (86.2)	
Preterm PROM			
Yes	1 (16.7)	9 (9.6)	0.57
No	5 (83.3)	85 (90.4)	
Term PROM			
Yes	2 (33.3)	15 (15.9)	0.27
No	4 (66.7)	79 (84.1)	
GA at delivery, weeks, median [range]	39.4 [29.7–41.9]	39.6 [32.1–42.6]	0.92
PTB < 34 weeks			
Yes	1 (16.7)	1 (1.1)	0.008*
No	5 (83.3)	93 (98.8)	
PTB less than thirty-seven weeks			
Yes	1 (16.7)	4 (4.3)	0.18
No	5 (83.3)	90 (95.7)	
Sex			
Male	3 (50)	52 (55.3)	0.80
Female	3 (50)	42 (44.7)	
Birth weight, kg, median [range]	2.7 [1.1–4.2]	3.1 [1.46–4.31]	0.47
Apgar score after1 minute			
Low Apgar score (< 7 points)	1 (16.7)	14 (14.8)	0.91
≥ 7 points	5 (83.3)	80 (85.2)	
Apgar score after 5 minutes			
Low Apgar score (< 7 points)	1 (16.7)	10 (10.6)	0.65
≥ 7 points	5 (83.3)	84 (80.4)	
NICU admission			
Yes	1 (16.7)	11 (11.6)	0.72
No	5 (83.3)	83 (88.4)	
Neonatal GBS disease			
Yes	0 (0.0)	0 (0.0)	1
No	6 (100)	94 (100)	

GA: gestational age GDM: Gestational diabetes mellitus PROM; Premature rupture of membranes PTB; Pulmonary Tuberculosis. GBS; Guillain-Barré syndrome.

This table demonstrates a significant association between PTB less than thirty-four weeks of gestation and each of diabetes mellitus, and GBS-positive in the initial stages of pregnancy. There was a significant association between PTB less than thirty-seven weeks of gestation and Group B Streptococcus-positive in the initial stages of pregnancy (Table 3).

Table 3: Comparison of case characteristics categorized by PTB

Variable	PTB < thirty-four weeks of gestation					PTB < thirty-seven weeks of gestation				
	Yes n (%)	No n (%)	OR	95%CI	p-value	Yes n (%)	No n (%)	OR	95%CI	p-value
Maternal age, years	33.3 ± 4.2	33.1± 3.9	0.95	(0.85–1.1)	0.75	33.8 ± 4.3	33.4± 4.5	0.95	(0.9–1.01)	0.22
Nullipara										
Yes	1(1)	49(99)	0.32	(0.08-1.36)	0.129	2(4)	48(96)	0.67	(0.38–1.19)	0.169
No	1 (1)	49(99)	Ref	Ref		3(6)	47(94)	Ref	Ref	
Overweight (BMI ≥ 25)										
Yes	0 (0.0)	50 (100)	–	–	–	2 (1.9)	103 (98.1)	0.374	(0.09–1.57)	0.177
No	5(10)	45 (90)				3(4.9)	47(95)	Ref	Ref	
Diabetes mellitus										
Yes	3 (6)	47 (93)	10.5	(2.1–52.5)	0.005*	5 (10)	2 (4)	2.36	(0.65–8.1)	0.17
No	3 (6)	49 (99)	Ref	Ref		2 (4)	47 (95)	Ref	Ref	
Thyroid disease										
Yes	0 (0.0)	50 (100)	–	–	–	2 (4)	47 (95)	0.8	(0.26–2.82)	0.81
No	1 (1)	45 (90)				47 (4.7)	959 (95.3)	Ref	Ref	
GDM										
Yes	0 (0.0)	50 (100)	–	–	–	2 (1.6)	126 (98.4)	0.30	(0.07–1.24)	0.094
No	1 (1)	45 (90)				5 (5.0)	45 (95)	Ref	Ref	
BV in the initial stage of pregnancy										
Yes	0 (0.0)	50 (100)	–	–	–	2 (4)	46 (95.9)	0.84	(0.25–2.83)	0.72
No	1 (0.9)	45 (90)				5(4)	47 (95)	Ref	Ref	
GBS-positive in the initial stage of pregnancy										
Yes	2(6)	43 (93)	14.1	(3.71–54.4)	< 0.001*	5 (10)	45 (90)	2.43	(1.01–5.92)	0.042*
No	1 (2)	49 (99)	Ref	Ref		4(4)	44 (94)	Ref	Ref	
BV during the third trimester										
Yes		–	–	–		2 (2)	46 (96)	1.23	(0.28–5.3)	0.7
No	–				–	3 (3)	47(97)	Ref	Ref	
GBS-positive during the third trimester										
Yes	–	–	–	–	–	5 (5)	44 (94.9)	1.87	(0.7–5)	0.2
No						25(2.9)	47(97)	Ref	Ref	

According to multivariate analysis, this table demonstrates a significant association between PTB less than thirty-four weeks of gestation, diabetes mellitus, and GBS-positive in the initial stages of pregnancy. There was a significant association between PTB below thirty-seven weeks of gestation and Group B Streptococcus-positive in the initial stages of pregnancy (Table 4).

Table 4: Outcomes from a multivariable logistic regression analysis of the factors that are correlated with PTB.

	PTB less than thirty-four weeks			PTB less than thirty-seven weeks		
	Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Nullipara	0.32	(0.07–1.31)	0.4	–	–	–
Diabetes mellitus	8.3	(1.4–47.6)	0.017*	–	–	–
Group B Streptococcus -positive in the initial stage of pregnancy	15.2	(3.71–61.74)	< 0.001*	2.43	(1–6.1)	0.052*

DISCUSSION

Regarding prevalence of vaginal microorganisms, there was statistically insignificant distinction between the initial stage of pregnancy and throughout the third trimester as regard Nugent score and abnormal bacterial colonization, whereas there was statistically significant distinction between the 3rd trimester and during the early stage of pregnancy as regard GA at the examination.

The results match with the findings of **Son *et al.*** [6], who conducted an investigation involving 593 females to evaluate the presence of abnormal vaginal microorganisms in pregnant individuals across different trimesters ($p<0.001$). The research aimed to determine whether abnormal vaginal colonization is linked to a higher likelihood of miscarriage or preterm delivery. The research reported that there has been a significant distinction among the 1st, 2nd, and 3rd trimesters with regard to GA at examination ($p<0.001$). Nevertheless, the investigation also demonstrated that there has been a statistically significant distinction between the examined groups according to abnormal vaginal colonization. As well with **Donders *et al.*** [7] who aimed that the research demonstrated that there has been an insignificant distinction between the examined groups according to full bacterial vaginosis, whereas there has been a significant distinction between the examined groups according to abnormal vaginal flora. This has been carried out to assess the variance effects of AVF, partial and full bacterial vaginosis, and aerobic vaginitis on the rate of PTB in the 1st trimester. In contrast, **Severgnini *et al.*** [8] who aimed to investigate the characteristics of the vaginal environment belonging to a cohort of Caucasian females by a normal pregnancy at various GA, the research that has been conducted on sixty-three females established a significant distinction in Nugent score between the 1st, 2nd, and 3rd trimesters.

In the early stage of pregnancy, our findings indicated that there has been statistically insignificant distinction between positive and negative GBS in the following areas: GA at the examination, maternal age, overweight, diabetes mellitus, GDM, thyroid disease, preterm term premature rupture of membranes, premature rupture of membranes, GA at delivery, sex, birth weight, Apgar score after one minute, and after 5 minutes, NICU admission, and neonatal GBS disease. However, there has been a statistically significant distinction between positive and negative GBS in the initial stage of pregnancy in the following areas: nullipara, PTB fewer than thirty-four weeks, and PTB fewer than thirty-seven weeks. This finding was consistent with previous research.

Our results are supported with **Khalil *et al.*** [9] whose research, which evaluated the correlation between preterm delivery and Group B streptococci in urine culture during pregnancy, included 249 females with Group B streptococci positive and 5,765 females with Group B streptococci negative. The findings indicated that there has been statistically insignificant distinction between the 2 groups in terms of body mass index and age. However, there has been a significant distinction in terms of GDM and diabetes mellitus.

Also, in consistence with **Brigtsen *et al.*** [10] whose research, which was conducted on 1746 females with the objective of determining whether GBS colonization at delivery is correlated with an elevated risk of maternal prepartum infection, demonstrated that there has been insignificant distinction between non-colonized and colonized Group B streptococci females in terms of nulliparity maternal age, BMI, diabetes mellitus, and premature rupture of membranes.

In addition, **Yang and Zhang** [11] who aimed that the research found insignificant variations in premature rupture of membranes gestational weeks or premature delivery when comparing the invasiveness of GBS to various indices of pregnant mothers and newborns.

Furthermore, **Chen *et al.*** [12] found that there was a statistically insignificant distinction among positive and negative GBS in relation to GA, diabetes mellitus, as well as thyroid dysfunction. The objective of the investigation was to ascertain the prevalence of Group B Streptococcus among expectant women in Southern China, to identify the high-risk group of invasive Group B Streptococcus diseases, and to assess the efficacy of IAP therapy in enhancing intervention programs. **McDonald *et al.*** [13] also established that the rate of preterm labor (PTL) (fewer than thirty-seven weeks) was significantly distinct between positive and negative GBS females. Additionally, it has been demonstrated that there has been significant variation between the examined groups according to premature rupture of membranes.

There was a significant correlation between diabetes mellitus and GBS-positive in the early stages of PTB and pregnancy at fewer than thirty-four weeks of gestation in both bivariable regression and multivariable logistic regression analyses. GBS-positive in the initial stages of pregnancy has been significantly correlated with PTB at fewer than thirty-seven weeks gestation.

Our results align with those of **Sibai *et al.*** [14], whose research demonstrated that the control group had much lower rates of spontaneous and determined PTB contrasted with the pre-GDM group, which had significantly higher rates of both conditions. Their research aimed to compare the incidence of spontaneous and advised PTB among women who were healthy and those who had pre-GDM or chronic hypertension.

Similar to **Daskalakis *et al.*** [15]; their investigation was conducted on 1197 females to assess the correlation between preterm delivery and Group B Streptococcus colonization in the second trimester of pregnancy. The research determined that preterm delivery was inversely correlated with GBS colonization ($p = 0.05$). Furthermore, the outcomes of the multiple regression

analysis suggested that an increased GA at delivery was associated with GBS colonization.

Furthermore, **Tano *et al*. [16]** whose investigation involved 1079 pregnant women to examine the link among vaginal GBS colonization, a source of infection throughout pregnancy, and early PTB. An increased risk of PTB before thirty-seven weeks and before thirty-four weeks of gestation was found to be related to the colonization of GBS throughout early pregnancy, in accordance with the findings of the research, which was performed. Diabetes mellitus has been connected to an increased risk of PTB prior to thirty-four weeks of gestation in multivariable logistic regression models. This is in addition to the fact that GBS positivity within the first few weeks of pregnancy has been linked to this risk.

In addition, the current research agreed with **Bianchi-Jassir *et al.* [17]** who aimed to examine the relationship among maternal vaginal colonization by GBS and premature labor, concluding that the risk of preterm labor was approximately related to GBS culture positivity. In contrast **Khalil *et al.* [9]** reported that there was no link among females with positive GBS in urine and those who delivered early term, during 37- and 39-weeks' gestation, and those who delivered at 40 weeks' gestation or later.

CONCLUSION

In this investigation, the correlation between PTB as well as group B streptococcal colonization in pregnant females was evaluated. The findings demonstrated a significant association among GBS -positive and PTB in the early stages of pregnancy, including PTB at below thirty-seven and under thirty-four weeks of gestation. Additionally, diabetes mellitus was significantly correlated with PTB at a GA of less than thirty-four weeks.

DECLARATIONS

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Competing interests: None.

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