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Effect of Group B Streptococcus Infection on Perinatal Morbidity and Mortality

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Abstract: To study effect of Group B Streptococcus (GBS) infection on perinatal morbidity and mortality. The study included 986 pregnant females at 35-37 wks of gestational age attending the antenatal outpatient department at tertiary care hospital in northeastern India. All participants were screened by conventional method of two rectovaginal swabs for GBS colonization in Blood Agar media and secondly with serum for antigen detection by rapid latex test for use in qualitative detection of antigen from GBS by Wellcogen Strep B kit. Data of neonates born to GBS positive mothers were divided into Group A (GBS present) and Group B (GBS absent). Patients of Group A were alternatively divided into control Group (C) and Test Group (T). Only the Test Group [T] were given intrapartum antibiotics [IAP] whenever they went into labor. Antibiotics policy followed was as per CDC guidelines; Inj ampicillin 02gm I.V. *stat* followed by 01gm I.V. *q* 6 hours till delivery of the patient. Records of the clinical rupture of the membranes, its duration and any clinical signs of chorioamnionitis were maintained. Specific clinical signs that indicate high risk for early onset neonatal sepsis (EONS) by GBS such as fever >100.4°F, foul smelling liquor or fetal tachycardia were documented. All the neonates born to GBS positive mother with symptoms of EONS were recorded. A total of 986 antenatal women were screened for GBS carrier state between 35-37 weeks of gestation and were followed till delivery. 162 women tested GBS positive by both methods [16.4%] [Group-A] and 824 tested GBS negative [83.6%] [Group-B]. Two infants out of 81 in control group were colonized by GBS against none in the test group, which was not significant [P >0.05]. There was one case each of EONS of non-GBS origin, both in control group and test group. Only one infant was admitted in neonatal intensive care unit [NICU] which was not statistically significant. There was no neonatal mortality in the study. Screening of high risk women for GBS vaginal colonization early in labor with rectovaginal swab culture and rapid antigen detection tests is equally effective. No recommendation regarding administration of intrapartum antibiotics can be made on the basis of this study. A larger multicentric study needs to be conducted to study the effect of intrapartum antibiotics on GBS colonization among neonates born to GBS positive mothers.
Keywords: Group B streptococcus, EONS.

INTRODUCTION

Group B streptococcal (GBS) disease is the leading cause of early onset neonatal sepsis (EONS) in developed and developing countries [1]. Despite the widespread adoption of preventive strategies in the United States and Australia in recent years [2-4] uncertainty prevails as to whether early onset GBS sepsis is sufficiently common to justify widespread prophylaxis [5]. There are no firm recommendations for using intrapartum antibiotics. More recently the GBS Working Group of the Public Health Laboratory Service, UK issued interim recommendations for prevention of GBS neonatal infection, to be used while further data are collected. Evidence from both the United States and Australia shows that the adoption of prophylactic policies significantly decreases the incidence of neonatal GBS infection [4,6].

Little data is available on the prevalence of early onset GBS sepsis in India, and there are no population-based case-control studies on risk factors for GBS infection. The available data implies a prevalence of 0.5-1.15 cases per 1000 live births [7]. Part of the variation in prevalence probably relates to differing characteristics of populations, although some variation is almost certainly related to case ascertainment and, possibly, differences in case definition [7]. In addition, many neonates may become infected with GBS yet

sample taken from them do not grow bacteria on culture [8]. Interpretation of epidemiological studies may be complicated by the use of intrapartum antibiotic prophylaxis if local practices are not evaluated concurrently. Reports from the developing world infrequently identify the pathogen among newborn with sepsis because in resource limited countries, at times, adequate methods for diagnosis of GBS infection are not used [9].

We used both culture and antigen/antibody detection methods in our study. Universal screening of antenatal patients for GBS colonization and Intrapartum antibiotics prophylaxis [IAP] for patients found positive, is already and established routine practice in most developed countries [10]. At present there is no standard practice as no firm evidence of benefit of intrapartum antibiotics is statistically proven. More studies are required to be undertaken to ascertain GBS as cause of perinatal morbidity and mortality. This study was aimed to find out the effect of GBS infection on perinatal morbidity and mortality.

AIMS

To determine GBS as a cause of perinatal morbidity and mortality

Participants

The study included 986 pregnant females at 35-37 wks of gestational age attending the antenatal outpatient department at tertiary care hospital in northeastern India.

All participants were screened by conventional method of two rectovaginal swabs for GBS colonization in Blood Agar media and secondly with serum for antigen detection by rapid latex test for use in qualitative detection of antigen from group B Streptococci by Wellcogen strep B kit. Patients were followed till delivery. Neonates born to GBS positive mothers with signs of early onset neonatal septicemia (EONS) were screened with nasal swabs for GBS colonization in Blood Agar media and urine for antigen detection by wellcogen strep kit. Details with regard to labor and delivery were recorded in all pt. Data of neonates born to GBS positive mother were recorded.

Study Protocol

After explaining the procedure and aim of work, all participants were screened by conventional method of two rectovaginal swabs for GBS colonization in Blood Agar media and with serum for antigen detection by rapid latex test for use in qualitative detection of antigen. Only those women who tested positive for GBS by both methods (rectovaginal swab culture and antigen detection by Wellcogen strep B antigen detecting kit) were taken as GBS positive. Nasal swabs were collected for detections of GBS according to CDC Recommendation from the nares of neonates born to GBS positive mother. The nasal swabs were immediately plated on nonselective nonspecific Blood agar media. The growth of colonies of GBS was read after 24 h and maximum up to 72 hrs. Simultaneously, urine sample of the neonates collected for further testing of antigen for GBS in the patient by Wellcogen strep B antigen detecting kit. The rapid latex test for detection of antigen from GBS was done using polystyrene latex particles coated with group antibodies. Their latex particles agglutinate in presence of sufficient homologous antigen.

Specimen collection and preparation one ml of urine sample was collected using all standard precautions. The urine sample was heated for five minutes in a boiling water bath and then cooled to room temperature and clarified by centrifugation.

Test Procedure the latex reagents were shaken, for each test sample one drop of test latex was placed in one circle on a reaction card and one drop of control latex into a separate circle. Using a disposable dropper, one drop of test sample was dispensednext to each drop of latex. The contents of each circle were mixed with a mixing stick and spread to cover the complete area of the circle. The card was rocked slowly and observes for agglutination to 3 minutes, holding the card at normal reading distance (25 to 35cm) for the eyes. The used reaction card was discarded for safe disposal.

The sensitivity and specificity of antigen detection test is 82% and 98% as compare to 100% of GBS culture (Table 1)

Table- 1: **Correlation of Gbs Culture and Antigen Detection**

METHOD	SENSITIVITY	SPECIFICITY
GBS CULTURE	100% (162)	100% (162)
ANTIGEN DETECTION	82% (132/162)	98% (158)

INTERPRETATION OF RESULTS

Positive Results

Clear agglutination of the test latex accompanied by a lack of agglutination of the control latex indicated the presence of group B streptococcal antigen in the body fluid supernatant.

Negative Result

Lack of agglutination in both reagents means that no group B streptococcal antigen is detectable in the test fluid. The participants were divided into Group A (GBS present) and Group B (GBS absent). Patient of Group A were alternatively divided into control Group (C) and Test Group (T). As per CDC guidelines, only Test Group (T) were given intrapartum antibiotics

(IAP) when they went into labor. Antibiotics policy followed as per CDC guidelines [11], Inj ampicillin 02gm I.V. stat followed by 01gm I.V. q 6 h till delivery of the patient. Record of the clinical rupture of the membranes, its duration and any clinical signs of chorioamnionitis were kept. Specific clinical signs which are high risk for EONS by GBS such as fever >100.4, foul smelling liquor or fetal tachycardia were recorded. All the newborns to GBS positive mother (Group A) with symptoms of 1. Early onset sepsis (EONS), 2. RDS Respiratory distress syndrome, 3. Maternal fever >100.4°F, 4. Premature Rupture of Membranes (PROM)>18 h and 5. Meningitiswere screened for GBS antigen by collecting urine samples and swabs from both naresof neonates for GBS colonization. Results of neonates with presence of GBS antigen and GBS colonization in both control group and test group were tabulated.

RESULTS

A total of 986 antenatal women were screened for group B streptococcus carriage between 35-37 yrs of gestation and were followed till delivery. 162 cases were found to be GBS positive [16.4%]. Group A having 162 GBS positive cases were further divided into control group (C) and Test group (T) of 81 cases each. One case was lost to follow up in test group. Two cases in control group had PROM> 18 hand one case hadtemperature >100.2°F. Only two cases in test group had PROM(Table 2). Chorioamnionitis was not observed in any woman from either group by clinical criteria.

Table-2: Data of risk factors

RISK FACTOR	CONTROL GROUP[81]	TEST GROUP[80]
PROM > 18H	02	02
T>100.2°F	01	NIL

The neonate delivered to women with PROM > 18 hrs in control group developed EONS of GBS origin but none of the neonates born to the mother with PROM in test group were affected.One of the women in control group developed temperature >100.4°F but the neonatal outcome was normal.

As regards neonatal infection, two infants out of 81 in control group were colonized by GBS against none in test group which was not significant (P >0.05). There was one case each of EONS of non-GBS origin both in control and test group (Table 3). Only one infant was admitted in neonatal intensive care unit (NICU) which was not statistically significant. There was no neonatal mortality in the study.The data in table 3 is inconclusive in judging the role of intrapartum antibiotics in preventing EONS of GBS colonization in neonates born to GBS positive women because of its small sample size. The prevalence rate of EONS by GBS all around the world is 0.17- 1.0 per 1000 live births [9 ,12]. However, the role of intrapartum antibiotics in GBS positive cases is well established [12] as per CDC guidelines.

Table-3: Early onset neonatal sepsis (eons) in gbs positive

GBS Colonization	EONS inControl Group (81)	EONS in Test Group (80)
GBS Colonized	02	00
GBS Not Colonized	01	01

DISCUSSION

During the past two decades, GBS has emerged as an important cause of perinatal morbidity and mortality. It has been shown that early onset GBS septicemia is prevented by administering Inj ampicillin to women colonized by GBS during labor and delivery [12,13]. The sample size in this study was small with only 162 GBS positive cases. The observation of the results shows no cases of neonatal septicemia with GBS colonization in test group and only one case of EONS in which causative organism was other than GBS in test group (out of 80). There were three cases of EONS in control group (out of 81) which were not given IAP; out of these only two cases were of GBS origin and the third case was of non-GBS colonization. One out of two cases of EONS by GBS infection was among the woman of PROM >18 h (high risk) The results show P value > 0.16 which is not significant. Despite significant GBS colonization rates, reports of invasive neonatal GBS disease in India are infrequent and only about two per cent of colonized neonates develop true infection. During a ten-year study, the incidence of GBS infection in neonates was found to be 0.17% [9, 12]. The study because of small sample size is inconclusive regarding the effect of intrapartum antibiotics prophylaxis on perinatal morbidity and mortality in GBS positive women.

The study on EONS due to GBS in GBS positive women with or without intrapartum antibiotics is not significant [P >0.05] and inconclusive [02 cases of EONS out of 81]. Screening of high risk women for GBS colonization early in labor and subsequent selective administration of antibiotics to mother would be more cost effective in bringing down the incidence of GBS infection in the neonate rather than a routine antenatal screening program. The Royal College of Obstetricians and Gynecologists also recommends IAP

to GBS positive mothers [14]. There are rapid test kits available commercially which give reliable results in the presence of heavy colonization with GBS. The sensitivity of the tests depends on whether to identify all colonized patients or those with heavy colonization. Sensitivity of various test used varies from 40% to 97.7%. More importantly, the negative predictive value in most tests is reported to be above 95%. Such test can be used for detection of GBS antigen in women with high risk and thus help in identifying thepregnant women and neonates at risk and help in early administration of definitive treatment. It will also prevent unnecessary intrapartum antibiotics to all and ensure administration of necessary antibiotics to all GBS positive women and neonates and thus preventing the increase of resistant organisms in the neonates.

Prevention is of paramount importance in areas of high incidence of invasive GBS disease. It is impractical to administer antibiotic prophylaxis to all parturient mothers and neonates. The challenge therefore is to identify correctly the high-risk infants before they are born. The most effective way to prevent neonatal early-onset infection is maternal antibiotic administration during labor. The risk-based approach involves administration of antibiotics based solely on the presence of antenatal or intrapartum risk factors. Maternal risk factors for GBS neonatal sepsis are as follows: preterm labor or premature rupture of membranes (< 37 weeks' gestation); premature rupture of membranes (>18h); intrapartum fever >100.4°F (>38.0° C); history of a previous newborn with GBS disease; and GBS bacteriuria during pregnancy. In India, vaginal swab culture screening of all parturient women for GBS may be difficult to implement from a logistic as well as cost-effectiveness point of view. However, a strategy based on identifying maternal risk factors could potentially be used, which, according to one source, would require intrapartum antimicrobial prophylaxis in 18% of deliveries and would hypothetically prevent 70% of the cases of early-onset GBS disease [15]. There is a requirement of large population based multicentric study to clearly establish the role of intrapartum prophylaxis during labor in GBS positive women on perinatal morbidity and mortality in Indian population

CONCLUSION

The study on perinatal morbidity and mortality by GBS infection with and without intrapartum antibiotics prophylaxis is inconclusive because it is limited by the small sample size. Large population based multicentric studies are required to accurately evaluate

- The true incidence of GBS carriage in pregnant women
- Determine the neonatal morbidity and mortality and
- Whether the GBS screening by culture and rapid antigen tests are cost effective.

It is recommended that only high risk antenatal cases should be screened with rapid detection test kits for GBS antigen and GBS culture. The confirmed cases of GBS colonization should be treated with intrapartum antibiotics at the time of labor and delivery as recommended by CDC. Further guidelines are required to allow for patients' involvement in making decisions based on possible benefits and harm of universal antibiotic therapy for GBS carriers.

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