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GENITAL TRACT COLONISATION PRIOR TO INDUCTION OF LABOUR: MATERNAL AND NEONATAL SEPSIS

Gynaecology

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ABSTRACT

During Pregnancy genital tract colonisation is common. Those harbouring pathogenic organisms are asymptomatic prior to labour and may develop infection or sepsis during Intrapartum and postpartum. Neonatal sepsis is also acquired during the process of labour and delivery. To investigate this 2 groups of women (85 in each group) were screened for genital tract colonisation prior to induction of labour. Group1 consisted of women with risk factors for infection like diabetes and group 2 without risk factors for infection. Cervical, Vaginal, Rectal swabs were taken prior to induction of labour and subjected to bacterial culture on blood agar and selective media for Group B Streptococci. Cervical and Vaginal cultures were repeated during labour and immediate puerperal period. Puerperal and Neonatal sepsis were diagnosed as per clinical criteria. Infection was diagnosed on positive culture reports. Both the groups were compared for incidence of bacterial infection, bacterial profile and Maternal and Neonatal infection and Sepsis. Chi square test was done to compare proportions. The correlation between continuous variables was done using Pearson's correlation coefficient. All analyses were done using 2 tailed hypotheses and $p<0.05$ was considered significant. Bacterial genital tract colonisation was present in 40.5% and it was not different in women with risk factors and without risk factors. But significantly more number of colonised women with risk factors developed infection during Intrapartum and postpartum period. Non- colonised women also developed infection but this was not significant when compared to Colonised women. The most common organism was Escherichia Coli and Polymicrobial. Puerperal sepsis and Neonatal sepsis occurred in 15% and 8% respectively. It is desirable to screen pregnant women *with risk factors for infection* during Intrapartum or postpartum period and or adopt prophylactic antibiotic therapy to prevent sepsis. *Group B Streptococcus (GBS) colonisation or sepsis is very rare* in this cohort of South Indian Pregnant women.

KEYWORDS

Bacterial, Genital tract, Colonisation, Induction of Labour, Group B Streptococcus, Puerperal sepsis, Neonatal sepsis

INTRODUCTION

Genital tract sepsis is one of the causes of maternal as well as fetal morbidity and mortality in developing and developed countries. Pregnant women with genital tract infection (GTI) are often asymptomatic. Approximately 10 to 30 % of pregnant women are reported to be colonized with GBS in the vagina and rectum[1]. Maternal genital tract colonization present at the time of labor is the primary risk factor for early onset invasive neonatal GBS. *Group B streptococcal infection* (GBS) is the leading cause of neonatal morbidity and mortality due to early onset neonatal invasive GBS[2]. Non GBS pathogens like *Escherichia coli* are also responsible for perinatal sepsis. In the early neonatal period, the most common organisms causing septicemia are *E.coli* and GBS[3]. *Group A Streptococcus* (GAS) is the most common organism responsible for maternal sepsis that caused maternal deaths in UK[4]. Ascending infection is the most common cause for chorioamnionitis and fetal infection. Screening prior to induction of labor gives us an opportunity to diagnose genital tract infection thus preventing Intrapartum and postpartum sepsis as well as neonatal sepsis to certain extent.

Hence this study aimed to screen pregnant women undergoing induction of labor for genital tract infection (GBS & non GBS pathogens) at or beyond term with the following Objectives. 1. To determine the prevalence of genital tract colonisation and bacterial profile prior to cervical ripening in women undergoing induction of labour. 2. To determine if the GTI is more common in women with risk factors.3. To determine the incidence of maternal and neonatal sepsis among women undergoing induction of labour with asymptomatic genital tract infection.

MATERIALAND METHODS:

The study was undertaken in the department Obstetrics and Gynaecology, JIPMER, Puducherry, India. The primary variable for assessing outcome was prevalence of GTI. Assuming percent of exposure (GTI) among normal women to be 23% and risk of GTI among high risk group to be 2.6, 85 patients in each group would be required. Calculations were done based on 80% power, 2 sided 95% CI and ratio of exposed to unexposed to be 1. The total sample size was 170.

The Inclusion criteria were pregnant women more than 18 years of age undergoing induction of labour. Pregnant women with prior diagnosis of cervico -vaginal infections and premature rupture of membranes were excluded. The primary outcome measures were incidence of bacterial colonization and bacterial profile. The secondary outcome measures were early onset neonatal sepsis and puerperal sepsis.

After informed consent and noting the details of history and examination, prior to cervical ripening, cervical swab was collected and subjected to culture for aerobic bacteria. At the same time vaginal and rectal swabs were collected as per CDC guidelines[2]. The above cultures were repeated when the patient was in active stage of first stage of labour. After delivery, cervical swab was taken within the first 24 hours. All the specimens (Cervical swab, vaginal swab and rectal swabs- pre induction, during labor and post induction) were subjected for bacteriological cultures. They were processed as per standard bacteriological procedures. All specimens were inoculated on 5% sheep blood agar, MacConkey agar and Group B streptococcus selective agar (Himedia). Vaginal swabs and rectal swabs were inoculated on Blood agar and Group B streptococcus selective agar (Himedia) and were incubated at 37^0C for 24- 48 hours.

The isolates of Group B Streptococcus (GBS) were identified by Gram stain, colony morphology, CAMP test and confirmed by Lancefield grouping (Latex agglutination assay – Plasmatec, UK). Non-GBS pathogens were identified by Gram stain, colony morphology and biochemical reactions. Antibiotic susceptibility testing was done for all isolates by disc diffusion method following the guidelines by the Clinical and Laboratory Standards Institute..

Maternal sepsis during pregnancy and labour was diagnosed [5] if any two of the clinical criteria are satisfied for clinical chorioamnionitis viz; 1. Fever>101 ^{0}F 2. Unexplained tachycardia>100/min 3. Uterine tenderness 4. Foul smelling amniotic fluid/ vaginal discharge. 5. fetal tachycardia>160/min. Sepsis in the postnatal period was diagnosed if there was fever of more than 38^{0C} after 24 hours of delivery without any other causes. Subclinical chorioamnionitis was diagnosed by the positive culture reports only.

Neonatal sepsis was diagnosed based on the following clinical indicators of possible-early-onset neonatal infection[3]._**Red flags:** Respiratory distress starting more than 4 hours after birth, seizures, the need for mechanical ventilation in a term baby, signs of shock. Investigations for a suspected case of neonatal sepsis were done as per the Neonatology department protocol.

Statistical Analysis:
Data was presented as proportions and mean, SD. Chi square test was done to compare proportions. The correlation between continuous variables was done using Pearson's correlation coefficient. All analyses were done using 2 tailed hypotheses and $p<0.05$ was considered significant. SPSS version 20 was used for statistical analysis.

RESULTS:
The clinical profile of women at recruitment is shown in Table1. Women with risk factors were mostly GDM, Type DM and anemia with Pregnancy. Majority of women were between 39 to 40 weeks of gestation.

Table - 1 Clinical Profile Of Women Screened For GTI At Recruitment

Characteristics	Group 1 (risk factors) N=85(%)	Group 2 (No risk factors) N=85 (%)	Total N=170 (%)
Mean age(yrs) + SD	26.6± 2.8	25.0± 3.1	-
Gravidity Prim gravidae Multi gravidae	 43(50.5%) 42(49.41%)	 56(65.8%) 29(34.1%)	 99 (58.2%) 71(41.8%)
Gestational age (in weeks) 39-40 40+1-41 >41	 68(80%) 11(12.9%) 6(7.05%)	 43(50.5%) 33(38.8%) 9(10.5%)	 111 (68.2%) 44 (25.9%) 15 (8.8%)
Risk factors a. GDM b. Type II DM c. Anaemia	 68(80%) 5(5.8%) 12(14.1%)	 ----	 68 (40%) 5 (2.9%) 12 (7%)

The incidence of GTI and Bacterial Profile is shown in Table 2A. On the whole 40.5% were colonized with bacteria. Of the colonised the most common organism was Escherichia Coli (26%) followed by Klebsiella pneumonia (13%). More than 22% grew multiple organisms.

Table - 2a Genital Tract Colonisation Prior To Induction Of Labour

S. No	Genital tract Colonisation	Number (Percentage) N=170
A	**Culture Positive prior to induction**	**69 (40.5%)**
B	**Bacterial Profile**	
1	*Escherichia Coli*	**18 (26%)**
2	*Klebsiella pneumoniae,*	**9 (13%)**
3	*Coagulase negative streptococci*	**5**
4	*Group B streptococci*	**1**
5	*Enterobacter* species	**5**
6	*Staphylococcus aureus*	**7**
7	*Streptococcus* species	**10 (14.5%)**
8	*Multiple organisms*	**15 (21.7%)**

Table - 2B Incidence Of GTI In Women With Risk Factors

S. No	Parameter	GTI in women with Risk Factors N= 85	GTI in women without Risk Factors N=85	P Value
A	Incidence of GTI	36(42.3%)	33(38.8%)	0.622
B	Bacterial Profile	N=36 (100%)	N=33 (100%)	
1	E. coli	10 (27.8%)	8 (24.2%)	1
2	Klebsiella Pneumoniae	5 (13.9%)	4 (12.1%)	1
3	Coagulase negative Streptococci	2 (5.6%)	3 3.5%)	0.67
4	Group B Streptococcus	1 (2.8%)	0	-
5	Enterobacter Sps	2 (5.6%)	3 (9.1%)	0.67
6	Staphylococus aureus	3 (8.3%)	4(12.1%)	0.70
7	Streptococus	5 (13.9%)	5 (15.1%)	1
8	Multiple Organisms	8 (22.2%)	7 (21.2%)	0.70

Whether colonization is significantly more in women with risk factors was checked and this is shown in Table 2B. There was no significant difference in the incidence of colonization in women with risk factors and without risk factors (42.3 % Vs 38.8%) Mode of Delivery is shown in Table 3. More than 70 % delivered vaginally and only 12% underwent emergency caesarean section and there is no difference in rate of Caesarean section in women with or without risk factors. NICU admissions were high in women without risk factors but it is not statistically significant.

Table 3 Mode Of Delivery And Neonatal Outcome In Induced Labour

Outcome measure	Total	Group 1 Risk Factors	Group 2 No Risk Factors	P value
Mode of Delivery				
SVD	122 (71.7%)	59 (69.4%)	63 (74.1%)	0.495
Instrumental Delivery	28 (16.4%)	16 (18.8%)	12 (14.1%)	0.374
Caesarean section	20 (11.7%)	10 (11.7%)	10 (11.7%)	0.807
Neonatal Outcome				
APGAR Score <6 at 1 min	9 (5.2%)	3 (3.5%)	6 (7%)	0.304
NICU Admission	32 (18.8%)	13 (15.2%)	19 (22.3%)	0.239
Birth weight				
AGA	151 (88.8%)	75 (88.2%)	76 (89.4%)	0.807
LGA	2 (1.1%)	1(1.1%)	1 (1.1%)	-
SGA	17 (10%)	9 (10.5%)	8 (9.4%)	0.798

The incidence of intrapartum infection and postnatal infection in colonized women is shown Table 4. Intrapartum infection and postpartum infection was evident in women colonized with bacteria prior to labour as more than 60% yielded positive cultures. Significantly more number of women with risk factors showed postpartum infection. In non-colonized women though there were Intrapartum and postpartum culture positive women it was not statistically significant. This is represented in table 5. Table 6 shows the comparison between colononised and non-colonised women. Among colonised women 62.3% had intrapartum infection when compared 28.7% among non-colonised women. This is statistically significant (p=0.001). Similarly 59.4% colonised women prior to induction developed postnatal infection as against 44.5% non-colonised women prior to induction (p=0.056).

Table - 4 Intrapartum Infection And Postnatal Infection In Women With *Genital Tract Colonisation (colonised Women)*

CULTURES	Total N=69	Group 1 (Risk factors) N=36	Group 2 (No risk factors) N=33	P value
Intrapartum cultures positive	43 (62.3%)	23 (63.8%)	20 (60.6%)	0.764
Post natal cultures positive	42 (60.9%)	26 (72.2%)	16 (48.4%)	0.042

Table - 5 Intrapartum Cultures And Postnatal Cultures In Women With Negative Pre Induction Cultures *(non-colonised Women)*

CULTURES	Group 1 (Risk factors) N=49	Group 2 (No Risk factors) N=52	Total N=101	P value
Intrapartum cultures positive	15 (30.6%)	14 (26.9%)	29 (28.7%)	0.662
Post natal cultures positive	23 (46.9%)	22 (42.3%)	45 (44.5%)	0.639
Total Culture positive	38 (77.5%)	36 (69.2%)	74 (73.2%)	0.345

Maternal sepsis developed in 16% of colonised women when compared to 15% of non- colonised women (p=0.846) and there is no statistical significant difference. In colonised women though 11.5% of neonates developed sepsis when compared to 5.9% neonates of non-colonised women this was not statistically significant (p=0.187) . This is represented in Table 6.

Table - 6 Comparison Of Maternal And Neonatal Infection And Sepsis In Colonised And Non- Colonised Women

Outcome	Total N=170	Colonised Women N=69	Non-colonised women N=101	P value
Maternal Infection Intrapartum	72 (42.3%)	43 (62.3%)	29 (28.7%)	0.001
Postpartum	86 (50.6%)	41 (59.4%)	45 (44.5%)	0.056
Maternal sepsis (Puerperal Sepsis)	26 (15.3%)	11 (15.9%)	15 (14.8%)	0.846
Neonatal sepsis	14 (8.2%)	8 (11.5%)	6 (5.9%)	0.187

DISCUSSION:

Vaginal flora is in women of reproductive age dominated by species of anaerobic Lactobacillus species which included L.crispatus, L. gasseri, L. jensenii, and L. iners. It is the primary colonising bacteria of vagina in a healthy individual[6]. In some apparently healthy women, vaginal flora dominated by other bacterial species and it is not considered as abnormal or a sign of disease.

The other anaerobic species that are frequently found in vagina are gram positive cocci: Atopobiumvaginae, Peptostreptococcus spp, Staphylococcus sp, Streptococcus spp, and Bacteroides spp., Fusobacterium sp, Gardnerella vaginalis, Mobiluncus, Prevotella spp, and Gram-negative enteric organisms, such as Escherichia coli. Candida albicans, Mycoplasma and Ureaplasma are frequently found in the vagina. Some of the obligate and facultative anaerobic bacteria are associated with Bacterial vaginosis[7]. To protect women from genital infections and to maintain the natural healthy balance of the vaginal flora, the activity of Lactobacillus is essential. Lactobacillus produces acidic environment (hydrogen peroxide) in vagina is an important defense mechanism against the proliferation of different microbial pathogens.

In pregnancy vaginal flora of healthy asymptomatic women normally consists of many aerobic and anaerobic organisms, dominated by Lactobacilli[9].Lactobacilli play an important role in protecting the women from genital tract infection. Lactobacilli maintains vaginal PH acidic by producing lactic acid which is an important defence mechanism. It also maintains hydrogen peroxide in genital tract. Lactobacilli have the ability to inhibit the growth of microorganisms which are known to cause infection. Therefore any disruption in the vaginal lactobacilli results in bacterial vaginosis (BV).In bacterial vaginosis, Lactobacilli is replaced by mixed flora in which dominating organisms are anaerobic bacteria [6].

Keski- Nisula et al 2013[8] studied the role of maternal intrapartum antibiotic to decrease vertical transmission of Lactobacillus in 45pregnant women with singleton pregnancy. Ninety percent of pregnant women in third trimester were colonised by lactobacilli dominant mixed Flora, Ureaplasma urealyticum in 40%, Group B beta haemolytic streptococci in 9%. The cultures were obtained by processing the vaginal fluid swab samples from the upper part of vagina.

Beta haemolytic streptococci, represented by streptococcus agalactiae colonizes mainly vagina and epithelium of lower gastro intestinal tract in 10% to 40% of pregnant women. Brzycgczy-wtoch et.al[9], observed colonization of GBS in genitourinary and/or anus among 42 healthy pregnant women in all three trimesters. They found GBS in vagina in first trimester 24%, second trimester 18%, third trimester 17%. In anus among three trimesters, 19%, 24%,17% respectively. They also found the other normal flora of genital tract such as, Lactobacillus isolated from all pregnant women, Bifidobacterium in 53%, and Candida in 30%. Asymptomatic candidal colonisation of vagina was found in 30% to 40% of pregnant women. Most common species C.albicans followed by C.galbrata[10].

In chorioamnionitis, the source of infection is ascending polymicrobial infection from the lower genital tract and this most commonly occurs with genital mycoplasmas such as Ureaplasma species and Mycoplasma hominis. Haematogenous spread in chorioamnionitis is documented rarely with Listeria monocytogenes. These organisms are found in the lower genital tract of over 70% of women[11].

In the current study the most common organisms colonised were Escherichia coli in 26%, polymicrobial in 22%, streptococcus in 14.5% and Klebsiella pneumonia in 13%. Colonisation with Group B Streptococci is negligible in this cohort of South Indian population. A systematic review reported 10-15% of women to harbour GBS prior to labour and recommended antibiotic prophylaxis for prevention of neonatal GBS in high risk women for development of infection [12].

Sepsis is defined as infection plus manifestation of infection[13]. Organisms causing sepsis can be grouped as maternal genital tract flora, maternal gut flora, sexually transmitted infections, environmental and others[14]. WHO guidelines for management of puerperal sepsis identified streptococci, staphylococci, Escherichia coli, Clostridium tetani, Clostridium welchii, Chlamydia trachomatis and Neisseria gonorrhoea as important organisms[15]. In the current study Escherichia coli which is classified under maternal gut flora is the commonest organism that was responsible for puerperal sepsis. The incidence of puerperal sepsis and neonatal sepsis were not significantly high in women with prior colonisation when compared to those without colonisation. Maternal morbidity and mortality in puerperal sepsis are due to DIC and Septicaemia [16]. Such complications did not develop in women in this study as they were promptly treated with specific antibiotics as per culture reports.

The incidence of neonatal sepsis is reported as 30 per 1000 live births. Klebsiella pneumoniae (32.5%), followed by Staphylococcus aureus (13.6%) are the common causes of neonatal sepsis in India[17]. In the current study neonatal sepsis was diagnosed based on clinical criteria and not on laboratory criteria. This is due to the various protocols adapted by the neonatology department where the study was carried out. The most common organisms responsible for early neonatal sepsis were E.coli and GBS[3]. It is reported that 1 to 2% of neonates born to women colonised with GBS develop early onset neonatal sepsis and many of the clinical signs are nonspecific for sepsis and bacteraemia can occur in the absence of sepsis[18] and hence there is a need for laboratory investigations of neonatal sepsis and initiation of prophylactic antibiotics as preventive strategies. The nonspecific features of neonatal sepsis include hypothermia or fever, lethargy or poor cry, refusal to suck, poor perfusion, prolonged capillary refill time, hypotonia, absent neonatal reflexes, bradycardia or tachycardia, respiratory distress, apnea and gasping respiration, hypoglycaemia or hyperglycaemia, metabolic acidosis[18]. Prophylactic antibiotic therapy to the mother with risk factors for infection to be given at least 4 hours prior to delivery and to the neonates from birth when the risk factors for early onset neonatal sepsis are present.

Limitations of the study are that laboratory diagnostic criteria like C-reactive protein and blood culture for neonatal sepsis were not included due to the neonatal departments protocols not permitting the same. Late onset neonatal sepsis was not included in the analysis.

CONCLUSIONS:

1. Bacterial genital tract colonisation is common (40.5%) irrespective of risk factors for infection. The commonest organism was E.coli followed by polymicrobes and streptococcus in Colonised women.
2. Colonised women with risk factors developed GTI during intrapartum and postpartum when compared to non-colonised women
3. Puerperal sepsis and Neonatal sepsis occurred in 16% and 12% respectively. Hence women with prior bacterial colonisation with risk factors like diabetes complicating pregnancy should undergo screening for infection and or receive prophylactic antibiotic therapy prior to induction of labour.

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