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Analytical study on Uro-genital infections and their antibiotic response status in preterm and term labor patients in a tertiary care institute in Chennai

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Abstract
Delivery occurring prior 37 weeks of gestation account to the maximum incidence of Neonatal morbidity and mortality in India. Amongst the various factors that trigger Preterm birth presence of infections in the lower reproductive tract and the female urinary tract constitute to be a common cause. Such infections release noxious toxic radicals that not only initiate premature uterine contractions but also cause damage to the amniotic membrane resulting in pre-labor rupture of the membranes. The objective of this study was to evaluate the various vaginal micro- organisms present and their antibiotic response in women presenting with preterm labor and compare them with those in women who deliver after 37 weeks of gestation. A sample size of 100 women who presented with preterm labor pains were selected and were compared with 100 women who delivered beyond 37 weeks of gestation with matched demographic and physical parameters. The study was done in Institute of Obstetrics and Gynecology, Egmore, a tertiary care institute at Chennai, South India. High vaginal swab culture sensitivity was done along with mid-stream clean catch urine culture sensitivity for women who reported with labor pains prior to 37 completed weeks of gestation. The type of micro-organisms was also compared with those of women who had term delivery. The study revealed that genital infections were twice as more common in women with preterm labor when compared with women with term delivery. It was also evident that preterm labor was more common in multiparas as against primiparas and the age group of common occurrence was around 20-25 years. High vaginal swab culture was positive 52% and urinary pathogens were demonstrated in 66% of the study group women. The risk was high in women belonging to the low socioeconomic group and in women with short inter pregnancy interval. The most common organism isolated in the vaginal tract was *Staphylococcus aureus* followed by *E. coli* and Pseudomonas and the common pathogen in urine was *E. coli*. The organisms were sensitive to Linezolid , Amikacin and Vancomycin and resistant to cephalosporins and ciprofloxacin.

Keywords: preterm labor, high vaginal swab, urine culture senstivity

Introduction
Early neonatal death due to Preterm birth accounts to about nearly half of all neonatal deaths that occur in India. The various causative factors attributed for triggering preterm delivery include infections in the female lower reproductive tract especially vaginal infections and urinary tract infections as reported by Lockwood *et al*. [1], associated medical illnesses like hypertension, anaemia, diabetes, heart diseases and so on. The fetal factors leading to preterm birth are presence of congenital anomalies, chorioamnionitis, intrauterine growth restriction and multiple pregnancy. WHO has estimated that 9.6% of all births (about 13 million) in 2005 were preterm, Africa and Asia accounted for almost 11 million in them [2].

The common micro-organisms that are detected in the vagina are of two groups namely the Bacterial vaginosis group comprising of Gardnerella vaginalis and *Bacterioides* spp and a second group of enteropharyngeal organisms comprising *E. coli*, *Klebsiella* spp, *Haemophilus* spp., and *Staphylococcus aureus*. The *Bacterioides* spp are detected in nearly 12% of women who have preterm labor while it is present in only 6% of women with term delivery [3]. Bacterial vaginosis infection usually goes unrecognised by the pregnant mother but for a watery nonpruritic discharge with malodour and may be present silently in around 40% of pregnant women.

The theoretical basis postulated as to how infections of the vagina and bladder lead to preterm birth have been proven in various studies, Chabra and Patil have also reported in their study that 28% of women with preterm delivery showed presence of pathogens in either vaginal swab or urine specimen [4]. It is explained that the decidual invasion by the ascending micro-organisms resident in the vagina lead to attraction of leucocytes and macrophages followed by synthesis release of prostaglandins and interleukins from the amnion, chorion, decidua and myometrium. Prostaglandins have been evidenced to initiate uterine contractions.

and lead to preterm birth. The enzymes sialidase and mucinase released by these bacteriae cause breakdown of the amniotic membrane and lead to preterm pre labor rupture of membranes (PPROM). These enzymes also distort the cervical mucus plug and weaken it making it favourable for more ascents of micro-organisms from the vagina into the cervix, and thus the vicious cycle follows.

It has been also proven that presence of infectious pathogens in the urinary tract especially in the asymptomatic state can lead to preterm birth. Untreated asymptomatic bacteriuria in pregnancy can cause acute cystitis and even pyelonephritis in 20-40% of cases. Gram negative bacteriuria leads to release of endotoxins that can cause preterm birth, anaemia and in occasional instances septic shock too. Romero *et al* proved in their study that the risk of preterm birth was twice as less in women who were non bacteriuric compared to women who demonstrated bacteriuria [5]. It was also evidenced in their study that the organisms present in the urine sample were similar to the abnormal vaginal residents. Regular screening of asymptomatic bacteriuria and its treatment with appropriate antibiotics has proven to reduce the incidence of preterm birth and the economic burden of treating low birth weight infants. This prospective case control study was done to prove the association of uro-genital infections in women who presented with preterm labor**,** the study also analyses the different bacteriae that were isolated and their antibiotic susceptibility. The various demographic and other risk factors were also analysed in this study.

Study Methodology

This is a prospective case control study conducted at Institute of Obstetrics and Gynecology, Egmore; a premiere tertiary care hospital specialized in maternity care in Chennai. Sample population of 100 women who reported with preterm labor were selected and compared with 100 women who had term delivery. Preterm labor was documented according to ACOG criteria as four uterine contractions in 20 min or eight in 60 minutes associated with progressive changes in the cervix; cervical dilatation greater than 1 cm; and cervical effacement 80% or greater at gestation less than 37 completed weeks.

A detailed history was taken, age, parity, socioeconomic status, presence of medical illnesses and the previous obstetric outcome was elicited and general examination findings were recorded. High vaginal swab and midstream clean catch urine sample were collected for culture and sensitivity from both the categories.

Inclusion criteria

- 100 women presenting with threatened preterm labor and preterm labor with or without rupture of membranes after 28 weeks and before 37 completed weeks of gestation
- 100 age and demographics matched women with term pregnancy were studied

Exclusion criteria

- Women with multiple pregnancy, iatrogenic preterm induction of labor for maternal medical conditions and fetal conditions and women with antepartum hemorrhage were excluded from the study.

Observation and Interpretation

Table 1: Association of risk factors in preterm labor patients

Risk factor	Incidence n=100	Percentage%
Low socioeconomic status (Modified Kupuswamy Scale)	64	64
Medical risk factors		
Urinary tract infection	34	34
Anemia	30	30
Diabetes mellitus	20	20
Hypertensive disorders	16	16
Hypothyroidism	8	8
Obstetric risk factors		
Previous preterm labour	26	26
Short interpregnancy interval	24	24
Polyhydramnios	18	18

Table 2: Age and Gravidity analysis in preterm labor patients

Parameters	Number of cases (n=100)	Percentage (%)
Maternal age		
<20	10	10
21-25	64	64
26-30	21	21
>30	5	5
Gravidity		
Primi	29	29
Gravida 2	62	62
Gravida 3	9	9

It is evidenced that preterm labor was more common in women under the age group of 21-25 years and more common in second gravidas compared to primigravidas. Most of the women belonged to the lower socioeconomic group and the predominant risk factor associated were urinary tract infections, anemia and diabetes.

Table 3: Organisms isolated in HVS and Urine C/S of women presenting with Preterm labor and in women with term labor

Organisms isolated	Preterm labor cases (n=100)		Term labor cases (n=100)		P value
	HVS	Urine C/S	HVS	Urine C/S	
Staphylococcus aureus	18	13	4	3	<o.ooo1 for all isolates
MRSA	6	7	2	3	
Escherichia coli	16	31	5	8	
Pseudomonas spp	4	5	2	2	
Klebsiella spp	3	6	2	1	
Candida albicans	3	2	1	1	
Proteus mirabilis	2	2	1	1	
No growth	48	34	83	81	

Positive culture sensitivity was found in around 52% of preterm labor cases of which *Staphylococcus aureus* was the most common organism (n=18) isolated , 6 cases were Methicillin resistant Staphylococcus aureus, followed by *E. coli* in about 18% of cases. There was a significant reduction in the positive culture reports for pathogens detected in women who had term delivery, there was only 17 positive for vaginal pathogens and 19 positive report of urinary pathogens (P= 0.0001)

Table 4: Sensitivity pattern of the microbes isolated from HVS and Urine C/S in Preterm labor group

Organism	Total No	Antibiotic Susceptibility					Antibiotic Resistance				
		C	V	L	A	Cp	C	V	L	A	Cp
Staphylococcus aureus	18	12	10	14	15	9	6	4	2	3	9
MRSA	6	0	6	5	5	2	6	0	1	1	4
Escherichia coli	16	5	14	16	14	6	11	2	0	2	10
Pseudomonas	4	1	4	4	3	1	3	0	0	1	3
Klebsiella	3	1	3	1	3	3	2	0	2	0	0
Proteus	2	0	2	2	1	0	0	2	0	1	2

C= Cephalosporin V=Vancomycin L=Linezolid A=Amikacin Cp=Ciprofloxacin

Most of the organisms were susceptible to Vancomycin, Amikacin and Linezolid and exhibited resistance to Cephalosporins and Ciprofloxacin.

Discussion

WHO defines preterm labor as labor occurring with intact amniotic membranes after 28 weeks and before 37 completed weeks of gestation. It accounts to about 6-8% of deliveries in both the developed and the developing countries. Prematurity being the leading cause of neonatal morbidity and mortality poses a great challenge to the neonatologist. Various measures are being tried all over the globe to curtail the rate of preterm birth. The risk factors that predispose to preterm birth is multifactorial but yet the presence of infections in the lower reproductive and urinary tract is the most discussed. Detection and clearance of Uro-genital infections has proven to be a major milestone in the measures taken to decrease the rate of preterm birth in a particular community. In our study, genital infections were about 2 times more in women with preterm labour (52%) when compared to those in term pregnancy (17%). Staphylococcus aureus was the predominant organism isolated from the high vaginal swab of the preterm labour group of which 25% were MRSA followed by *E. coli* and *Psedomonas aeruginosa*.

Uro-genital infections are more common in women belonging to lower socio-economic group and in women with poor reproductive tract hygiene. The common microorganisms that can predispose to preterm labor are *Bacteroides* spp and enteropharyngeal organisms [6]. Apart from these social factors the other risk factors favouring the growth of pathogens in the lower reproductive tract and urinary bladder are medical complications associated with pregnancy like anaemia, diabetes, immune-suppressive states and HIV [7].

There are many studies conducted in India to prove the risk of infections as causative agent in preterm delivery, Ghungae V [8] found the presence of urogenital infections in 46% of the study group. In our study, the incidence was 52% in the women who had preterm delivery and 17% in women who had term delivery. The common age group was 21-25 years which was also found in the study done by Udayakumar *et al.* [9]

The predominant micro-organism found in the vaginal swab culture was GBS and *E. coli* in urine sample by the study done by Vermu *et al.* [10] In our study the bacteriae demonstrated were mostly Staphylococcus in HVS and *E. coli* in urine culture. The organisms tragically expressed resistance to the commonly used antibiotics like cephalosporins and ciprofloxacin probably due to common usage but were susceptible to the less commonly used drugs like linezolid, Vancomycin and amikacin. It has to be stressed here that the use of antibiotics are to be rationalised and also over usage has to be avoided to prevent drug resistance.

Summary and Conclusion

We conclude that Genital infections were 52% in women with preterm labor and 17% in women with term. The prevalence of silent infections in the Uro-genital system remains a constant threat to the obstetrician and the antenatal mother. Prematurity has to be dealt with care so as to reduce both the anxiety and the financial burden on the parents. One of the easily detectable and treatable risk factor for premature birth is screening and eradication of micro-organisms dwelling the female reproductive and urinary tract. The American College of Obstetricians and Gynaecologists (ACOG) recommends screening at the initial prenatal visit and additional screening as clinically indicated. Prevention of preterm labor in high risk group can be instituted by health education on personal hygiene so as to prevent urogenital infections, adequate hydration, early identification and treatment of anemia, glycemic and blood pressure control in women with Diabetes mellitus and Hypertensive disorders respectively and adequate spacing of births. A careful vigil on the patients who are prone to have preterm birth by risk assessment scoring and screening them for the presence of infections would be the most attractive and effective step to control occurrence of preterm births.

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