ORIGINAL ARTICLE

ASSOCIATION OF RISK FACTORS WITH SPONTANEOUS PRETERM LABOUR WITH INTACT FOETAL MEMBRANES

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Background: Spontaneous preterm labour refers to the onset of uterine contractions of sufficient strength and frequency to effect progressive dilatation between 24 and 37 weeks of gestation. The objective of the study was to determine an association between risk factors and spontaneous preterm labour with intact foetal membranes. **Methods:** A case control study was designed which was conducted in the Department of Obstetrics and Gynaecology, Ayub Teaching Hospital, Abbottabad. Sample size of 262 subjects was equally divided into two equal groups (131 cases and control each). Non-probability consecutive sampling was used collection of samples. Pregnant women presenting after 24 weeks of gestation with spontaneous preterm labour with intact membranes were considered as cases. While, pregnant women presenting after 37 complete weeks of gestation with normal pregnancy were considered as controls. The diagnosis of bacterial vaginosis was established by Amsel criteria. Asymptomatic bacteriuria was diagnosed by microscopy. Odds ratios were calculated as measure of association with calculation at 95% confidence interval. Level of 5% (p<0.05) was used to test for significant difference. **Results:** Mean±SD age of cases was 26.97±7.072. Subjects with young maternal age (<20 years) were 27 (10.3%) from cases and 12 (4.6%) from controls (OR=2.575, 95% CI: 1.242, 5.338). The subjects with advanced maternal age (>35 years) were 26 (9.9%) from cases and 15 (5.7%) from controls (OR=0.522, 95% CI: 0.262, 1.039). 25 (19.1%) cases and 6 (4.6%) controls had bacterial vaginosis (OR=4.914, 95% CI: 1.943, 12.426). Asymptomatic bacteriuria was present in 03 (2.3%) subjects from cases and 2 (1.5%) from controls (OR=1.512, 95% CI: 0.248, 9.199). **Conclusion:** The study concluded that risk factors like young maternal age and bacterial vaginosis are significantly associated with spontaneous preterm labour with intact foetal membranes. While, association of other risk factors like advanced maternal age and asymptomatic bacteriuria with spontaneous preterm labour is still debatable.

Keywords: Spontaneous preterm labour; Intact foetal membranes; Risk factors

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INTRODUCTION

Spontaneous preterm labour (sPTL) is the labour between 24 weeks to 37 weeks of gestation.[1] It has tremendous outcomes for neonates, children, and their families.[2] Approximately 15 million births per year occur as preterm and 1.1 million children die from its complications.[3] Four distinct mechanisms for the pathogenesis of preterm labour have been described and include premature activation of the foetal hypothalamic pituitary axis, mechanical stretch, inflammation/matrix re-modelling, and placental abruption.[4] The risk factors of preterm labour are multipartite, foetal anomaly, prenatal care, smoking, not consuming folic acid and iron supplements, in vitro fertilization, history of infertility and trauma, amniotic fluid leak, rupture of membranes, cephalic presentation, vaginal bleeding, oligohydramnios, preeclampsia, uterine abnormalities, cervical insufficiency, and short time since last delivery.[5] Overall incidence of preterm labour is 6–15% and 40–50% of these occur spontaneously with intact membranes. The incidence of sPTL with intact membrane is higher than preterm, pre-labour rupture of membranes (25%).[6] The preterm babies have high risk of cerebral palsy, vision/hearing impairments, intellectual disabilities, and immaturity of multiple organ systems.[7] The biochemical markers like C-reactive protein, alpha fetoprotein, cervical foetal fibronectin, and interleukin-6 have good diagnostic value to identify pregnancies that have a risk of sPTL.[8]

Infection is an important and frequently occurring mechanism of sTPL in preterm deliveries. Microbial studies suggest that infection accounts for about 25–40% of all preterm births.[9] At earlier age of gestation, the leading cause of spontaneous preterm delivery is intra-amniotic inflammation[2]. Bacterial vaginosis (BV) is a clinical condition described by

off- white, thin, homogenous, and adherent vaginal discharge. It is more often present after menses and intercourse with pH greater than 4.5. Positive Whiff test, few lactobacilli, presence of clue cells, and small number of polymorphonuclear leucocytes are other characteristic features.[10] Lactobacilli, gram positive bacteria, and of Enterobacteriaceae members are most prominent isolates present in the vaginal samples[11]. The incidence of preterm labour with BV is 5–18% of total deliveries and causes morbidity like neurodevelopmental deficit e.g., cerebral palsy but in some communities, its prevalence is up to 50%.[1,12] It can be treated with metronidazole but can relapse within 3–6 months in 50% cases. It is the risk factor for post-Caesarean section endometritis, spontaneous preterm birth, and second-trimester miscarriage.[12]

Asymptomatic bacteriuria (ASB) is defined as a measurable count of $>100\times10^6$ colony-forming units of bacteria per litre (CFU/L) of urine without any particular symptoms of a urinary tract infection.[13] Verma *et al*. documented that the prevalence of ASB is 12.27% in pregnant women. Pregnant females with ASB have higher incidence of delivering premature, low birth weight, and preterm infants. They also more likely have anaemia, preeclampsia, and preterm labour[14]. Bacteria in lower genital tract produce enzymes like mucinase and sialidase which act on cervical mucosa and weaken it thus allow invasion of bacteria in upper genital tract. The microorganisms cultured in urine are gram positive bacilli, gram negative bacilli, gram negative coccobacilli, enterococcus faecalis, staphylococcus aureus, candida albicans, proteus vulgaris, and E coli. There is also an association of urogenital infections with preterm labour.[15] It is highly prevalent in third trimester (61.77%) than in the second trimester (32.35%) and the first trimester (5.88%) and can be treated by antimicrobial therapy.[16,17] This study not only helps clinicians to identify risk factors associated with sPTL but will also help patients regarding prevention strategies and treatment.

MATERIAL AND METHODS

A case control study was designed which was conducted in the Department of Obstetrics and Gynaecology, Ayub Teaching Hospital, Abbottabad. The duration of study was six months. Sample size was calculated using the WHO software for sample size determination in health studies, using the proportion of estimating Odds Ratio with relative precision in case control study with the following assumptions: Confidence level = 95%, power of test = 90%, proportion of exposure of (BV) in preterm = 25%, proportion of exposure (BV) in full term = 11.3%. Sample size thus calculated is 262 (131 cases and control each). Non-probability consecutive sampling was used collection of samples. Pregnant women presenting after 24 weeks of gestation with spontaneous preterm labour with intact membranes were considered as cases. While, pregnant women presenting after 37 complete weeks of gestation with normal pregnancy were considered as controls as per our operational definitions. Period of gestation was calculated from first day of last menstrual period or by antenatal ultrasound scan. The subjects with preeclampsia and eclampsia, antepartum haemorrhage, intra-uterine growth retardation (IUGR), intrauterine foetal death, foetal congenital anomalies, multiple gestation, and uterine and cervical anomalies diagnosed by relevant investigations and clinical examination were excluded from the research as these conditions act as confounders and might introduce bias in the study result.

After getting fully informed, understood, and written consent from the subjects, all participants were subjected to detailed history, clinical examination, and routine baseline investigations. Period of gestation was calculated from first day of last menstrual cycle or by antenatal ultrasound scan.[18] Spontaneous Preterm labour was diagnosed by presence of uterine contractions at least one every 10 minutes associated with cervical effacement of 80% and dilatation of more than 2 cm before 37 weeks and 6 days of gestational period and with intact foetal membranes on clinical examination. Young maternal age of <20 years and advanced age of >35 years were considered as extreme maternal ages. The diagnosis of bacterial vaginosis was established by Amsel criteria.[19] Asymptomatic bacteriuria was diagnosed by microscopic presence of $>10^5$ colony-forming units (CFU)/ml of same bacteria in mid steam urine sample on high power field in the absence of acute urinary tract symptoms. Data obtained was first entered in the Microsoft Excel sheet to generate a database which was exported in the SPSS version 20.0. Data was analysed for description, i.e., for categorical variables like extreme maternal age (young/advanced), bacterial vaginosis, and asymptomatic bacteriuria; frequencies and percentages were calculated and for continuous variables like age and period of gestation; mean±standard deviation (SD) were calculated. Odds ratios were calculated as measure of association with calculation of 95% confidence interval. Level of 5 % (p<0.05) was used to test for significant difference.

RESULTS

Descriptive statistics of mean±SD of age (years) in cases and controls:

Mean±SD age of cases was 26.97±7.07 years while 27.85±5.55 years was mean±SD age of controls depicted in table-1.

Odds ratios (OR) and 95% confidence intervals (CI) for young and advanced maternal ages,

bacterial vaginosis, and asymptomatic bacteriuria with cases and controls:

Pregnant women with young maternal age were 27 (10.3%) from cases and 12 (4.6%) from controls. Odds ratio and 95% confidence intervals were 2.575 and 1.242 and 5.338 respectively for extreme young maternal age of cases and controls. However, subjects with advanced maternal age were 26 (9.9%) from cases and 15 (5.7%) from controls while with no advanced maternal age were 105 (40.1%) from cases and 116 (44.3%) from controls. The patients found with bacterial vaginosis were 25 (19.1%) from cases and 6 (4.6%) from controls while with no bacterial vaginosis were 106 (80.9%) from cases and 125 (95.4%) from controls. Odds ratio and 95% confidence intervals for bacterial vaginosis (OR=4.914, 95% CI: 1.943, 12.426) of preterm cases and controls are shown in table 2.

Similarly, patients with asymptomatic bacteriuria were 03 (2.3%) from cases and 2 (1.5%) from controls while with no patients with asymptomatic bacteriuria were 128 (97.7%) from cases and 129 (98.5%) from controls. Odds ratio was 1.512 while 95% confidence intervals for asymptomatic bacteriuria were 0.248 and 9.199 of cases and controls (Table-2).

Table 1: Descriptive statistics of mean±SD of age (years) in cases and controls

Age (years)	Cases n=131	Controls n=131	Total n=262
Mean	26.97	27.85	27.41
Std. Deviation	7.07	5.55	6.36

Table-2: Odds ratios (OR) and 95% confidence intervals (CI) for young and advanced maternal ages, bacterial vaginosis, and asymptomatic bacteriuria with cases and controls

Variables	Cases	Controls	Total	*p*-value	Odds ratio	95% Confidence Interval	
						Lower	Upper
Young Maternal age (years)	27 10.3%	12 4.6%	39 14.9%	0.00*	2.575	1.242	5.338
No.	104 39.7%	119 45.4%	223 85.1%				
Total	131 50.0%	131 50.0%	262 100.0%				
Advanced Maternal age (years)	26 9.9%	15 5.7%	41 15.6%	0.06	0.522	0.262	1.039
No.	105 40.1%	116 44.3%	221 84.4%				
Total	131 50.0%	131 50.0%	262 100.0%				
Bacterial Vaginosis	25 (19.1%)	6 (4.6%)	31 (11.8%)	0.00*	4.91	1.943	12.426
No.	106 (80.9%)	125 (95.4%)	231(88.2%)				
Total	131 (100.0%)	131 (100.0 %)	262 (100.0%)				
Asymptomatic Bacteriuria	3 (2.3%)	2 (1.5%)	5 (1.9%)	0.65	1.512	0.248	9.199
No.	128 (97.7%)	129 (98.5%)	257 (98.1%)				
Total	131 (100.0%)	131 (100.0 %)	262 (100.0%)				

DISCUSSION

In this study, age of selected cases was 26.97±7.07 years while cases with young maternal age were 27 (10.3%) compared to controls 12 (4.6%) (OR=2.575, 95% CI: 1.242, 5.338, p = 0.00*). Similarly, 26 (9.9%) cases were presented with advanced maternal age while 15 (5.7%) were controls (OR=0.522, 95% CI: 0.262, 1.039, p = 0.06). The association between advanced maternal age and premature labour is still controversial. The maternal age between 30–34 years is associated with lowest risk of premature deliveries while, maternal age 40 years or above is associated with preterm deliveries.[20] This study shows that the incidence of spontaneous preterm labour with intact foetal membranes is more in extreme of young maternal age < 20 years while as advance maternal age >35 year had poor association and it is similar to the study done by IP M *et al*.[21] A study also concluded that maternal age is not associated with

preterm delivery.[18] In this study, only young maternal age was significantly associated with sPTL. Contrary, other studies have documented that both maternal ages (below 19 years and advanced) are associated with increased risks of preterm deliveries.[22–24]

Bacterial vaginosis was present in 25 (19.1%) cases and in 6 (4.6%) controls (OR=4.914, 95% CI: 1.943, 12.426, p=0.00*) and was significantly associated with sPTL. A study concluded that BV is significantly associated with preterm delivery (risk ratio [RR], 2.68; 95% confidence interval [CI], 1.44–4.98).[25] Similarly, another study documented same findings like our study that BV is significantly associated with preterm labour (OR=7.3, 95% CI =1.9–27.5, p=0.03*).[1] Patients with asymptomatic bacteriuria were 03 (2.3%) from cases and 2 (1.5%) from controls. There was no significant association of asymptomatic bacteriuria with sPTL in our selected subjects (OR=1.512, 95%, CI: 0.248, 9.199, p=0.65). Results of studies conducted in the past have shown controversial findings about association between ASB and sPTL. Some studies documented an association between ASB and preterm labour, foetal, and maternal morbidities (p = 0.02).[15,16] While, the study conducted by Verma et al. found no significant association between asymptomatic bacteriuria and preterm delivery (OR=3.231 CI: 1.108, 9.418, p>0.05).[14] Tahir *et al*. has also reported no significant adverse perinatal outcome in the form of premature delivery associated with ASB (p>0.05).[26] The study also documented an increased incidence of preterm labour [RR 3.27, 95% CI 1.38-7.72] in late ASB detected women (32-34 weeks), whereas no significant difference was seen in early detected women (till 20 weeks) as compared to ASB negative women [RR 0.632, 95% CI 0.20–1.93, p = 0.52].[27]

CONCLUSION

The study revealed that risk factors like young maternal age and bacterial vaginosis are significantly associated with spontaneous preterm labour with intact foetal membranes. As other risk factors like advanced maternal age and asymptomatic bacteriuria have been reported in cases, therefore it is recommended that timely identification, prevention, and management of all risk factors must be done to avoid spontaneous preterm labour and its subsequent neonatal and maternal morbidities and mortalities.

AUTHORS' CONTRIBUTION

UZ: Data Collection, lab work, discussion. AN: Data collection, lab work, review, discussion. AT: Data entry, review and data analysis,. IS: Data analysis, references. SF: Tables, analysis, interpretation. HJ: Proof reading, write-up, data collection.

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