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Original Research Article

Pre-pregnancy and prenatal care risk factors for spontaneous premature delivery in Western Uganda: a hospital based unmatched case-control study

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ABSTRACT

Background: We aimed to establish pre-pregnancy and prenatal care risk factors for spontaneous premature delivery at Kampala international university teaching hospital (KIUTH) so as to enable us draw a platform upon which specific interventions can be formulated.
Methods: This was a hospital based unmatched case-control study conducted in the months of March to June 2019. A total of 110 cases and 330 controls admitted at KIUTH maternity and postnatal units were enrolled into the study. Interviewer administered questionnaires and respondent's medical records were used to collect data. Chi square test and multiple logistic regression analysis were performed to establish the risk factors for spontaneous premature delivery at this facility. All data analyses were done using SPSS statistics version 20.
Results: Nulliparity, previous premature delivery, history of premature rupture of membranes, previous cervical procedures, history of not having received preconception care, urinary tract infections during pregnancy and maternal obesity were independently associated with spontaneous premature delivery at this hospital.
Conclusions: Guided by these factors, a high index of suspicion for spontaneous premature delivery among all pregnant women attending prenatal care is vital towards ameliorating this obstetric complication at KIUTH.

Keywords: Spontaneous premature delivery, Premature birth, Premature labor, Preterm birth, Preterm labor

INTRODUCTION

Spontaneous premature delivery continues to be enigmatic to many obstetricians and pediatricians all over the world. The condition is responsible for more than 70% of all premature births and accounts for about 75% of all neonatal deaths across the world with several associated devastating perinatal, neonatal and infant morbidity.[1-3] Vicious long term morbidities such as cerebral palsy, neurodevelopmental delay and cognitive impairment have also been reported in the later life of the children who are born prematurely.[4,5] Spontaneous premature delivery poses great impact on the survival and quality of life as well as psychological and emotional stress on mothers and their families.[6] Mothers who suffer recurrent spontaneous premature delivery are prone to psychological upsets and social stigma usually arising from failure to achieve normal delivery and/or the problems of her premature baby among other morbidities.[7] Up to present, the etiology of this obstetric complication in the largest portion of the pregnant women remains unclear.[8] However, different factors have been reported to increase the risk of its occurrence. Whereas several studies have been conducted in various parts of the world to ascertain the associated factors, there is no evidence for any of such studies conducted in this

area despite the many cases of spontaneous premature deliveries observed during our day-to-day practice. We are not certain however if such factors apply in this particular population as well. The current study specifically aimed to establish the pre-pregnancy and prenatal care risk factors for spontaneous premature delivery at KIUTH so as to enable us draw a platform upon which specific interventions can be formulated.

METHODS

A hospital based unmatched case-control study was conducted in the months of March 2019 to June 2019 with an aim of establishing the pre-pregnancy and prenatal care risk factors for spontaneous premature delivery at Kampala international university teaching hospital. The study was conducted in the hospital's maternity and post-natal units. KIUTH is a 700-bed capacity private not for profit teaching hospital for Kampala international university located in southwestern Uganda's district of Bushenyi, about 370 kilometers from the country's capital Kampala. Only term and spontaneous premature deliveries conducted at the hospital were included for the study. A sample size of 440 deliveries was considered. This was determined using Epi tools for specified values. Expected proportion in controls was 0.136 based on a study conducted in Mulago hospital in Uganda, assumed odds ratio of 2, confidence level of 0.95, power 0.8, and a ratio of 1:3 for cases: controls.[9] Therefore, 110 singleton spontaneous premature deliveries and 330 singleton term deliveries were considered. The cases were the mothers who had had spontaneous preterm delivery of before 37 weeks and 0 days of gestation but above 28 weeks and 0 days of gestation following spontaneous uterine contractions with intact membranes. The latter weeks of gestation were considered based on the Uganda definition for preterm delivery since below 28 weeks and 0 days of gestation is regarded as a miscarriage.[10] All women who had had preterm delivery following preterm premature rupture of membranes and/or following medical intervention such as induction (regardless of indication) were therefore not part of this inclusion criterion. The controls were all women who had delivered at 37 weeks and 0 days or more of gestation but prior to 42 weeks and 0 days of gestation. Gestational age was estimated basing on the last normal menstrual period and/or first trimester obstetric ultrasound scan for those who could not remember their last menstrual period. We did not encounter any respondent where neither of the two was available.

This study was strictly conducted in accordance with the principles of the declaration of Helsinki. We ensured voluntary enrollment of all the study participants both adults and emancipated minors. The informed written consent was obtained after explaining the details of the study in Runyankole, the popular local language as well as English, the national official language for the few participants who either did not understand the local language or were generally well conversant with the English language. Participants were not forced to participate if they did not wish to. Each participant was free to withdraw from the study at any time she wished without coercion or compromise of care that she had been entitled to. We used pretested interviewer administered questionnaires and patient's medical records to collect the data on all our variables. Where further information regarding specific respondent's previous data was thought necessary, consultation of the respective respondent's health facility prenatal care register was made. Information regarding whether the respondent had at any point of her pregnancy been diagnosed with a urinary tract infection was taken from the respondent's general medical records as well as the laboratory reports in the patient's prenatal care records. This was regardless of which time of pregnancy the infection was diagnosed. According to the Uganda ministry of health protocol, urinalysis is routine for all pregnant women during their routine first prenatal care visit in all the health facilities. We therefore took advantage of this since all our respondents had at least had a prenatal care visit at some point during their pregnancy. We had no incidents of missed records. Information regarding each respondent's weight (kg) and height (m) was also obtained from the respondent prenatal care records and the respective pregnancy body mass indices computed accordingly. Those whom it had already been calculated, a repeat calculation was made to confirm the one already documented. Although most of these were first trimester parameters, we had some cases whom their first antenatal care attendance was in second trimester and therefore these parameters were accordingly considered. All the collected data were entered into Microsoft excel version 2010 from where it was imported into IBM SPSS statistic software version 20 for analysis. Frequency tables for all the variables were constructed and cross tabulation on associations between the independent and dependent variable was done to generate chi square and comparisons made accordingly. Statistical significance was assessed using a chi square test and a $p<0.05$ was considered statistically significant. Multivariable logistic regression analysis was performed to check for any confounding and adjusted odds ratios; their corresponding 95% confidence intervals and p values were accordingly computed. All variables in the final multivariate model were significant when $p<0.05$.

RESULTS

Socio-demographic characteristics of the study participants

Four hundred forty participants (n=110 for the cases and n=330 for the controls) were enrolled in the study. Most participants were aged between 20 and 30 years for both the cases and controls. Majority were married for both the cases and controls. The highest level of education was relatively similar among both groups with about half of the participants not having attended secondary and

tertiary schooling. We noted a higher proportion of peasant farmers (53.6%) among the cases than control group (40.6%). Most of the women who were employed in civil service, non-governmental organizations, or business were noted to be under the control group. The proportion of participants earning less than 200,000 Uganda shillings (1US Dollar=3,690 Uganda shillings) was higher in the cases than controls. More than 50% of the participants in the control group earned more than 200,000 Uganda shillings. This is shown in Table 1.

Pre-pregnancy and prenatal care factors for cases and controls

The proportions of nulliparous women were notably higher in the cases group than the controls. There were many women with previous premature delivery in the cases group (42.7%) than in the control group (29.4%). Similar observation was noted with the women with history of premature rupture of membranes (20%), prior cervical procedures (17.3%), prior miscarriage (25.5%), and prior caesarean delivery (37.3%) in the cases group than in the control group (5.2%), (2.4%), (18.8%), (27.6%) respectively. Women who had received preconception care were generally low for both the cases and controls. The proportion of women who had attended first, second and third trimester prenatal care visits was relatively similar for both the cases and controls. 60% of cases and 40.6% of controls had suffered urinary tract infection during the pregnancy. Regarding body mass index, there was no difference between the cases and controls for underweight (BMI <18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2) and overweight (25-29.5 kg/m^2). However, the largest proportion of women with obesity (BMI ≥30 kg/m^2) was noted under the cases (11.8%) than the controls (3.9%) shown in Table 2.

Risk factors for spontaneous premature delivery

Chi square analysis revealed seven pre-pregnancy and prenatal care factors, that is; nulliparity, previous premature delivery, history of premature rupture of membranes, previous cervical procedures, urinary tract infection during the pregnancy, history of no preconception care, and maternal obesity (body mass index≥30 kg/m^2) significant (p value of<0.05). These factors retained the significant association even after checking for confounding with multivariable analysis. Accordingly, the odds of previous premature delivery were 5.2 times higher in women who delivered preterm compared to those who delivered at term (aOR=5.2, 95%CI: 1.6-9.31, p value of<0.0001), while that of premature delivery were 3.3 times greater in women with history of premature rupture of membranes compared to the women who delivered at term (aOR=3.3, CI: 1.4-7.12, p<0.0001). The odds of prior cervical procedures were 4.37 times greater in the women who had premature delivery compared to those who delivered at term (aOR=4.37, CI: 1.42-9.97, p<0.0001), while nulliparous women had 2.1 times the odds of spontaneous premature delivery compared to term delivery (aOR=2.1, CI: 1.01-5.42, p=0.0394). Women who had not received preconception care had 1.67 times the odds for spontaneous premature delivery among the cases than controls (aOR=1.67, CI: 0.93-3.95, p=0.0389). Meanwhile, the odds of spontaneous premature delivery were more than twofold higher in the women with BMI≥30 kg/m^2 compared to the women who delivered at term (aOR=2.6, CI: 0.61-6.11, p=0.0096). This is shown in Table 3.

Table 1: Baseline socio-demographic characteristics for both the cases and controls at KIUTH.

Variables	Cases (n=110)	Controls (n=330)	X^2	P value
Age (year)				
<20	12 (10.9)	31 (9.4)	3.316	0.1905
20-30	85 (77.3)	235 (71.2)		
>30	13 (11.8)	64 (19.4)		
Marital status				
Single	0 (0)	12 (3.6)	8.886	0.0308*
Married	106 (96.4)	312 (94.6)		
Widowed	4 (3.6)	3 (0.9)		
Separated	0 (0)	3 (0.9)		
Highest education level				
No formal education	4 (3.6)	11 (3.3)	0.063	0.9959
Primary	51 (46.4)	157 (47.6)		
Secondary	25 (22.7)	74 (22.4)		
Tertiary	30 (27.3)	88 (26.7)		
Occupation				
Peasant farmer	59 (53.6)	134 (40.6)	9.935	0.0415*
House wife	17 (15.5)	63 (19.1)		
Civil servant/NGO	13 (11.8)	72 (21.8)		
Business woman	13 (11.8)	72 (21.8)		
Others	8 (7.3)	14 (4.3)		

Continued.

Variables	Cases (n=110)	Controls (n=330)	X^2	P value
Average monthly income (in Ugx)				
<200,000	59 (53.6)	156 (47.3)	5.969	0.1131
200-449,999	22 (20)	96 (29.1)		
450,000-900,000	29 (26.4)	72 (21.8)		
>900,000	0 (0)	6 (1.8)		

NGO=Non-Governmental Organization, Ugx=Uganda shillings.

Table 2: Comparison of pre-pregnancy and prenatal care risk factors for spontaneous premature delivery for cases and controls at KIUTH.

Variables	Cases (n=110)	Controls (n=330)	X^2	P value
Nulliparity				
Yes	47 (42.7)	97 (29.4)	6.6617	0.0099*
No	63 (57.3)	233 (70.6)		
Previous premature delivery				
Yes	38 (34.5)	50 (15.2)	19.3939	<0.0001*
No	72 (65.5)	280 (84.8)		
History of PROM				
Yes	22 (20)	17 (5.2)	22.5172	<0.0001*
No	88 (80)	313 (94.8)		
Prior cervical procedures				
Yes	19 (17.3)	8 (2.4)	31.5798	<0.0001*
No	91 (82.7)	322 (97.6)		
Previous miscarriage				
Yes	28 (25.5)	62 (18.8)	2.2535	0.1333
No	82 (74.5)	268 (81.2)		
Previous cesarean delivery				
Yes	41 (37.3)	91 (27.6)	3.6941	0.0546
No	69 (62.7)	239 (72.4)		
Preconception care				
Yes	6 (5.5)	4 (1.2)	6.6853	0.0097*
No	104 (94.5)	326 (98.8)		
First trimester PNC attendance				
Yes	60 (54.5)	166 (50.3)	0.5944	0.4407
No	50 (45.5)	164 (49.7)		
Diagnosed with UTI during pregnancy				
Yes	66 (60)	134 (40.6)	12.5156	0.0004*
No	44 (40)	196 (59.4)		
Pregnancy BMI ≥30 kg/m^2				
Yes	13 (11.8)	13 (3.9)	9.211	0.0024*
No	97 (88.2)	317 (96.1)		

*P<0.05, PNC=Prenatal care, UTI=Urinary tract infection, BMI=Body mass index

Table 3: Risk factors for spontaneous premature delivery at KIUTH before and after controlling for the potential confounders.

Variables	uOR	95%CI	aOR	95%CI	P value
Nulliparity					
Yes	1.79	1.15-2.8	2.1	1.01-5.42	0.0394*
No	1				
Previous premature delivery					
Yes	2.96	1.8-4.85	5.2	1.6-9.31	<0.0001*
No	1				
History of PROM					
Yes	4.6	2.34-9.05	3.3	1.4-7.12	<0.0001*
No	1				

Continued.

Variables	uOR	95%CI	aOR	95%CI	P value
Prior cervical procedures					
Yes	8.4	3.56-19.82	4.37	1.42-9.97	<0.0001*
No	1				
Preconception care					
Yes	4.7	1.3-16.98	1.67	0.93-3.95	0.0389*
No	1				
Diagnosed with UTI during pregnancy					
Yes	2.19	1.41-3.41	3.7	1.8-4.56	0.0016*
No	1				
Pregnancy BMI ≥30 kg/m^2					
Yes	3.27	1.47-7.29	2.6	0.61-6.11	0.0096*
No	1				

*P<0.05, PNC=Prenatal care, UTI=Urinary tract infection, BMI=Body mass index

DISCUSSION

Spontaneous premature delivery remains a major trouble to many obstetricians across the world with worst incidence in the developing countries of which Uganda (where this study was conducted) is among. Given the low resources in the developing countries, it is extremely hard to manage the prematurely born babies following spontaneous premature labor, which actually justifies the high perinatal morbidly and mortality observed in these countries. Prediction based on the risk factors and prevention of spontaneous premature delivery would therefore offer the best opportunity to prevent such complications. Unfortunately, to the best of our knowledge, information regarding the risk factors in western Uganda is not available. Here we discuss the findings of our study to fill this gap.

Literature from Wudie et al, Chen et al, Delnord et al, and Koullali et al have revealed that nulliparous women are at high risk for spontaneous premature delivery than those who have had deliveries before.[11-14] Our study findings were indeed no different. Accordingly, nulliparous women had slightly more than twofold the odds of delivering prior to term compared to those who delivered at term (aOR=2.1, CI: 1.01-5.42, p=0.0394). The naivety of pregnancy by nulliparous women usually characterized by poor prenatal care seeking behavior coupled with the fact that nulliparous women are usually of young age and of low educational status, which per se have been associated with spontaneous premature delivery may perhaps explain this observation.[11,12,15,16] The study further established that the odds of premature delivery at this hospital was 5.2 times greater in women with previous history of premature delivery compared to women who delivered at term (CI: 1.6-9.31, p<0.0001). Prior studies in Iran, Peru, Nepal, Brazil and Palestine have reported similar findings.[15,17-20] The mechanism for this however has not clearly been ascertained. It is possible that recurrent factors among these women are responsible.

In the present study, the odds of spontaneous premature delivery among women with history of premature rupture of membranes in any of their prior pregnancies were more than threefold compared to those who delivered at term (aOR=3.3, CI: 1.4-7.12, p<0.0001). Similar observations have been reported by Ayebare and colleagues before.[9] It is now fairly clearly to us that certain risk factors responsible for premature rupture of membranes overlap with those of spontaneous premature delivery in various parts of the world. Moreover, more than one-third of spontaneous premature delivery lies on account of preterm premature rupture of the membranes.[21,22] The extent to which these factors overlap however remains an important aspect for future research.

The current study has also established that women diagnosed with urinary tract infection during pregnancy have 3.7 times the odds for spontaneous premature delivery compared to those who deliver at term (CI: 1.8-4.56, p=0.0016). We noted consistency of this result with previous studies such as Wagura et al in Kenya and Mahapula et al in Tanzania.[23,24] Urinary tract infections have been noted to be a potential reservoir for bacteria that ascend via the pregnant woman's lower genital tract to access the fetal membranes where they release a number of proteolytic enzymes such as collagenases and gelatinases with subsequent inflammation and weakening of the involved membranes.[25] In some cases therefore, occult contractions ensue with resultant spontaneous premature labor and delivery.[17,25]

Women with prior history of cervical procedures showed a significant association with spontaneous premature delivery at this hospital. The odds of prior cervical procedures were 4.37 times greater in the women who had spontaneous premature delivery compared to those who delivered at term (CI: 1.42-9.97, p<0.0001). It is possible that these women have had complications of cervical incompetence arising from the cervical procedures per se or probably have suffered recurrent spontaneous premature deliveries and therefore the prior need for cervical procedures. A common example here

could be a Macdonald stitch usually placed in women with history of recurrent painless second trimester pregnancy miscarriages. A previous study in Tanzania reported cervical incompetence as an independent risk factor for premature delivery.[24] There is indeed remarkable consensus in the literature regarding the role of previous precancer cervical lesion treatment and risk of spontaneous premature delivery.[26,27] Sasieni and colleagues have suggested three plausible mechanisms by which cervical treatment could for example increase the risk of spontaneous premature delivery.[27] These include mechanical weakening of the cervix, more subtle histological alterations within the cured cervical tissue thus affecting the tensile strength, and altered cervical antimicrobial mechanisms such as mucus plug formation which allows microbial access to the uterine cavity.

A large proportion of women who had not received preconception care were observed under the cases group than the controls group with odds of 1.67 (CI: 0.93-3.95, p=0.0389). Although not many women had received preconception care and counseling for both study groups (6 out of 110 for cases and 4 out of 330 for controls), the conclusion that this variable is a risk factor for spontaneous premature delivery calls for special attention to encourage women planning to conceive to seek for this service through continuous health education and sensitization awareness campaigns as part of tools that could ameliorate this problem. Health facilities need to formulate preconception care protocols in a way that enhances effectiveness of preconception care services.

Regarding BMI, the current study has revealed an independent significant association between obese women and spontaneous premature delivery. The odds of spontaneous premature delivery were more than twice higher in the women with BMI≥30 kg/m^2 compared to the women who delivered at term (CI: 0.61-6.11, p=*0*.0096). Maternal overweight and obesity have both been implicated in increasing the risk for spontaneous premature delivery by previous researchers.[28,29] Whereas normal weight gain during pregnancy has been shown to decrease the risk of having a premature delivery no matter the pre-pregnancy BMI, our findings stress the need to counsel and advise all women on weight control as well as the need for weight reduction for those who are already obese prior to conception so as to minimize such associated obstetric complications.[29]

Last but not least, despite our core target being pre-pregnancy and prenatal care risk factors for spontaneous premature delivery; our socio-demographic characteristics results deserve an extra comment in here. Although no significant association was observed between the two (socio-demographics and spontaneous premature delivery), we noted that a large proportion of the women who were working as peasant farmers and also those with low total monthly family income of less than 200,000 Uganda shillings in the cases group than the controls group. Similar observations have been presented before by other scholars such as Ayebare et al, Leal et al, Hidalgo-lopezosa et al, and Carcavalli et al where a mixture of socio-demographic characteristics like rural residence, un employed status, low levels of schooling, and a generally low socio-economic status were independently associated with spontaneous premature delivery.[9,15,16,30]

CONCLUSION

A high index of suspicion for spontaneous premature delivery guided by these factors among all pregnant women attending KIUTH is crucial towards ameliorating spontaneous premature delivery in this area.

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