

Research

Maternal, reproductive and obstetric factors associated with preterm births in Mulago Hospital, Kampala, Uganda: a case control study



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Abstract

Introduction: Preterm birth, a leading cause of neonatal mortality accounts for 35 percent of all neonatal deaths worldwide. Uganda's high preterm birth rate of 13.6 per 1000 live births ranks 28th in the world. Efforts at reducing these pre-term births must entail interventions that target any associated risk factors. This study therefore aimed at identifying and describing the risk factors for preterm births among mothers delivering in Mulago Hospital. **VMethods:** This was a case control study among postpartum women in Mulago Hospital. Ninety nine women with preterm newborns were recruited as cases and 193 with full term babies were the controls. A semi-structured questionnaire was used to collect data. Data was entered into Epidata version 3.1 and exported to STATA 11 for univariate analysis and multivariate analysis by logistic regression. **Results:** Risk factors for preterm birth included maternal height less than 1.5 meters (OR 131.08 (20.35-844.02)), rural residence (OR 6.56(2.68-16.10)) and failure to attend antenatal care clinic (OR 8.88(1.44-54.67)). Pregnancy related risk factors included PPROM (OR 287.11(49.26-1673.28)), antepartum haemorrhage (OR 7.33(1.23-43.72)) and preeclampsia/eclampsia (OR 16.24(3.11-84.70)). **Conclusion:** Preterm birth is more likely to occur in women of short stature, living in rural areas and those who do not attend antenatal care clinic. The preterm birth risk is higher for women who get PPROM, APH and preeclampsia/eclampsia in pregnancy. Early recognition and management of these high risk conditions among pregnant women may lead to a reduction in preterm birth rates.

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Introduction

Preterm birth defined as delivery of a baby before 37 completed weeks of gestation, is associated with complications that lead to one million child deaths annually among neonates. It is also associated with increased risk of post neonatal mortality, long term neurological impairment, stunting and development of non-communicable diseases in adulthood [1]. Preterm birth is a major public health problem worldwide occurring in six to 10 percent of births in high income countries and up to 15 percent in low income countries. The highest burden (85%) for preterm birth is concentrated in Africa and Asia [2]. In sub-Saharan Africa, studies conducted in Gambia and Tanzania estimated the preterm birth incidence of 10.9 and 12 percent respectively [3, 4]. Uganda is the 28th country worldwide with a high preterm births rate of 13.6 per 1000 live births [5]. These preterm births are directly responsible for 25 percent of the 27 neonatal deaths per 1,000 live births [6, 7]. In order to achieve the new global targets for neonatal mortality of less than 10 deaths per 1000 live births by 2035 [1], Uganda indeed has to work harder than before to reduce preterm birth incidence. This will require identifying ways to address preventable causes of preterm birth as a priority in low income countries [2]. Whereas several demographic, social, obstetric and pregnancy related risk factors contributing to preterm births have been identified in other countries, these vary in different regions of the world with major disparities evident between high and low income countries [2]. However, there is limited evidence about the risk factors for preterm birth in the local setting that would be central in formulating preventive interventions. This study therefore examined factors associated with preterm birth so as to inform formulation of interventions for reducing preterm births.

Methods

Study design, site and population: This was a case-control study conducted in Mulago Hospital postnatal ward and Special care Unit (SCU). Mulago hospital is the National referral and teaching hospital for Uganda located in Kampala city. The postnatal ward admits approximately 50-80 admissions daily of women who deliver from the labour ward. The SCU is the neonatal intensive care unit for the hospital. It admits preterm and sick full term babies born either in Mulago Hospital or in other neighbouring health centres. Women whose babies are in SCU remain on the postnatal ward until their babies are discharged. All women who gave birth either vaginally or by Caesarean section were recruited into the study. The New Ballard's Score (NBS) for estimating maturity was used to assess the gestational age of the newborns at birth [8]. Cases were selected using the LNMP based gestational age but at analysis, only those babies with NBS scores of 10 to 31 corresponding to gestational ages 28 to 37 weeks were considered as cases. The allocation to control or cases group was based only on the NBS score irrespective of their gestational age by LMNP.

Case definition: A preterm birth was defined as birth of a baby before 37 completed weeks of gestation [9]. All women who gave birth to preterm babies at hospital or at home, and were admitted in Mulago Hospital during the study period, within 72 hours after delivery and consented to the study were included. The controls were women who gave birth to full term babies from Mulago Hospital during the study period, within 72 hours after delivery and who consented to the study. Only women who were 72 hours postpartum or less were selected for the study to ensure accuracy of the NBS tool for estimating prematurity. We excluded all women who were very sick/weak and unable to answer the questions; those with critically ill babies.

Sample size determination: The Kelsey formula for estimating sample size for case control studies was used [10]. Basing on a study on risk factors associated with preterm births in Gaza, where attendance of less than 4 antenatal visits was a risk factor for preterm births [11] and a case to controls ratio of 1:2, we enrolled a total of 296 participants (99 cases and 197 controls). However, some of the data from controls was incomplete therefore only 193 participants were included in the analysis.

Sampling procedure: Consecutive sampling was used because of the limited number of preterm deliveries. Controls were selected following the cases from the birth register in the labour ward. Once a case was recruited, the two subsequent women with full term babies were selected as controls. In case a selected woman did not fit the criteria or declined to consent, the next woman on the register would be selected. Interviewer administered semi-structured questionnaires were used to collect information from the mothers enrolled in the study.

Quality control: A two days training for research assistants (qualified nurses) was conducted on topics such as; recruitment process, eligible participants, obtaining consent, filling the questionnaire, using the NBS, accessing information from the medical records and research ethics. The questionnaires were pre-tested among women who had delivered from a midwifery led labour ward and adjusted to capture the intended information.

Data management: Data was collected using a structured questionnaire, entered into a database using EPI DATA 3.1 and analysed using STATA version 11. Bivariate analysis was conducted on the socio-demographic, maternal and pregnancy related factors by comparing with the outcomes to obtain crude odds ratios. P-values below 0.05 were considered significant at confidence intervals of 95%. Maternal and infant characteristics were compared among cases and controls using descriptive statistics. Factors with a p-value of less than 0.1 were entered into logistic regression by backward stepwise method to identify factors independently associated with preterm birth.

Ethical considerations: This study was conducted in accordance with the declaration of Helsinki guidelines for protection of human participants. Approval to carry out this study was obtained from the institutional review board of the school of health sciences, Makerere University (SHSREC REF 2013-24) and Mulago Hospital Ethics Committee (MREC 400). Written informed consent was obtained from all the mothers enrolled in the study and serial numbers were used instead of participants' identifying information.

Results

As presented in Table 1, the mean age of mothers with preterm births of 24 years (SD = 5.2) was similar to that of the controls: 24 years (SD = 5.3). The median maternal height was 1.56 (range, 1.2-2.0) metres for the cases lower than for controls which was 1.60 (range, 1.41-1.76) metres. As shown in Table 2, the mean gestational age according to the NBS was 32.7(SD = 2.4) weeks for the cases and 41.9(SD = 1.1) weeks for controls. The median age since birth for the babies was 22(range, 2-72) hours among the cases, higher than 14 (range 2-69) hours among the controls.

Bivariate analysis: Bivariate analysis results are presented in Table 1, Table 3 and Table 4. Factors found to be associated with preterm birth at bivariate analysis were maternal height less than 1.5 metres, body mass index equal or more than 25.0kg/m², rural

residence of mothers and failure to attend all the antenatal visits. Factors in the index pregnancy found statistically significant were; pre-eclampsia/eclampsia ($p = 0.014$), PPRM ($p = <0.001$), APH ($p = <0.001$), and trauma to the abdomen in index pregnancy ($p = 0.033$). No medical condition in pregnancy showed an association with preterm birth.

Multivariate analysis of factors associated with preterm birth: As presented in Table 5, Risk factors independently associated with preterm birth were height less than 1.5 metres (aOR = 131, 95% (CI: 20.35-844.02)); rural residence (aOR=6.56, 95% CI: (2.64-16.10)); being unemployed (aOR= 0.36, 95%(CI: 0.15-0.86)); failure to attend antenatal clinic (aOR=8.88 (95% CI: 1.44-54.67)); and PPRM, APH or preeclampsia/eclampsia in the index pregnancy with p -values of <0.001 , 0.03 and 0.001 respectively .

Discussion

The mean age of mothers of preterm newborns and that of full term newborns was comparable at 24 years. This could be due to the fact that the median age at first birth in Uganda is 19 years and the study included both primiparous and multiparous women [6]. Women with height less than 1.5 metres were more likely to have preterm birth as opposed to their taller counterparts. Although most studies [3, 12] have shown a positive association between maternal height and small for gestational age babies, an association with preterm birth also exists. In Norway and Gaza women of short stature (less than 1.63metres) had a higher likelihood for getting a preterm birth than taller women [11, 13]. Short stature may be a reflection of previous poor socioeconomic conditions and inadequate nutrition during childhood and adolescence [6]. In this study being unemployed reduced the chances of getting a preterm birth by 64 percent. On the contrary, a case control study in Portuguese maternities found that women getting pregnant while unemployed were 1.5 times more likely to have preterm births than working women [14]. Type of employment may however have an impact on a pregnant woman depending on whether it is manual or labour intensive. In Korea, women employed in jobs with manual labour were more likely to have preterm births compared to those in non-manual work [15]. In 2011, the UDHS showed that only 69 percent of Ugandan women were employed. In addition, majority (57%) of women were reported to work in the agricultural sector which is labour intensive while only five percent were in managerial positions [6]. Women residing in rural areas were more likely to have preterm birth in this study. Other studies have also shown that women residing in areas of lower education levels, with manual work and far from health facilities like rural areas are more likely to have poor birth outcomes [16, 17]. This is contrary to a study in Beijing which found women in cities and urban centres to be more likely to have preterm births [18]. In Uganda, rural women are more likely to be of low education, involved in manual work such as farming and have poor access to health facilities.

Studies in Beijing, Gaza and USA established the increased risk of preterm birth among women who do not get antenatal care in line with findings of this study [12, 18, 19]. In Zimbabwe also, lack of antenatal care attendance was found to double the risk of preterm birth [20]. Interventions during antenatal care such as CenteringPregnancy and other health education interventions were shown to reduce preterm birth rates by 47 percent in a low income setting [21]. Preterm premature rupture of membranes was independently associated with preterm birth. Moreover, it has been associated with 40 to 45% of all preterm deliveries [22]. This could be due to the reduced ability to prolong pregnancies due to facility and individual factors in low income countries. Similar to studies

conducted in Gambia and Zimbabwe, women who had experienced antepartum haemorrhage were more likely to have a preterm birth in this study [4, 20]. Although APH is one of the danger signs of pregnancy which are communicated to pregnant women during antenatal care, its management depends on how quickly the woman gets to a health facility. In the case of placenta previa, it would be diagnosed on ultrasound in the third trimester but this is not common practice in Uganda. Pre-eclampsia/eclampsia is a major cause of poor birth outcomes worldwide including preterm birth, intra uterine growth retardation and intra uterine foetal death. Studies have shown preeclampsia/eclampsia to be another cause of medically induced preterm delivery [23]. This study found that mothers with preeclampsia or eclampsia were 16 times more likely to have a preterm birth. Studies in Gambia and Beijing and Australia found similar findings [4, 18, 24].

Limitations: This being a case control study in design, recall bias could have occurred where some of the mothers were unable to remember some events in their previous pregnancies or even in the index pregnancy. Self-report was used for most of the parameters such as malaria during pregnancy which could have affected the findings. This limitation was overcome by review of the participants' medical records. Including primiparous women in this study may have reduced the ability of this study to establish relationships between previous pregnancy factors and preterm birth.

Conclusion

Women with height < 1.5 metres; those residing in the rural areas; who did not attend antenatal care are more likely to have preterm births. The same is true for women who get preterm premature rupture of membranes, antepartum haemorrhage and preeclampsia. Early identification and prompt management of these factors can help reduce the rates of preterm births.

What is known about this topic

- Preterm birth is one of the leading causes of neonatal mortality;
- Some of the intrapartum risk factors include preeclampsia, preterm premature rupture of membranes and antepartum haemorrhage;
- Interventions to prevent preterm births have been suggested including use of antenatal corticosteroids and tocolytics in preterm labour.

What this study adds

- First, maternal height is a risk factor for preterm birth in the Ugandan setting;
- Secondly, antenatal attendance is still a key factor in reducing adverse pregnancy outcomes such as preterm birth;
- Lastly, multiple pregnancies present a real risk for preterm birth therefore, they should be managed in health facilities with adequate facilities for care of preterm babies.

Competing interests

The authors declare no competing interests.

Authors' contributions

Elizabeth Ayebare conceived of the study, participated in proposal development, data collection, analysis and drafting of the manuscript, Gorrette Nalwadda participated in proposal development, data analysis and writing of the manuscript, Peter Ntuyo participated in proposal development and manuscript writing. Oliver Ombeva Malande participated in data collection, analysis and manuscript writing. All authors read and approved the final manuscript.

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Tables

Table 1: Maternal socio-demographic characteristics

Table 2: Demographic characteristics of newborns examined using New Ballard's score

Table 3: Association between reproductive factors and preterm birth

Table 4: Association between obstetric factors and preterm birth

Table 5: Crude and adjusted odds ratios of factors associated with preterm birth after logistic regression

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| Table 1: Maternal socio-demographic characteristics | | | | |
|--|--------------------|------------------------|----------------------------|------------------|
| Variable | Case (n=99) | Control (n=193) | cOR(CI) | p-value |
| Mother's Age* | | | | |
| Less than 18yrs | 4 | 9 | 0.86 (0.26- 2.85) | 0.800 |
| 18yrs and above | 95 | 183 | 1 | |
| Marital status | | | | |
| Married | 88 | 173 | 1 | |
| Single | 11 | 20 | 1.08(0.51-2.36) | 0.844 |
| Height (m) | | | | |
| Less than 1.5 | 35 | 3 | 34.63(10.30-116.46) | <0.001 |
| 1.5 and above | 64 | 190 | 1 | |
| Pre-pregnancy BMI | | | | |
| Less than 25.0 | 53 | 147 | 1 | |
| 25.0 and above | 46 | 46 | 2.77(1.66-4.64) | <0.001 |
| Post pregnancy BMI | | | | |
| Less than 25 | 47 | 126 | 1 | |
| 25.0 and above | 52 | 67 | 2.08(1.23-3.51) | 0.003 |
| Employment | | | | |
| Yes | 60 | 92 | 1 | |
| No | 39 | 101 | 0.59(0.36 - 0.97) | 0.037 |
| Residential area | | | | |
| Urban | 40 | 143 | 1 | |
| Rural | 59 | 50 | 4.22(2.44-7.29) | <0.001 |
| Nature of Work | | | | |
| Light/Moderate Manual | 83 | 172 | 1 | |
| Heavy Manual | 16 | 21 | 1.57 (0.73-3.36) | 0.199 |
| Standing for >4 consecutive hours in a day | | | | |
| Yes | 26 | 66 | 1.19(0.64-2.18) | 0.549 |
| No | 42 | 127 | 1 | |
| Level of education | | | | |
| Primary and below | 44 | 64 | 1.64(1.00- 2.70) | 0.051 |
| Secondary and tertiary | 54 | 129 | 1 | |
| *One missing age | | | | |

| Variables | Cases (%) n=99 | Controls (%) n=193 |
|-------------------------------|-------------------|-----------------------|
| Birth Weight* | | |
| Low birth Weight <2500g | 96(97.0) | 9(4.7) |
| Normal birth weight ≥2500g | 3(3.0) | 183(95.3) |
| Sex of baby | | |
| Male | 42(42.4) | 95(49.6) |
| Female | 57(57.6) | 98 (50.8) |
| Mode of delivery | | |
| SVD | 75(75.7) | 92(47.7) |
| IVD | 2(2.0) | 63(32.6) |
| Elective C/S | 6(6.1) | 11(5.7) |
| Emergency | 16(16.2) | 27(14.0) |
| Birth Type^a | | |
| Singleton | 81(81.8) | 193(100) |
| Multiple | 18(18.2) | 0(0) |

* Frequency is 291 due to 1 missing weight. SVD- spontaneous vaginal delivery; IVD-Induced vaginal delivery; C/S-caesarean section

| Variable | Case (%) | Control (%) | cOR (CI) | | P values |
|--|-----------|-------------|-------------------|--------|----------|
| Parity | | | | | |
| Primipara | 36(36.4) | 83(43.0) | 0.76(0.46-1.25) | 0.275 | 0.275 |
| Para 2- 9 | 63(63.6) | 110(57.0) | 1 | | |
| Antenatal clinic attendance | | | | | |
| Attended | 91(91.9) | 189(97.9) | 1 | | |
| Did not attend | 8(8.1) | 4(2.1) | 4.15(1.22 -14.15) | 0.023 | 0.023 |
| No. of antenatal visits* | | | | | |
| 1- 3 visit(s) | 72(79.2) | 83(43.9) | 1 | | |
| 4 or more visits | 19(20.8) | 106(56.1) | 0.21(0.11 -0.38) | <0.001 | <0.001 |
| Gestational age at first ANC attendance** | | | | | |
| First trimester ≤12 weeks | 20(22.0) | 42(22.2) | 1.01(0.55-1.84) | 0.98 | 0.98 |
| 2 nd or 3 rd trimester | 69(75.8) | 146(77.8) | 1 | | |
| Inter-pregnancy interval*** | | | | | |
| ≤12 months | 6(9.2) | 23(19.5) | 0.42(0.16-1.09) | 0.075 | 0.075 |
| More than 12 months | 59(90.8) | 95(80.5) | 1 | | |
| Use of family planning methods | | | | | |
| Yes | 53(53.5) | 75(38.9) | 1.81(1.11-2.96) | 0.017 | 0.017 |
| No | 46(46.5) | 118(61.1) | 1 | | |

*Out of 280 participants who attended antenatal clinic. ** 2 participants not sure of age at first ANC attendance.
***Frequency out of 186 participants

| Table 4: Association between obstetric factors and preterm birth | | | | |
|---|--------------|-----------------|----------------------------|------------------|
| Variable | Cases | Controls | cOR (CI) | p- value |
| Previous Pregnancy factors | n=66 | n=120 | | |
| Previous preterm birth | | | | |
| Yes | 2 | 1 | 3.72(0.19-221.17) | 0.287 |
| No | 64 | 119 | 1 | |
| Previous abortion | | | | |
| Yes | 19 | 48 | 0.61(0.30-1.21) | 0.128 |
| No | 47 | 72 | 1 | 1 |
| Bleeding before 28 weeks in previous pregnancy | | | | |
| Yes | 1 | 4 | 0.45(0.01-4.64) | 0.657 |
| No | 65 | 116 | 1 | |
| Previous still birth | | | | |
| Yes | 4 | 7 | 1.04(0.21-4.29) | 0.950 |
| No | 62 | 113 | 1 | |
| Index pregnancy obstetric factors | n=99 | n=193 | | |
| PPROM | | | | |
| Yes | 39 | 2 | 62.08(15.08-537.86) | <0.001 |
| No | 60 | 191 | 1 | |
| Antepartum Haemorrhage | | | | |
| Yes | 12 | 4 | 6.52(1.89-28.32) | <0.001 |
| No | 87 | 189 | 1 | |
| Pre-eclampsia/eclampsia | | | | |
| Yes | 9 | 5 | 3.76(1.08-14.64) | 0.014 |
| No | 90 | 188 | 1 | |
| Bleeding before 28 weeks of gestation | | | | |
| Yes | 8 | 11 | 1.45(0.49-4.12) | 0.435 |
| No | 91 | 182 | 1 | |
| Incompetent cervix | | | | |
| Yes | 4 | 3 | 2.67(0.44-18.50) | 0.189 |
| No | 95 | 190 | 1 | |
| Trauma to abdomen | | | | |
| Yes | 6 | 28 | 0.38(0.12-0.98) | 0.033 |
| No | 93 | 165 | 1 | |

| Table 5: Crude and adjusted odds ratios of factors associated with preterm birth after logistic regression | | | |
|---|----------------------------------|------------------------------------|------------------|
| Variable | Crude Odds Ratios (95%CI) | Adjusted Odds Ratio (95%CI) | P- value |
| Height(metres) | | | |
| Less than 1.5 | 34.63(10.30-116.46) | 131.08(20.35-844.02) | <0.001 |
| 1.5 and above | 1 | 1 | |
| Educational level | | | |
| Primary or None | 1.64(1.00-2.70) | 1.46(0.61-3.49) | 0.395 |
| Secondary and above | 1 | 1 | |
| Prepregnancy BMI (Kg/m²) | | | |
| Less than 25.0 | 1 | 1 | |
| 25.0 and above | 2.77(1.66-4.64) | 1.49(0.62-3.60) | 0.372 |
| Employment status | | | |
| Employed | 1 | 1 | |
| Unemployed | 0.59(0.36-0.97) | 0.36(0.15-0.86) | 0.021 |
| Residential area | | | |
| Urban | 1 | 1 | |
| Rural | 4.22(2.44-7.29) | 6.56(2.68-16.10) | <0.001 |
| Antenatal attendance | | | |
| Attended | 1 | 1 | |
| Did not attend | 4.15(1.22-14.15) | 8.88(1.44-54.67) | 0.019 |
| Family planning Use | | | |
| Yes | 1.81(1.11-2.96) | 2.11(0.86-5.20) | 0.104 |
| No | 1 | 1 | |
| PPROM | | | |
| Yes | 62.08(15.08-537.86) | 287.11(49.26-1673.28) | <0.001 |
| No | 1 | 1 | |
| APH | | | |
| Yes | 6.52(1.89-28.32) | 7.33(1.23-43.72) | 0.029 |
| No | 1 | 1 | |
| Preeclampsia/Eclampsia | | | |
| Yes | 3.76(1.08-14.64) | 16.24(3.11-84.70) | 0.001 |
| No | 1 | 1 | |
| Trauma to the abdomen | | | |
| Yes | 0.38(0.12-0.98) | 0.20(0.36-1.05) | 0.057 |
| No | 1 | 1 | |