RISK FACTORS ASSOCIATED WITH PRETERM BIRTH AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA: UNMATCHED CASE CONTROL STUDY

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By

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CERTIFICATION

The undersigned certifies that she has read and hereby recommends for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled*:* ***Risk factors associated with preterm birth at Muhimbili National Hospital, Dar es salaam, Tanzania: Unmatched hospital-based case-control study,*** in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine in Obstetrics and Gynaecology of the Muhimbili University of Health and Allied Sciences.

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Dr. Fadhlun M. Alwy, MD, MMed, MPH

(Supervisor)

_____

Date

DECLARATION AND COPYRIGHT

I,Dr. Mujuni R. Njunwa, declare that this **dissertation** is my own original work, and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature…… **Date**……

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DEDICATION

This thesis is dedicated to my family, Dad, Mum, my siter , my bother, my sister in law and my nephew.I would like to thank them for their love, encouragement and support through this long journey. You are so special to me in an unspeakable ways.

ABSTRACT

Background

Preterm birth, birth of a baby prior to 37 weeks gestation age, is one of the major public health burdens worldwide. It has far reaching consequences to the mother and the newborn with both short-term and long-term effects. It is estimated that more than one in ten babies were born prematurely worldwide in 2010 making approximately 15 million preterm births, of which more than 1 million died due to the complications of preterm birth. Dealing with premature babies has been seen to pose a number of challenges due to inadequate care provided to these babies. In order to combat this burden, reduction of preterm birth should be highly emphasized. This can be done by first identifying the risk factors associated with preterm birth and then come up with appropriate preventive measures.

Objective

The objective of this study was to determine the risk factors associated with preterm birth at Muhimbili National Hospital, Dar es Salaam, Tanzania.

Methodology

Unmatched hospital-based case-control study was conducted between Feb 2015 and April 2016 involving 140 cases who were women who delivered preterm babies between 28 and 36 weeks and 280 controls who were women who delivered term babies at 37 weeks gestation or more at Muhimbili National Hospital. Data collection was through face to face interview using a questionnaire which contained information on socio-demographic characteristics of the women, maternal factors and fetal factors and it was supplemented by maternal data from the case notes and antenatal cards. Data analysis was done using IBM SPSS version 20. Chi square and Odds ratio (OR) with 95% CI were used to assess the relationship between independent variables and dependent variables. T-test was used for continuous variables. Logistic regression was done to find independent risk factors associated with preterm birth. *P* value < 0.05 was considered significant.

Results

The prevalence of prematurity in this study was 17.9%. Factors that were independently associated with preterm birth after adjusting for confounders were few number(<2) of antenatal visits (AOR=2.8, 95%CI 1.5-5.1), antepartum hemorrhage (AOR = 6.2, 95% CI 3.3-11.8), maternal hypertension (AOR = 4.9, 95% CI 3.5-6.9), premature rupture of membranes (AOR = 8.4, 95% CI 5.3-13.4), history of preterm birth (AOR = 2.2, 95% CI 1.2-3.9) and history of stillbirth (AOR = 2.1, 95% CI 1.0-4.3) and multiple gestation (AOR = 2.3, 95% CI 1.3-3.9).

Conclusion

Prematurity still remains one of the major public health burdens. This study has highlighted the prevalence of prematurity in our setting and its associated risk factors. Therefore, early detection of these risk factors is recommended in order to help to improve prenatal care especially in high risk pregnancies in order to prevent preterm birth hence reducing significantly neonatal morbidity and mortality.

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LIST OF ABBREVIATIONS

ANCS	Antenatal Corticosteroids
ANC	Antenatal Care
BMI	Body Mass Index
HIV	Human Immunodeficiency Virus
IVH	Intra-ventricular Hemorrhage
LNMP	Last Normal Menstrual Period
MNH	Muhimbili National Hospital
MOHSW	Ministry of Health and **S**ocial Welfare
MUHAS	Muhimbili University of Health and Allied **S**cience
NBS	New Ballard Score
NEC	Necrotizing Enterocolitis
NICU	Neonatal Intensive Care Unit
PI	Principal Investigator
PROM	Premature Rupture of Membranes
RA	Research Assistant
SPSS	Statistical Package for Social Science
SVD	Spontaneous Vaginal Delivery
TDHS	Tanzania Demographic Healthy **S**urvey
UN	United Nations
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Preterm birth

It is defined as any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the woman's last normal menstrual period (1)

Gestation age

It is the age of an embryo or fetus in weeks often calculated from the first day of the woman's last menstrual period to the current date.

Antepartum hemorrhage (APH)

This is defined as bleeding from or into the genital tract, occurring from 28th week of pregnancy and prior to the birth of the baby(2).

Preterm Premature Rupture of Membranes

It is defined as a spontaneous rupture of the fetal membranes before the onset of labor any time beyond 28th week of pregnancy but less than 37 weeks gestation(3)

INTRODUCTION

Preterm birth is defined as any birth before 37 completed weeks of gestation, or fewer than 259 days since the first day of the women's last normal menstrual period. It can be subcategorized based on gestational age into either extremely preterm (<28 weeks), very preterm (28–<32 weeks), or moderate or late preterm (32–<37 completed weeks of gestation. The subcategories are directly linked to increased neonatal morbidity and mortality, physical and neurological disabilities and the need for intensive care (1).

Preterm birth is one of the major public health burdens worldwide and it poses problems due to its short-term and long-term consequences(4). It is estimated that more than one in ten babies were born prematurely worldwide in 2010 making it approximately 15 million preterm births, of which more than 1 million died due to the complications of preterm birth(5,6).

Apparently the number of preterm births is on the increase from 9.6% in 2005 to 10% in 2010(4). The percentage of infants born late-preterm (34 to 36 weeks of gestation) in the US increased from 8.2% in 2000 to 8.8% in 2008 while the percentage of newborns delivered early-preterm (less than 34 weeks of gestation) was 3.6 percent in 2008 which was higher compared to 1.93 percent in 2000(7,8).

The global distribution of premature birth rates seems not to be uniform. The lowest incidence of preterm birth has been reported in Europe (6.2%) and Oceania mainly Australia and New Zealand (6.4%)followed by Latin America & the Caribbean (8.1%) and Asia (9.1%) and finally Africa of which the incidence has been shown to be as high as (11.9%) (4). Studies which were done in some West African Countries like Gabon, Togo and Cameroon showed the variation in the rate of prematurity ranging from 11.1% to 57% (9). One study done in Tanzania found that 12% of mothers who had live births gave birth to preterm babies(10).

Prematurity is the leading cause of death for newborns in the first month of life and the second most important cause of death in children under five years worldwide after pneumonia (11)**.** Its effects are not on the neonatal deaths only, children who are born prematurely also have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory diseases as compared to children born at term(4). The morbidity associated with preterm

deliveries often prolongs to later life, resulting in huge physical, psychological and economic problems(12). One study conducted across Tanzania, Kenya and Uganda trying to ascertain an association between prematurity and neonatal mortality found that 28% of neonatal mortality was associated with prematurity(13). According to Tanzania Ministry of Health, Social and Welfare, the complications of preterm birth contribute to about 23% of newborn deaths. (14).

Dealing with premature babies has been seen to pose a number of challenges. In many low- and middle- income countries there is still lack of minimum care of preterm babies and for those with these services, the quality is still insufficient resulting in short- and long- term consequences such as neurodevelopmental impairment among the survivors(15). In order to combat this burden, reduction of preterm birth should be highly emphasized. This can be done by identifying the risk factors associated with preterm births and then come up with appropriate preventive measures.

LITERATURE REVIEW

Given the key role that preterm birth plays in causing adverse neonatal and childhood outcomes, it is important to know the risk factors that are associated with it. The etiologies of preterm birth are complex and multifactorial. One challenge in attempting to control preterm births worldwide is over half of preterm births remain of idiopathic causes(16).Various studies done worldwide suggest that there are some socio-demographic, maternal and fetal factors that are associated with preterm birth and they are going to be discussed here.

Maternal age has been shown to be an important determinant of adverse pregnancy outcome. One cohort study done in Utah looking at an association of young maternal age with adverse maternal outcome involving 134088 teenage mothers aged 13 to 24 years old, found that, those aged 13-17years old had higher risk of preterm births (17). The reason for this association was thought to be the biological immaturity of these teenage mothers. Advanced maternal age of 35years or older has also been found to be associated with higher incidences of preterm birth, early neonatal mortality, low birth weight and NICU admissions when compared with women aged 20-34 (18). This is due to the fact that advanced aged women tend to be associated with untoward medical and obstetrical conditions such as hypertension, diabetes mellitus, antepartum hemorrhage, placenta praevia and chromosomal abnormalities which can lead to fetal congenital malformation (19,20).

Maternal nutritional status is another determinant factor on the pregnancy outcome. It has been shown that the risk of spontaneous preterm birth is high in women having low body mass index BMI(<19) before conceiving or gaining little weight during pregnancy as well as those with pre-pregnancy obesity (21–23). Low body mass index is associated with diminished amount of some important nutrients like minerals, vitamins and amino acids necessary for the maintenance and wellbeing of any pregnancy

More studies have shown that low socioeconomic status of a woman has an effect on preterm birth. This has been evident in some studies done in the US whereby high preterm birth rates were observed among black Americans(16-18%) who are supposedly having low socioeconomic status compared to white Americans(5-9%) (24,25). Similar findings were

observed in an ecological study done in the UK which came out with a conclusion that women from very deprived areas had nearly twice the risk of having very preterm birth as those living in the least deprived areas (26). Level of education is another socio-demographic factor that has been found to be associated with preterm birth. It has been seen that the lower the level of education the higher is the likelihood of having preterm birth (27).

More maternal factors have also been implicated in the adverse pregnancy outcome. Preterm PROM has been seen to be highly associated with spontaneous onset of labor leading to preterm delivery (24).This leaves the fetus prone to infections due to lack of barrier preventing the ascending microbes from getting into the uterus. Obi et al in their retrospective study on pre-term premature rupture of fetal membranesfound that large percent of women having PPROM ended in delivering preterm babies (28). Preterm PROM on the other hand has been seen to be associated with antepartum vaginal bleeding in more than one trimester, current cigarette smoking and previous preterm delivery. One study found that the relative risk of preterm PROM to be 7.4, 2.1 and 2.5 among women with antepartum vaginal bleeding in more than one trimester, current cigarette smoking and previous preterm delivery respectively (29).

Preterm birth has also been seen to be having the tendency of recurrence making the subsequent pregnancies at risk of preterm births as well. Both subtypes of preterm births, spontaneous preterm birth and medically induced preterm birth are implicated. Among other reasons, inflammation of the placental membranes seems to be a contributing factor to this condition (30,31).One prospective study done in Tanzania by Mahande et al found that 17% of women with preterm birth had 2.7-fold risk of recurrent preterm birth in the subsequent pregnancies as compared to those with previous term birth (32).

Furthermore, short interval between one pregnancy and the other increases the risk of preterm birth. Although no optimal inter-pregnancy interval has been established, most studies have found that the risk of preterm delivery is greater when the interval is less than 12 months (33–35).This is likely due to the fact that the mother has not yet replenished essential nutrients for

maintaining the pregnancy such as iron and folic acid depleted by the previous pregnancy(36).

Inadequate number antenatal visits have been found to increase the odds of preterm birth. In Cameroon one cross-sectional study done by Chiabi et al found that the risk of preterm births was higher among those women who had few antenatal care visits(9). Similar findings were observed in another study done in Nigeria where they also found that the likelihood of preterm birth was higher among women with few(<4) number of antenatal care visits as compared to those with adequate visits(37).

Additional studies have shown that some infections like chorioamnionitis, urinary tract infection, bacterial vaginosis, malaria, sexually transmitted infections like syphilis and HIV during pregnancy are highly associated with preterm birth.(38–41).

More over, stressful life events during pregnancy such as domicile misunderstandings and conflicts, strenuous work, standing for a long time as well as social stress, may expose a woman to preterm delivery(42,43). The explanation behind this association is that stress activates maternal and fetal Hypothalamic-Pituitary-Adrenal axis which in turn stimulates preterm labor pathways.

Risk behaviors such as smoking and excessive alcohol consumption play significant role in preterm birth as well (38). With regards to alcohol consumption, one population-based study done in USA found that prenatal alcohol use elevated the risk of preterm birth (44). Smoking indirectly increases the risk of early preterm birth by increasing the likelihood of preterm premature rupture of membranes and preterm labor (45). More studies have shown an association between substance abuse and preterm birth (46).

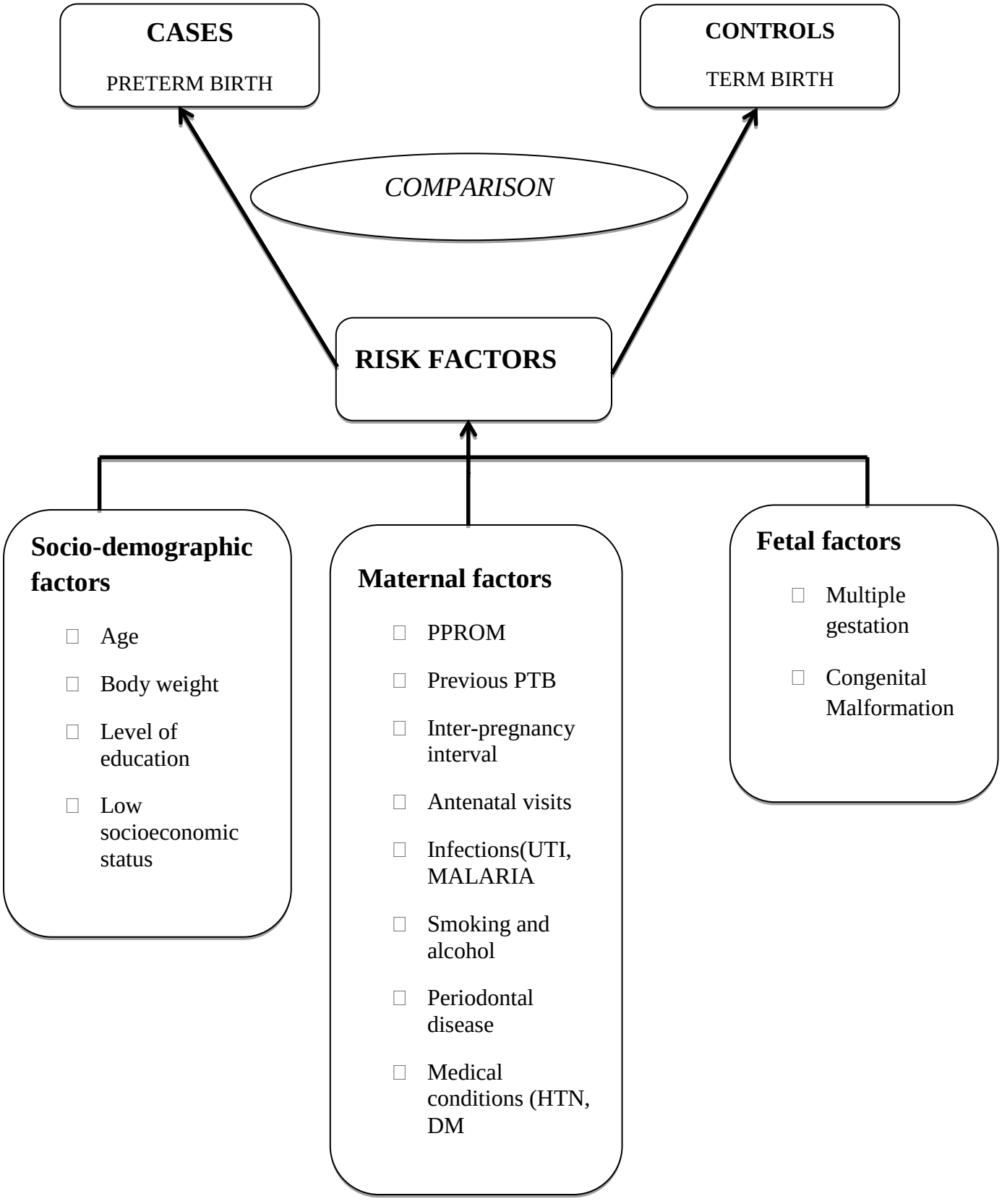
There is inconsistency of results on periodontal disease as a risk factor for preterm birth. One meta-analysis found the likelihood of preterm births among women with periodontitis to be 2.73 (47). In contrast, another meta-analysis found that periodontal disease treatment during pregnancy did not confer a general protection against preterm birth and low birth weight (48).

However, according to American Dental Hygienists Associations women with periodontal disease are 3 to 5 times at greater risk of preterm birth compared with healthy women with no periodontal disease.

Various studies demonstrated that maternal medical and obstetric disorders play important role in scaling up preterm birth rates globally. Conditions like antepartum hemorrhage, pregnancy-induced hypertension, diabetes mellitus, thyroid dysfunction have been shown to increase the odds of preterm birth (49–53).

Fetal factors commonly associated with preterm birth are multiple gestation and congenital malformations. A cross-sectional study done by Chiabi et al in Cameroon found that the likelihood of delivering premature babies for women with multiple gestation and those with fetuses having congenital malformations was3.82 and2.78 times respectively(9).

CONCEPTUAL FRAMEWORK OF THE ASSOCIATED RISK FACTORS FOR PRETERM BIRTH



Dependent variable will be preterm birth. The study aimed at determining the independent variables which are associated with the dependent variable. These include socio-demographic, maternal and fetal factors. In order to be able to ascertain this association adequately between these factors and preterm birth, a control group consisting women with term births was included.

Problem statement

Most of the risk factors for preterm birth are known but are non-specific and show considerable geographical variations. These variations may affect the rates of preterm birth among the regions simply because preterm birth rates depend on the proportion of determining factors at a particular area. Studies in the country are done on the contribution of prematurity on the neonatal outcomes and have not looked on the risk factors associated with preterm birth. Hence, there is a need to find these risk factors in the local setting.

Rationale of the study

The management of preterm babies and their complications still faces considerable challenges especially in developing countries due to lack of necessary care and facilities such as standard neonatal intensive care units (NICU) which would otherwise improve their survival(15,54).Since prematurity contributes enormously to the burden of neonatal mortality and morbidity, identification of the risk factors that contribute to preterm birth in our setting is necessary if we want to come up with strategies for its prevention that are etiologically based and region specific. The information obtained will possibly be used as a platform for future researches and facilitate the planning and implementation efforts for preterm birth prevention in Tanzania.

Research question

Are there factors related to the increased risk of preterm birth at MNH, Dar es Salaam?

Objectives

General objective

To determine risk factors associated with preterm birth at MNH, Dar es Salaam, Tanzania.

Specific objectives

1. To find out the proportion of preterm birth between 28 and 36 weeks gestation among women who deliver at MNH.
2. To identify socio-demographic factors associated with preterm birth at MNH.
3. To determine maternal factors associated with preterm birth at MNH.
4. To identify fetal factors associated with preterm birth at MNH.

METHODOLOGY

Study design

This study was an unmatched hospital based case-control study involving 140 cases which were women who delivered preterm babies between 28 36 weeks compared with 280 controls which were women who delivered term babies at 37 weeks gestation to determine factors associated with preterm birth at MNH, Dar es Salaam.

Study duration

The study was conducted between 23rd October and 4th December 2015.

Study setting

The study was conducted at a tertiary, national referral hospital, Muhimbili National Hospital. The hospital is a teaching hospital for the Muhimbili University of Health and Allied Sciences (MUHAS). Maternity block has four neonatal wards, the labour ward, maternal high dependency unit and four maternity wards which can accommodate 40 antenatal and postnatal women each. MNH offers specialized obstetrics services for Dar es Salaam city and suburban population (4 million people) (National population and housing census 2012). Maternity unit receives women directly from home as well as referred from almost all regional and district hospitals in Dar es Salaam.

The labour ward has four labour rooms which attends about 30-40 deliveries per day. The estimated number of preterm deliveries averages between 60 and 80 per month. This has been extrapolated from the labor ward registry. One of the four labour rooms is for private patients (Intramural Private Practice Muhimbili-IPPM). After delivery, patients are observed in the labor ward for some time before transferred to the wards.

All women admitted at the labour ward have RCH4 card, which summarizes the antenatal visits. Once admitted in the labour ward, women are assessed by a midwife and doctor on call and if they are in true labour, a partograph is started. Progress of labour, delivery data, maternal and neonatal outcome is also recorded in the partogram and case notes. All this information is finally summarized in midwifery book before entering them into the obstetrics data base. Once the baby is born, immediate care is provided. This includes immediate and thorough drying, skin to skin contact of the new born with the mother, cord clamping and

cutting and initiation of early breastfeeding. For newborns who do not start breathing on their own, the resuscitation starts within one minute while the preterm newborns are directly taken to the neonatal unit.

Muhimbili National Hospital has a special neonatal care unit which provides neonatal care to premature newborns and sick babies born at MNH and surrounding hospitals. The neonatal unit has got four rooms and premature babies are admitted in one of the rooms. The hospital has the only public neonatal unit in Dar es Salaam. It has 130 baby cots and admits between 12-25 neonates per day where one third of them are premature. There are two neonatologists and four pediatricians, registrars, resident doctors, intern doctors and nurses. It is important to highlight that, MNH receives a lot of in-utero transfers for preterm care and high risk obstetric women.

Study population

All women who delivered at the gestational age of 28weeks or more at MNH labor ward during the study period

Inclusion criteria

Cases:

All women who delivered at MNH during the study period preterm babies between 28 and 36 weeks and consented to participate in the study.

Controls:

Women who delivered at MNH during the study period term babies at 37weeks gestation or more and consented to participate

Exclusion criteria

Women who were too sick to give consent or refused to participate.

Sample size estimation

Sample size was calculated by using the following formula (73).

$$n = (\frac{r+1}{r}) \frac{(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

Where,

n= Sample size in the case group

r = ratio of controls to cases is 2:1

$\bar{p}$ =The average proportion exposed

Z_{β}= 0.84 for power (1-β) of study is 80%

Z_{α}=desired level of statistical significance, for 0.05 significance level= 1.96

(Z_{α}= the standard normal deviate at 95 confidence level=1.96 for two-sided comparisons depending on the hypothesis being tested).

p_1 = The proportion exposed in the case group

p_2 = The proportion exposed in the control group

Considering that the proportion of hypertension in pregnancy among pregnant women attending ANC at MNH is 16%(55)

To get proportion of cases exposed:

$$p_{case\exp} = \frac{ORp_{controls\exp}}{p_{controls\exp}(OR-1)+1} \quad , \quad p_{case\exp} = \frac{2.0(.16)}{(.16)(2.0-1)+1} = \frac{0.34}{1.17} = .28$$

Average proportion exposed ($\bar{p}$) = (p_1 + p_2)/2=0.28-0.16 /2= 0.22

Thus assuming that, the ODDs ratio =2

r = 2:1

$\bar{p}$ =0.23

Z_β=for 80% power is 0.84,

Z_α= for 0.05 significance level= 1.96

p_1 =0.28

p_2 =0.16

$$n(numberofcases) = (\frac{2+1}{2}) \frac{(0.22)(1-0.22)(0.84+1.96)^2}{(0.28-0.16)^2}$$

=140cases.

Ratio of controls to cases =2:1. Thus controls = 140*2=280 controls.

Thus,

n= cases=140, controls=280 making a total sample size (N) of **420.**

Sampling technique

A non-probability convenience sampling was employed in selecting cases which were women who delivered preterm babies between 28 and 36 weeks gestation. Controls were selected by picking the next two women who delivered term babies after the selected case. Gestation age was estimated from the first day of last normal menstrual period using Naegele's formula and for those not sure of dates, extrapolations from gestation age on booking recorded on antenatal card(ANC) was done.

Recruitment of Patients

Cases and controls were selected from the labour ward registry, which contains a summary of all deliveries from the labour ward as well as from the high dependency maternal unit. The selected cases and control were followed to their admission wards or observation rooms for

face to face interviews after they were clinically stable. The purpose and procedure of the study was explained and those who gave consent and agreed to participate in the study were enrolled in the study consecutively until the sample size was reached.

Data collection

Data collection was done using a well-structured questionnaire. This was a validated questionnaire obtained from some other similar studies and adapted to suit our situation(56–58)**.** It consisted of three parts. The first part included socio-demographic characteristics of the women namely age, occupation, marital status and level of education. The second part of the questionnaire was comprised of maternal factors such as parity, HIV sero-status, past obstetric history (history of previous preterm delivery, stillbirth), infections such as malaria and urinary tract infections and other medical illnesses like hypertension and diabetes during pregnancy. The last part contained questions pertaining to fetal factors such as multiple gestation and congenital malformations. These predictor variables were defined as follows. Hypertension included those who had the blood pressure $\geq$140/90mmHg, malaria included those had symptoms and positive peripheral blood smears for malaria parasites, urinary tract infection (UTI) included those who had symptoms or urine analysis showing urinary tract infection and diabetes mellitus included those who were diagnosed of having raised plasma glucose prior or during pregnancy.

The questionnaire was developed in English then translated into local language: Swahili. Data collection started early in the morning in order to be able to interview the participants especially those who had delivered by spontaneous vaginal delivery (SVD) before they got discharged. Before the commencement of data collection, the questionnaire was tested by interviewing few women for the sake of rectifying the questions to avoid biased responses which might lead to unreliable results. The questionnaire was supplemented by maternal data from the case notes and RCH 4 antenatal card.

Data analysis

Data entry was done after developing the template on IBM SPSS version 20. Before data analysis quick frequency table were run to check for consistency and missed data. After data cleaning, frequencies, means and proportions of variables were computed and tests of significant difference or association between independent variables and dependent variables were done using Chi‑square test or Fisher's exact test where appropriate as well as Odds ratio (OR) with 95% CI. T-test was used for continuous variables. *P* value < 0.05 was considered significant. To determine the independent risk factors for preterm birth, an initial univariate analysis was done to determine maternal socio-demographic, obstetric and fetal factors that were significantly associated with preterm birth. Variables that were significant in univariate analysis were then entered into multivariate analysis in order to find risk factors that were independently associated with preterm birth. The results were reported as adjusted odds ratios (AORs) and 95% confidence limits.

Ethical consideration

Ethical clearance was sought and obtained from MUHAS research and publication committee as well as permission to conduct the study from the Executive Director of MNH. The participants were explained about the research, its purpose, confidentiality and safety. Interviews were done in a manner that observed privacy and the data collected was properly kept to observe confidentiality. Informed consent was sought from all the patients who were eligible for the study. Participation was voluntary and participants were informed that withdrawal from the study at any stage of the interview was acceptable if they so desired without any consequences or prejudice. After the interview, participants were explained about the risk factors of preterm birth, its adverse outcomes and the preventive measures.

RESULTS

During data collection from 23rd October to 04th December 2015, there were 891 deliveries at MNH, of these, 160 were preterm births making a prevalence of 17.9%. The study involved 140 cases which were women who had preterm deliveries (28-36weeks) and 280 controls which were women who had term deliveries (≥37 weeks). Mean gestation age in weeks for cases was 33.01(SD 2.4) while for controls was 38.93(SD 1.4). Mean birth weight in kilograms for cases was 1.9(SD 0.4) while for controls was 3.3(SD 0.4). Slightly over half of the preterm births were induced (51.4%) and spontaneous preterm births were48.6%. Of all deliveries, 39.5% were by spontaneous vaginal delivery (SVD) and 60.5% were by cesarean section (C/S).

Table 1: Socio-demographic and baseline characteristics of the study population

Variables	**Cases n=140(%)**	**Controls n=280(%)**	***p*-Value**
Participant's age			
<18	1 (0.7)	6 (2.1)	
18-34	113 (80.7)	218 (77.9)	0.512
>34	26 (18.6)	56 (20.0)	
Mean ± S.D	***27.99*** *± 6.05*	***28.46*** *± 6.18*	
Education level			
No formal education	4 (2.9)	21(7.5)	
Primary education	66 (47.1)	128(45.7)	0.266
Secondary education	52 (37.1)	102 (36.4)	
College education	18 (12.9)	29 (10.4)	
Marital status			
Single	12 (8.6)	17 (6.1)	
Married/cohabiting	128 (91.4)	263 (93.9)	0.341
Participant's occupation			
Housewife	57 (40.7)	95 (33.9)	
Self employed	56 (40.0)	117 (41.8)	0.318
Employed	27 (19.3)	68 (24.3)	
Parity			
1	54(38.6)	100(35.7)	0.85
2	36(25.7)	75(26.8)	
3+	50(35.7)	105(37.5)	

As shown in table 1, the age of participants ranged from 14 to 45 with the mean age of all study participants of 28.3 years with standard deviation (SD) 6.1. For cases the mean age was 28 years (SD 6), while for controls it was 29 years (SD 6.2) (t = 0.7, P < 0.46).Maternal age, education level, marital status, occupation and parity were not significantly different between the two groups**.**

Table 2. Maternal factors associated with preterm birth

Variables	**Cases n=140(%)**	**Controls n=280(%)**	**OR**	**95%CI**	***p*-Value**
Number of antenatal visits					
0-2	47(33.6)	24(8.6)	5.4	3.12-9.31	**<0.001**
>2	93(66.4)	256(91.4)			
HIV infection					
Yes	9(6.4)	16(5.7)	1.1	0.49-2.63	0.771
No	131(93.6)	264(94.3)			
Urinary tract infection					
Yes	39(27.9)	58(20.7)	1.5	0.93-2.36	0.102
No	101(72.1)	222(79.3)			
Malaria during pregnancy					
Yes	29(20.7)	69(24.6)	0.8	0.49-1.31	0.370
No	111(79.3)	211(75.4)			
Antepartum hemorrhage					
Yes	13(9.3)	4(1.4)	7.1	2.26- 22.09	**< 0.001**
No	127(90.7)	276(98.6)			
Diabetes mellitus					
Yes	0(0)	3(1.1)	1.5	1.41-1.61	0.219
No	140(100)	277(98.9)			
Maternal hypertension					
Yes	64(45.7)	31(11.1)	6.8	4.10-11.15	**< 0.001**
No	76(54.3)	249(88.9)			
Premature rupture of membranes					
Yes	45(32.1)	8(2.9)	16.1	7.33-35.39	**< 0.001**
No	95(67.9)	272(97.1)			
Smoking					
Yes	0(0)	1(0.4)	1.5	1.40-1.61	0.479
No	140	279			
Living nearby smoking person					
Yes	1(0.7)	1(0.4)	2	0.13-32.33	0.616
No	139(99.3)	279(99.6)			
Alcohol					
Yes	0(0)	4(1.4)	1.5	1.408	0.155
No	140(100)	276(98.6)			

Maternal factors that were significantly associated with preterm birth were few number (≤ 2) of antenatal visits, antepartum hemorrhage, maternal hypertension and premature rupture of membrane (Table 2)

Table 3. Maternal past obstetric and foetal factors associated with preterm birth

Variables	**Cases n=140(%)**	**Controls n=280(%)**	**OR**	**95C.I**	***p-Value***
History of preterm delivery [a]					
Yes	23(16.4)	12(6.6)	5.1	2.42-10.95	< **0.001**
No	63(73.3)	169(93.4)			
History of stillbirth [a]					
Yes	13(15.1)	4(2.2)	5.6	1.97-16.13	< **0.001**
No	73(84.9)	177(97.8)			
Interval between this and the previous pregnancy [a]					
< 12 months	8(9.3)	8(4.4)	2.2	0.83-6.125	0.12
≥ 12 months	78(90.7)	173(95.6)			
Birth outcome					
Twins or more	13(9.3)	12(4.3)	2.3	1.01-5.15	**0.046**
Singleton	127(90.7)	268(95.7)			
Congenital malformation					
Yes	1(0.7)	3(1.1)	0.66	0.07-6.45	0.722
No	139(99.3)	277(98.9)			

[a]-54 of the cases and 99 of controls were primipara.

Maternal past obstetric and foetal factors that were associated with preterm birth were, history of preterm delivery, stillbirth and multiple gestation. There was no association established between Inter-pregnancy interval, congenital malformation and preterm birth. (Table 3)

Table 4. Multivariable analysis of factors associated with preterm birth at MNH

Variables	ADJUSTED OR	95 %CI	*P*- Value
Number of antenatal visits			
>2	1		
0-2	2.1	1.4 - 3.0	<0.001
Antepartum hemorrhage			
No	1		
Yes	5.6	2.9 - 10.9	<0.001
Maternal hypertension			
No	1		
Yes	5.1	3.6 - 7.2	<0.001
Premature rupture of membranes			
No	1		
Yes	7.2	4.5 – 11.6	<0.001
History of preterm delivery			
No	1		
Yes	2.3	1.3 – 3.9	0.004
History of stillbirth			
No	1		
Yes	2.2	1.0 - 4.6	0.032
Birth outcome			
Singleton	1		
Twin or more	2.1	1.2 – 3.8	0.013

As shown in table 4, women who had two or less antenatal visits were at least 2 times more likely to have preterm birth compared to those with more than two antenatal visits (aOR = 2.1; 95% CI: 1.4, 3.0). Likewise, women who experienced antepartum hemorrhage were almost 6 times more likely to have preterm birth compared to those who did not (aOR = 5.6; 95% CI: 2.9, 10.9). Similarly, women who had hypertension during pregnancy were 5 more likely to experience preterm delivery compared to those who were normotensive (aOR = 5.1; 95% CI: 3.6, 7.2). Women with preterm premature rupture of membrane were found to be at least 7 times more likely to end up with preterm birth compared to those who had intact membranes (aOR = 7.2; 95% CI: 4.5, 11.6). Those who had previous history of preterm birth were 2 times more likely to have preterm birth in the current pregnancy compared to those who never had such a previous experience (aOR = 2.3; 95% CI: 1.3, 3.9). Similarly, those who had previous history of stillbirth were more than 2 more times likely to have preterm birth compared to

those who never had such a history (aOR = 2.2; 95% CI: 1.0, 4.6). It was observed that multiple gestation increased the odds of preterm birth by 2- folds (aOR = 2.1; 95% CI: 1.2, 3.8).

DISCUSSION

This study was designed to investigate the risk factors that contribute to preterm birth at Muhimbili National hospital. The prevalence of prematurity in our study was 17.9%. This is greater than Europe (6.2%), North America (10.6%), 8.5% reported by Etuk and his colleagues in their study done in Nigeria and 12% reported in one study done in Mwanza, northern Tanzania (4,10,59). This high prevalence can be explained by the fact that Muhimbili National hospital is the national referral hospital with a specialized neonatal unit and it receives a lot of in-utero transfers for premature care as well as high risk obstetric patients from other health facilities. Majority of our study participants were aged between 18-34 years. This was harmonious with other studies(9,37).

Fewer number of antenatal visits is associated with increased risk of preterm birth, women who attended once or twice were more at risk and this is consistent with other studies done in sub-Saharan Africa (9,37). The reason could be missing antenatal visits is a missing opportunity for other risk factors such as hypertension, anemia, infections and others. A low risk woman is expected to have made at least 3 visits using focused antenatal care visits by 32 weeks of gestation, whereas a high risk pregnant woman need more antenatal visits and should have more than 5 visits by 32 weeks of her pregnancy. This study did not investigate specific gestation age and number of visit. However, as the mean gestation age of cases was 33 weeks we would have expected them to have made more than 3 visits, which was not the case in most cases. Improving the coverage, quality and increasing the frequency of prenatal care may mitigate this problem of preterm birth among high risk women.

Maternal bleeding in the third trimester was an independently associated risk factor for preterm birth.The prevalence of antepartum hemorrhage was significantly higher among the cases than in controls, (9.3% versus 1.4%) ($P< 0.001$), and women with history of antepartum hemorrhage were more than six times likely to end up having preterm delivery. This association was also observed in other studies done elsewhere(24,37,60). Bleeding in the third trimester often times leads to maternal complications such as anemia and preterm labor or fetal complications such as fetal growth retardation due to chronic placental insufficiency caused by repeated small bouts of hemorrhage. Such women need early detection and expectant management.

With regard to the effect of maternal hypertension on preterm birth, it was found that having hypertension during pregnancy increased the odds of having preterm birth. This was compatible with some other studies(49,50,61).Those with maternal hypertension were more than five times likely to deliver preterm babies. The pathogenesis of maternal hypertension in pregnancy involves impaired placental implantation which leads to placental hypoperfusion as a result of ischemia, necrosis and even placental infarction causing decreased blood flow to the fetus hence causing poor fetal growth and prematurity among other adverse outcomes (62).This calls for special focus on those women with risk factors of developing hypertension during pregnancy such as primigravida, those with family history of hypertension and diabetes mellitus, multiple gestation and ensuring that they get effective antenatal care or early intervention in case of severe forms of hypertension.

Concerning premature rupture of membrane, thirty two percent of women who delivered preterm babies had more than seven times risk attributable to premature rupture of membrane when adjusted for other risk factors. Premature rupture of membrane has been reported to be associated with preterm delivery in other studies(28,61,63,64).

With regards to the association between previous history of preterm birth and preterm delivery, this study found that previous history of preterm birth was associated with 2.3-fold increased risk of preterm birth. This finding from is consistent with other studies done elsewhere. (37,59,65).A study done in Malawi found that women with prior history of preterm delivery carried a 2.13-fold increase in the risk of preterm delivery in the current gestation compared to those with no prior history of preterm delivery (66).One systematic review showed that there is significantly increased risk of preterm birth recurrence in women having preterm deliveries (67).These women necessitate proper follow-up before delivery in order to be able to pick problems that may surface and manage them accordingly.

Mothers with positive history of stillbirth had 2.2-fold increased risk of having preterm birth in the current pregnancy as compared to their counterparts. Abu Hamad and colleagues in their study reported that women with previous history of stillbirth had a 4-fold increased risk of

delivering preterm babies in their next pregnancy (68). Another study done by Meis et al also found an association between preterm birth and history of previous preterm birth(69).Preventive strategy in this case may involve identifying the causes of stillbirth and deal with them since they may be risk factors for preterm birth in the subsequent pregnancies.

Inter-pregnancy interval wasn't found to have any relationship with preterm birth in this study. This finding is not in agreement with other studies which observed this association(68,70). This inconsistency could be influenced by the differences in the utilization of family planning in these populations.

Likewise concerning fetal factors, this study found an association between multiple gestation and preterm birth. Those women who had multiple gestation had 2.1 times chances of having preterm birth as compared to those who had singleton deliveries. This association has also been reported by other various studies (9,59). Therefore, women with multiple gestation should be regarded as having high risk pregnancies hence proper prenatal care in a specialized facility capable of taking care of premature neonates is highly advocated in case labor starts before term.

However, there wasn't any association found between maternal age and preterm birth. This lack of association was also found in other studies as well(56).In contrast, some studies have reported positive relationship between maternal age $\geq$ 35 years and preterm birth(9,59).The difference here may be because majority of our study participants were aged between 18 and 34 years which is a protective age group for preterm birth.

Smoking and alcohol was not found to be associated with preterm birth in this study as well. However this finding is inconsistent with other studies which showed that women who smoke and/or take alcohol have increased odds of having preterm birth(44,71,72). This may be explained by the fact that culturally and socially smoking is more for men than women hence only few women do smoke in Tanzania.

CONCLUSION

In conclusion, preterm birth is one of the major public health burdens and its risk factors are complex and multifactorial. Identifiable risk factors associated with preterm birth in our setting are antepartum hemorrhage, maternal hypertension, eclampsia, premature rupture of membrane, prior history of preterm birth and stillbirth, multiple gestation and fewer (≤2) antenatal visits.

STUDY LIMITATIONS

- Some important independent variables associated with preterm birth (e.g. pre-pregnancy BMI) could not be studied because most women did not know their weights before conceiving.
- Some risk factors (e.g. Diabetes in pregnancy) were not prevalent which made it hard to establish any association with preterm birth.
- Since this was a hospital-based study, it might not be a reliable reflection about the general population.
- Like any other case control study, this study might have suffered a recall bias since most participants tend to not recall correctly their past experience.
- Since many women tend not to recall accurately their menstrual cycle patterns, the method used to ascertain gestation might have also been a source of limitation.

RECOMMENDATIONS

- Since most risk factors are preventable, improving the quality and quantity of prenatal care will mitigate the problem of preterm birth because high risk women will be identified early and receive specialized care for better perinatal outcome.
- In order to understand better about these risk factors that lead to preterm delivery, multicenter study including even much larger sample size should be devised in order to be able to establish the risk factors associated with preterm birth.

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APPENDICES

Appendix I. Informed Consent (English Version)

MUHIMBILIUNIVERSITY OF HEALTH AND ALLIED SCIENCES
DIRECTORATE OF RSEARCH AND PUBICATIONS, MUHAS
INFORMED CONSENT FORM

ID-NO | | | | |

Consent to participate in a research study

Greetings! My name is Mujuni Rutasera Njunwa and I am a student at Muhimbili University undertaking Masters of Obstetrics and Gynaecology. Currently I am working on this research study on associated risk factors for preterm birth at Muhimbili national hospital.

This study is going to help us determine the proportion of babies who are preterm between 28 and 36 weeks gestation, identify risk factors which are associated with preterm birth at Muhimbili national hospital.

What Participation Involves

If you agree to participate in this study you will be required to spend a few minutes for an interview.

Confidentiality

All information recorded will be entered into computers with only the study identification number. However no participant's name will be published. We do not expect that any harm will happen to you after joining this study.

Rights to Withdraw and Alternatives

Taking part in this study is completely your choice. You are free to choose either to participate in this study or not. You can decide to stop participating in this study any time you wish even if you have already given your consent. Refusal to participate or withdrawal from the study will not involve penalty or loss of any benefits to which you are otherwise entitled

Benefits

If you agree to take part in this study there are no direct benefits that you will get from this study. We believe the information you will provide will help in improving the prevention of preterm birth and its adverse consequences. A small group of scientific experts who are involved in implementing this study will monitor the results of this study and how we conduct this research.

Risks

We do not expect that you will get any physical injury resulting from participating in this study. However, if any injury resulting from participating in this study occurs, we will provide you with medical treatment according to current standard of care in Tanzania. There will be no additional compensations to you.

Who to Contact

If you ever have questions about this study, your rights as a participant, you should contact the principal investigator Mujuni Rutasera Njunwa at the department of obstetrics and gynaecology, Muhimbili University of Health and Allied Sciences, P.O. Box 65015, Dar es Salaam, through Mobile 0655 328494

Or contact Prof. Mainen Moshi of the University Research and Publications Committee, P.O. Box 65001, Dar es Salaam. Tel: 21503026.

Signature

Do you agree to participate?

He/she has agreed…….. He/she has refused…….

I……. have read the content in this form. My questions have been thoroughly answered. I agree to participate in this study

Signature of participant……..

Signature of witness (if participant cannot read) ……

Signature of Researcher…….

Appendix II. Informed Consent (Swahili version)

CHUO KIKUU CHA AFYA NA SAYANSI SHIRIKISHI MUHIMBILI
KURUGENZI YA UTAFITI NA UCHAPISHAJI
FOMU YA RIDHAA

NambayaUtambulisho				

Ridhaa ya kushiriki katika utafiti

Salaam!

Jina langu ni Mujuni Rutasera Njunwa ni Mwanachuo katika chuo kikuu cha Muhimbili ninayesomea shahada ya pili katika uzazi na magonjwa ya wanawake. Kwa sasa ninafanya utafiti kutambua sababu zinazopelekea watoto kuzaliwa kabla miezi tisa haijafika kwenye hospitali ya rufaa ya Muhimbili. Kama utakubali kujiunga katika utafiti huu utatakiwa kujibu maswali utakayoulizwa.

Utafiti huu utatuwezesha kujua kiwango cha wanawake wanaojifungua ndani ya miezi saba na miezi nane na kutafuta sababu zinazochangia hao wanawake kujifungua kwenye hiyo miezi kwenye hospitali ya rufaa ya Muhimbili.

Kushiriki Inahusisha nini?

Ukikubali kushiriki katika utafiti huu utahitajika kutumia muda kidogo kwa ajili ya kujibu maswali utakayoulizwa na mtafiti

Usiri

Majibu yote yatakusanywa kutoka katika eneo la utafiti na yataingizwa kwenye compyuta kwa kutumia namba ya utambulisho tu. Hakuna jina la mshiriki litakalochapishwa. Hatutegemei kwamba kutakuwa na madhara yoyote kwawewe kujiunga na utafiti huu isipokuwa kutumia muda wako tu katika majadiliano.

Haki ya Kutoka na Mbadala

Kushiriki katika utafiti huu ni uchaguzi wako, na una uhuru wa kukubali au kukataa kushiriki katika utafiti huu. Pia unaweza kuacha kushiriki katika utafiti huu muda wowote utakapojisikia hivyo hata kama umeshakubali kushiriki. Kukataa kushiriki au kuacha kushiriki katika utafiti huu hakutakufanya upate adhabu au ukose kufaidika na yale unayostahili kupata.

Faida

Ukikubali kushiriki katika utafiti huu hakuna faida ya moja kwa moja utakayopata lakini tunaamini maelezo utakayoyatoa yatasaidia kupendekeza njia zinazofaa katika kuzuia wanawake kujifungua kabla miezi tisa haijafika na madhara yake. Kundi dogo la wataalam wa utafiti ambao hawahusiki katika kutekeleza utafiti huu watasimamia matokeo ya utafiti huu najinsi utafiti huu utakavyofanyika.

Madhara

Hatutegemei kwamba utapata madhara yoyote ya kimwili kwa kushiriki katika utafiti huu. Hata hivyo ikiwa kutakuwa na madhara yoyote yatakayotokana na kushiriki katika utafiti huu, tutakupa huduma ya matibabu kulingana na viwango vya huduma za afya vya Tanzania. Hakutakuwa na fidia ya nyongeza kwako.

Mawasiliano

Kama utakuwa na swali lolote kuhusu utafiti huu unaweza kuwasiliana na mkuu wa utafiti huu Daktari Mujuni Rutasera Njunwa wa Chuo Kikuu cha Afya ya Tiba ya Sayansi Muhimbili, S.L.P. 65015, Dar es Salaam. Na ukiwa na swali lolote kuhusu haki zako kama mshiriki, wasiliana nami kwa namba 0655328494 au Profesa Mainen Moshi ambaye ni Mwenyekiti wa Kamati ya Utafiti ya Chuo, S.L.P. BOX 65001, Dar es Salaam. Simu: 2150302-6

Sahihi

Je umekubali?

Mshiriki amekubali……..…Mshiriki Hajakubali…….……

Mimi.....nimesoma maelezo ya fomu hii. Maswali yangu yamejibiwa. Nimekubali kushiriki katika utafiti huu.

Sahihi ya mshiriki……...

Sahihi ya shahidi (kama mshiriki hawezi kusoma) ……..

Sahihi ya mtafiti……..

Tarehe ya ukubali wa kushiriki……...

Appendix III. Questionnaire (English Version)

Associated risk factors for preterm birth: case-control study

ID_____

Date: _____/_____/_____

A. Socio-demographic factors

1. Maternal age at delivery (years)….

2.Place of residence…….

3.Marital status

- Single
- Married or cohabiting
- Divorced
- Widow

4. Level of education

- No formal education
- Primary education
- Secondary education
- College education

5. Occupation

- Not employed
- Self employed
- Employed

B. Maternal factors

6. Parity…….

7. Gestational age at delivery…….

8. Mode of delivery

- SVD
- C/S

9. HIV Serostatus

- Positive
- Negative

10. Did you do any antenatal care visits?

- Yes
- No

11. What was the gestational age at the first antenatal visit? (weeks) ……..

12. How many antenatal care visits did you do? .....

13. Were you smoking cigarettes during this pregnancy?

- Yes
- No……..skip question 12

14. If Yes, how many cigarettes per day?.....

15. Do you live/work near a smoking person?

- Yes
- No

16. Were you taking alcohol during pregnancy?

- Yes
- No……..skip question 15

17. If Yes, how many bottles per day?.....

18. Were you taking illicit drugs use during pregnancy?

- Yes
- No

19.Did you ever get urinary tract infection during pregnancy?

- Yes
- No

20. Did you ever suffer from Malaria during this pregnancy?

- Yes
- No

21. Did you havediabetes mellitus during this pregnancy?

- Yes
- No

22. Did you experience any vaginal bleeding after 7 months of pregnancy?

- Yes
- No

23. Did you get hypertension during this pregnancy?

- Yes
- No

24. Did you experience vaginal watery discharge before labor?

- Yes
- No

Skip this part if the patient is Primigravida.

25. Have you ever had any preterm delivery before?

- No
- Yes

26. Have you ever had any stillbirth?

- Yes
- No

27. What is the interval between this and the last pregnancy (months)? …….

C. Fetal factors

28. Number of babies delivered_____

29.Any congenital malformation?

- Yes…….Which one…….
- No

30. Weight of the baby…….(kg)

Appendix IV. Questionnaire (Swahili Version)

Associated risk factors for preterm birth: case control study

Nambari ya utambulisho(ID)_____

Tarehe ya mahojiano: _____/_____/_____

A. Demografia

1. Umri wa mama (Miaka)……

2.Mahali anapoishi……

3.Hali yako ya ndoa
- Sijaolewa
- Nimeolewa
- Tumetarakiana
- Mjane

4. Umesoma mpaka darasa la ngapi?
- Sijasoma
- Elimu ya msingi
- Elimu ya sekondari
- Chuo na zaidi

5. Unafanya kazi gani
- Mama wa nyumbani
- Nimejiajili
- Nimeajiliwa

B. Taarifa za ujauzito wa huyumtoto(wa)

6. Umezaamarangapi?

7.Umriwamimbawakatiwakujifungua……

8. umejifunguakwanjiagani?
- Kawaida
- Upasuaji

9. Je una maambukizi ya VVU
- Ndio

- Hapana

10. Je uliwahi kwenda kliniki wakati wa ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

11. Ulianza kliniki mimba ikiwa na umri gani(wiki)? ……..

12. Ulienda kliniki mara ngapi? .....

13. Je ulikuwa unavuta sigara kwenye ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana……..ruka swali no. 12

14. Kama ndio je ulikuwa unavuta sigara ngapi kwa siku?.....

15. Je ulikuwa unaishi au kufanya kazi karibu na mtu anayevuta sigara wakati wa ujauzito wa huyu mtoto?
    - Ndiyo
    - Hapana

16. Je ulikuwa unakunywa pombe wakati wa ujauzito wa huyu mtoto?
    - Ndio
    - Hapana……..ruka swali no. 15

17. Kama ndio, je ulikuwa unakunywa chupa ngapi kwa siku?.....

18. Je ulikuwa unatumia madawa ya kulevya wakati wa ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

19. Je uliwahi kuwa na maumivu wakati wa kukojoa na homa kwenye ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

20. Je uliwahi kuugua malaria kwenye ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

21.Je ulikuwa na kisukari kwenye ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

22. Je uliwahi kutokwa na damu baada ya miezi saba ya ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

23. Je ulipata ugonjwa wa kupanda kwa shinikizo la damu kwenye ujauzito wa mtoto huyu?
    - Ndiyo
    - Hapana

24. Je kwenye ujauzito wa mtoto huyu, ulitokwa na maji ukeni (chupa kupasuka) kabla ya uchungu kuanza?
    - Ndiyo
    - Hapana

25. Je umejifungua watoto wangapi kwenye ujauzito huu?.....

26. Je mtoto(wa) amezaliwa na ulemavu wowote?

Taarifa za mimba zilipita

27. Je ulishawahi kujifungua mtoto ambaye hajatimiza miezi tisa (wiki 28-36)?
    - Ndiyo
    - Hapana

28. Je umewahi kujifungua mtoto aliyefia tumboni?
    - Ndiyo
    - Hapana

29. Je umepita muda gani kati ya mimba hii na iliyopita (miezi)? …….

30. Je umepita muda gani kati ya mimba hii na iliyopita (miezi)? …….