PREVALENCE, UNDERLYING CAUSES, AND UPTAKE OF INTERVENTIONS FOR PREVENTING RECURRENT PRETERM BIRTHS AT KENYATTA NATIONAL HOSPITAL– A CROSS-SECTIONAL STUDY

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DECLARATION

I do declare that this research is to be undertaken in partial fulfillment of the Masters of Medicine in Obstetrics and Gynecology from the University of Nairobi and will be my original work and that it has not been undertaken and presented for the award of a degree in any other university.

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DEDICATION

I dedicate this work to the manani family: Dr. Quek meichi whose indelible sacrificial care was pertinent to its fruition; To my parents, lecturers, and statistician. I am eternally indebted.

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LIST OF ABBREVIATIONS

CKD:	Chronic Kidney Disease
HDP:	Hypertensive Disease in Pregnancy
HIV:	Human Immunodeficiency Virus
IPI:	Inter Pregnancy Interval
KCMC:	Kilimanjaro Christian Medical Centre
KNH:	Kenyatta National Hospital
LMIC:	Low and Middle-Income Countries
PTB:	Preterm Birth
RSAs:	Recurrent Spontaneous Abortions
SGA:	Small for Gestation Age
WHO:	World Health Organization

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ABSTRACT

Background: Globally, the prevalence of recurrent preterm births is between 9.6% and 31.6% with 81% of preterm births occurring in sub-Saharan Africa according to the World Health Organization (WHO). Ten percent (10%) of mortalities in this cohort are attributed to prematurity-related complications, the majority of which are preventable. Progesterone, low-dose aspirin, heparin, and antihypertensive treatments are effective interventions for decreasing preterm births. In Low- and Middle-income countries, local data on rates of recurrent preterm births, causes of recurrent preterm births, and interventions for preventing recurrent preterm births, which is critical for prevention and management, are limited.

Objectives: To determine the prevalence, underlying causes, and uptake of interventions for preventing recurrent preterm births at Kenyatta National Hospital between 2019 and 2020.

Methodology: This was a descriptive cross-sectional study where hospital files of 211 postpartum women with a history of preterm birth at <37 weeks in the immediately preceding pregnancy who delivered at the Kenyatta National Hospital, between December 2019 and December 2020 were used. The files were retrieved from the records department and maternal demographic and reproductive characteristics, treatment modalities, and birth outcomes were recorded. Uptake of interventions for preventing recurrent preterm birth such as aspirin, progesterone, or cervical cerclage was also extracted. Data analysis was conducted using version 25 of the Statistical Package for Social Scientists (SPSS) software. Descriptive data were summarized in a table and the prevalence of recurrent preterm births determined using the Clopper Pearson method at 95% confidence level and presented in a pie chart. The causes of recurrent preterm birth and uptake of interventions analyzed using frequency distribution and percentages.

Results: The hospital files of 211 women with a mean age of 29.4±5.8 years were evaluated. Most were in age group <35 years (76.9%), married (88.0%), and unemployed (57.6%); had an interpregnancy interval (IPI) of 2-5 years (44.1%) and did not use alcohol (99.1%) or cigarettes (99.5%). About 28.4% had comorbidities, mainly preeclampsia/eclampsia (75.0%). Prevalence of recurrent preterm births was 40.3% (95% CI=33.6-47.2%) with spontaneous preterm births accounting for 64.5% (95%CI=53.6-74.8) of recurrent preterm births. Comorbidities, diabetes, hypertension, and congenital anomalies were associated with 44.7%, 1.2%, 10.6%, and 1.2% of recurrent preterm birth cases, mostly provider-initiated. Human Immunodeficiency Virus (HIV), fibroids, cervical insufficiency, and Urinary Tract Infections (UTI) were associated with 2.4%, 3.5%, 17.6%, and 8.2% of recurrent preterm births, mostly spontaneous. The prevalence of cervical cerclage, vaginosis treatment, progesterone use, heparin treatment, and aspirin use were 14.1%, 8.2%, 1.2%, and 3.5%. The uptake of progesterone, bacterial vaginosis treatment, and cervical cerclage were higher among patients who had spontaneous recurrent preterm births (12.7%, 0.2%, and 18.1%) compared to provider-initiated recurrent preterm births (0.0%, 0.0%, and 0.0%). Heparin treatment and aspirin treatment were higher among patients who had provider-initiated preterm births (3.3% and 6.7% respectively) compared to spontaneous preterm birth (0.0% and 0.2% respectively).

Conclusions: The prevalence of recurrent preterm births was high at 40.3%. Most recurrent preterm births were spontaneous at 64.5%. Comorbidities, mainly hypertension, cervical insufficiency, and UTIs, were the main risk factors. Patients who have provider-initiated recurrent preterm births are likely to receive aspirin and heparin treatment, while those who

have spontaneous preterm births are more likely to receive progesterone, bacterial vaginosis treatment, and cervical cerclage.

CHAPTER ONE

1. INTRODUCTION

1.1 Background

Preterm birth refers to the delivery of a live baby before 37 weeks of gestation (1). The real prevalence of preterm births is not known due to insufficient accurate data, especially in Low- and Middle-income Countries (LMIC). However, it is estimated to afflict approximately 5% and 18% of pregnancies worldwide and is the leading cause of mortality of children under five years of age(1). Annually, 15 million babies are born moderately preterm (32-37 weeks), very preterm (28-32 weeks), and extremely preterm (<28 weeks), with the greater burden of births (60%) reported in Sub-Saharan Africa and Asia(2,3). More than one in ten preterm babies die from a range of prematurity-related complications, but75% of these cases are preventable with routine ultrasonic and clinical evaluations, fetal monitoring, and antenatal steroid injections (1,3).

Preterm birth is recurrent whenever a mother delivers two or more babies before 37 weeks gestation(4) and can be provider-initiated or spontaneous (with ruptured or intact membranes). From published data, the risk of recurrent preterm births seems to be significantly higher among women with a history of spontaneous preterm births in the first observed pregnancy. In Georgia, 16.3% of women with a history of preterm birth have recurrent preterm births, with its incidence being significantly higher among black women than white (5). In the United States of America, recurrent preterm deliveries vary between 9.6% and 31.6% in different populations(5–8), while the prevalence in Tanzania has been reported to reach 17% (9). Kenya is ranked as a medium-risk country for preterm deliveries with the prevalence range estimated to be between 5-9%(10).

Among the affected mothers, preexisting co-morbidities such as diabetes mellitus, high blood pressure, and preeclampsia are among the leading maternal causes of preterm birth(11,12). Reproductive factors such as short interpregnancy interval after preterm birth and the gestation of preterm births; lifestyle factors such as cigarette smoking; and neonatal factors such as congenital anomalies and placental or amniotic problems have also been reported (2,4,8,11–16).

Even though the risk of recurrence is thought to be higher among women of African origin, accurate data on recurrent preterm births in public hospitals such as the Kenyatta National Hospital is limited. This study aims to determine the prevalence, causes, and uptake of interventions for preventing recurrent preterm births to bridge the existing knowledge gap.

CHAPTER TWO

2 LITERATURE REVIEW

2.1 Prevalence of recurrent preterm birth

According to Mazaki-Tovi and colleagues, preterm birth is considered recurrent whenever a mother delivers two or more babies before 37 weeks gestation(4). Recurrentpreterm births are provider-initiated or spontaneous (preterm labor with ruptured/ intact membranes). To determine the rates and predictors for recurrent preterm deliveries in Georgia, Adams and others(5)did a population-based Cohort study using fetal death/ birth certificates of mothers who delivered in Georgia from 1980 to 1995. The data of 56,174 black women and 122,722 white women with singleton deliveries in first and second pregnancies were reviewed and the recurrence of preterm deliveries evaluated. From the results, the prevalence of recurrent preterm births was 14.2% (8.2% at 20-31 weeks) among white women and 18.4% (13.4% at20-31 weeks and 23.4% at 32-36 weeks) among black women, translating to an overall prevalence of 16.3%.

The risk of recurrent preterm births seems to be significantly higher among women with a history of spontaneous preterm births in the first observed pregnancy. In a preterm prediction study in Maryland, USA, Iamset al.(6)screened for spontaneous preterm births by evaluating fetal fibronectin levels in the cervix and vagina at 22-24 weeks and 30 weeks gestation, the cervical length, and obstetric history of 2929 pregnant women. Among the 378 women found to have a history of spontaneous abortions in the second trimester, the prevalence of recurrent preterm deliveries varied between 14% and 15%. Adams et al. had similar findings in Georgia in an earlier descriptive study in 2002 (5), while Ekwo et al. found the prevalence of recurrent preterm births in Illinois to be 9.6% in a second pregnancy and 12.9% in the third, peaking among African American women (18.2% and 24.5%) (7).

In a consecutive pregnancies study, Loughton et al. (8)demonstrated a significantly higher prevalence of recurrent preterm delivery among women whose first pregnancy resulted in preterm birth. The study was a retrospective review of the medical data of 51,086 women who delivered in Utah between 2002 and 2010. Of the 3836 who delivered preterm in the first pregnancy, the rate of recurrent preterm delivery for indicated, spontaneous, and elective preterm births was 23.0%, 31.6%, and 27.4%. From the data, having a prior indicated preterm delivery increased the risk of subsequent spontaneous and indicated preterm delivery by about 1.61 and 5.64 times. Having a prior spontaneous preterm delivery increased the risk of subsequent spontaneous and indicated preterm delivery by 2.7 and 9.1 times.

From 1241 data points of107 countries analyzed by Chwanpaiboonet al. (10) in 2014, close to 81.1% of preterm births occur in Sub-Saharan Africa and Asia. Regional rates range from 6.3–30·9% in North Africa, while the preterm birth rate in Kenya was found to reach 5-9%. Recent data from Africa show that the prevalence of recurrent preterm delivery in Africa might be comparable to the 8.9-30.7% rate reported globally, even though the data is limited.

In East Africa, Mahandeet al. (9) conducted a registry-based study in Northern Tanzania in which the prevalence of recurrent preterm births and its association with perinatal mortality was evaluated among 18,176 women with a singleton delivery between 2000 and 2008 at the Kilimanjaro Christian Medical Centre (KCMC) in Dar-es-salaam. From the findings, the prevalence of recurrent preterm birth was 17%, with the risk of its development estimated to be 2.7 fold higher with a history of preterm births(9). However, the causes of recurrent preterm deliveries, the underlying causes of recurrent preterm births, and the effect of management strategies on its prevalence were not studied, presenting a knowledge gap.

2.2 Types of recurrent preterm births

Recurrent preterm deliveries are of two broad types - spontaneous and provider-initiated. A recurrent spontaneous preterm birth refers to delivery due to spontaneous onset of labor with preterm PROM or intact membranes(17). Spontaneous preterm births happen before 37 weeks gestation (18)and account for most preterm births (65-70%) (19). Provider-initiated preterm deliveries happen due to fetal indications such as distress, fetal growth restriction, or malformations and maternal indications such as hypertensive disease in pregnancy (HDP), placenta previa, placenta abruption, and severe clinical conditions during pregnancy(20). It accounts for 30-35% of all recurrent preterm births (19) and contributes more to early neonatal deaths compared to spontaneous preterm deliveries (21). Therefore, to lower the risk of premature births and associated adverse outcomes, a reduction of provider-initiated preterm deliveries should be a priority. Provision of adequate obstetrics care, optimal timing of high-risk pregnancies, and avoiding provider-initiated preterm deliveries in women with maternal complications such as HDP can be effective, according to Morisaki et al.(22).

2.3 Causes of recurrent preterm birth

The etiology of recurrent preterm births is multi-factorial and can be divided as maternal or fetal, spontaneous or provider-initiated.

2.3.1 Provider initiated factors

2.3.1.1 Medical condition of the mother

In literature, the maternal causes of recurrent preterm deliveries are diverse. While examining data of163,889 mothers–first child–second triads, Yang et al. (11) demonstrated a strong link between pre-existing comorbidities and the risk of recurrent preterm deliveries in California, the

USA from 2005 to 2011. Data were collected from birth certificates and logistic regression analyses were used to compute adjusted risk ratios for preterm deliveries.

From the study, women who delivered at 32 weeks gestation with preeclampsia and pre-existing hypertension were 88.2 times more likely to have a preterm birth in the subsequent pregnancy. Pre-existing diabetes increased the odds of recurrent preterm birth by 4.3 times, while women with urinary tract infections were 9.0 times more likely to have a recurrent preterm delivery in the subsequent pregnancy. In another historical cohort study of maternally linked birth records in Utah, USA, the presence of any pre-existing medical condition in the subsequent pregnancy increased the adjusted risk of having a recurrent preterm delivery by 38% (12).

While the association between HIV infection and recurrent preterm birth has not been studied sufficiently, especially in Africa, antiretroviral therapy seems to influence perinatal outcomes negatively, key among them preterm births. In a systematic review on the "Determinants of preterm birth among mothers in East Africa," Laelago et al. (23) demonstrated a 2.59 fold (95% CI = 1.84–3.66) increase in adjusted odds for delivering preterm among with HIV compared to without. Even though the odds of a recurrent preterm birth among women with HIV compared to without was not evaluated, their data hinted a positive association, which should be factored in while designing interventions for preserving the wellness of babies.

In another 2016 study evaluating HIV as a risk factor for preterm births, Lopez et al. (24) observed a statistically significant association between first-trimester CD14 levels among HIV-infected women and preterm delivery. Overall, inflammatory markers were significantly higher among HIV-positive women compared HIV negative women and were associated with a higher incidence of preterm delivery. Among HIV-positive women, other factors such as the timing of

antiretroviral therapy (ART) have been reported to upregulate the immune system's reaction to the fetus, increasing the risk of a preterm birth even further.

In a 2017 systematic review in The Lancet, Uthman et al. (25) observed a significant increase in preterm births when ART was initiated before conception compared to after. Even though most studies reported a strong association between ART and preterm births, the association between HIV and recurrent preterm births was rarely studied, presenting a knowledge gap.

From literature, women with bacterial infections, predominantly vaginosis, have a higher risk of preterm birth than those who do not. In a systematic review by Laelago et al.(23) discussed previously, pregnant women with urinary tract infections (UTI) and a purulent vaginal discharge of a bacterial origin bore a 5.27 fold (95% CI=2.98–9.31 and 5.33 fold (95% CI=3.19–8.92) adjusted odds for delivering preterm compared to pregnant women who did not have infections. Infection-mediated preterm births were also a common occurrence in a 2019 study by Stinson and Payne (26), while Romero et al. (27) demonstrated the role of bacterial infections in preterm labor and delivery in a comprehensive review of the literature.

2.3.1.2 Gynecological problems of the mother

Gynecological problems of the mother have been strongly associated with an increased risk of recurrent preterm births, especially without proper management. This was reported by Sneideret al. (28) in a prospective study of 9602 Danish women with first extreme preterm birth or second-trimester miscarriage between 1997-2012. From the data, recurrent preterm births were reported in 7.3% of patients, most of whom had cervical insufficiency (28%). Cervical insufficiency has a strong genetic component. But, when managed correctly, the risk of recurrent preterm births can drop by 53%-86% in women at risk of a second-trimester repeat miscarriage. According to

Sneideret al. (28), recurrence of preterm births in women with cervical insufficiency dropped by 53% with vaginal cerclage and 86% with abdominal cerclage after multivariable analysis.

2.3.1.3 Foetal congenital anomalies

Even though maternal causes of recurrent preterm deliveries are the commonest in literature, neonatal causes are also common and diverse. While studying the risk factors for recurrent preterm deliveries in the USA, Simonsenet al. (12)demonstrated a strong association between neonatal development and the risk of preterm deliveries among multiparous women with a history of preterm births. In the study, the presence of a fetal anomaly increased the risk of recurrent preterm birth by 67% and 44% in the second and third subsequent birth.

2.3.1.4 Intrauterine growth restriction

Growth retardation and low birth weight for gestation can increase the risk of recurrent preterm birth by 24% and 14% in second and third pregnancy, highlighting the need for stringent fetal monitoring and pregnancy management when a previous delivery was preterm. In retrospective studies, low birth weight for gestation has been found to increase the risk of recurrent preterm birth(29,30). Uterine, amniotic, umbilical, and placental problems such as trauma, Abruption, intrauterine infections, or asphyxia also interfere with growth, causing preterm birth (2,8,15,16).

2.3.2 Inter Pregnancy Interval

Factors such as interpregnancy interval after preterm birth and the gestation of the immediate preterm birth can influence the occurrence of repeat preterm births. In the study by Yang et al. in the USA (11), women who had an IPI less than six months between pregnancies were 3.3 times more likely to have a preterm birth in the subsequent pregnancy. In another study, women who had a short IPI (<6 months) compared to a long IPI (2-3 years) were 1.77 and 1.43 times more

likely to have a recurrent preterm birth in the second and third subsequent pregnancy respectively (12). In a retrospective study of 997,000 index pregnancies in Australia, an IPI <3months increased the rate of recurrent preterm births compared to an IPI of 9-12 months by up to two times (31). Even though the WHO recommendation concerning IPI after a pregnancy loss (<6 months) might be practical in advanced countries with robust health care systems, women in LMIC should be advised to wait for at least a year to lower the risk of another pregnancy loss.

2.3.3 Spontaneous factors

2.3.3.1 Lifestyle factors

Lifestyle factors such as cigarette smoking and alcohol consumption during pregnancy have been reported to increase the risk of recurrent preterm births statistically significantly. In a population-based retrospective cohort study by Wallace et al. in 2016(32), a positive, statistically significant association between smoking and recurrent preterm births was evident among 36,432 women from Ohio, USA, with singleton nonanomalous live births.

From the data, women with at least one prior preterm birth had an inherently higher risk of recurrent preterm birth. Soneji et al. (33)reported similar findings in a cross-sectional study of over 25 million pregnant women from Lebanon. Finally, At less than four drinks per week, the risk of recurrent preterm birth among drinkers compared to non-drinkers is unchanged (34).

2.3.3.2 Demographic factors

In literature, demographic factors such as age, race, and body mass index have been found to influence the development of spontaneous recurrent preterm births statistically significantly. In a cross country study of 4.1 million singleton pregnancies for Europe and America by Ferrero et al (35), age was a risk factor for spontaneous recurrent preterm delivery with women aged 35+

years having a 1.4 fold higher odds of having a spontaneous preterm birth compared to younger women (<35 years). Jacobson et al. reported similar findings in 2004 in a population-based cohort study of 1,566,313 deliveries. The risk of spontaneous preterm delivery was 2.4 higher among women aged 45+ years old compared to younger women (36). Moreover, the spontaneous preterm delivery rate of women of African descent is approximately 40% higher than that of white women (37), while extreme ranges of Body Mass Index (BMI) have been reported to increase the risk of having spontaneous preterm delivery by about1.3 and 3.0 times (38,39).

2.4 Management of recurrent preterm birth

Progesterone administration is a common procedure for the management of preterm births that has demonstrated promising results. Progesterone maintains uterine quiescence in the second half of the pregnancy through inhibition of prostaglandin production and suppression of gene expression of contraction-associated receptors proteins and gap junctions.

In a placebo-controlled, double-blind randomized control trial by Fonseca et al. (40), daily administration of 100mg progesterone to patients with a previous spontaneous preterm delivery lowered the prevalence of recurrent preterm delivery by 14.7% compared to a control/placebo group. In another placebo-controlled, double-blind trial in the USA (41), weekly injections of 250 mg17 alpha-hydroxy-progesterone to women with a history of spontaneous preterm delivery lowered the risk of recurrent preterm birth by 66%and need for supplemental oxygen, intra-ventricular hemorrhage, or necrotizing enterocolitis compared to women who received inert oil placebo injections (41). While the efficacy of 17 alpha-hydroxyprogesterone in twin gestations is debatable(42), its ability to inhibit cervical reopening, downregulate gap junction formation, and conserve myometrial quiescence makes it suitable for preventing recurrent preterm births

(43,44), especially if administered vaginally. While comparing vaginal versus oral progesterone in the prevention of preterm labor among 100 women with a short cervix, AbdElgaber et al. demonstrated a high percentage of deliveries at term with vaginal progesterone compared to oral progesterone. Adverse drug side effects and adverse neonatal outcomes such as respiratory distress and admission to NICU were lower with vaginal compared to oral progesterone(45). Recent data also advocates for the treatment of bacterial vaginosis(46–48), prophylactic cervical cerclage, and heparin therapy in women at risk of preterm birth with complications(49–51).

2.4.1 Uptake of progesterone to prevent recurrent preterm births

Many recent studies support the use of progesterone to lower the risk of preterm births or recurrent preterm births. In a systematic review and meta-analysis of 79 distinct studies on oral progesterone for the prevention of recurrent preterm birth by Boelig et al. (52), progesterone was effective for the prevention of perinatal morbidity and recurrent preterm births in asymptomatic singleton gestations, albeit with increased adverse effects.

In another systematic review by Norwitz et al. (53), various preparations of progesterone could prevent recurrent preterm births, with self-administered vaginal progesterone gel found to be the most effective for women with a history of spontaneous preterm deliveries. However, uptake of progesterone after a preterm delivery is poorly understood because data is limited.

2.4.2 Uptake of aspirin to prevent recurrent preterm births

Platelets have a role in the development of preeclampsia, suggesting that the provision of antiplatelet agents, including aspirin, could slow/prevent HDP and linked adverse outcomes. According to Visser et al., administration of Aspirin before 16 weeks gestation not only inhibits

thrombocyte aggregation but also prostaglandin synthesis, which in turn lowers the risk of ischemic placental disease and preterm birth (54). Recent studies on using low-dose aspirin to prevent recurrent spontaneous births have highlighted several of its benefits.

In a meta-analysis of 27 randomized control studies by Bujold et al. (55) the effect of aspirin on the development of preeclampsia and spontaneous preterm births was evaluated. From the results, provision of low dose aspirin at 16 weeks gestation compared to after 16 weeks gestation lowered the risk of severe preeclampsia by 99% and preterm delivery by 78%.

In a meta-analysis of 32,217 individual patient data and their 32,819babies from 31 randomized control trials (RCTs), the provision of antiplatelet agents lowered the risk of preeclampsia 0.90 fold and the risk of delivering before 34 weeks gestation 0.98 fold(56). Agents such as aspirin were well tolerated and did not have a significant risk on the health of babies. Duley et al. (57) and Uzan et al. (58)found similar results in the United Kingdom (UK) and France. The uptake of aspirin to lower the risk of recurrent preterm births is, however, poorly explored.

2.4.3 Uptake of heparin to prevent recurrent preterm births

The risk of venous thrombo-embolism is high during the puerperium and pregnancy but is treatable with low molecular weight or unfractionated heparin administered subcutaneously or intravenously. Heparin not only manages the underlying conditions for HDPsbut can also lower the risk of recurrent spontaneous abortions. In a 2007 study of the association between thrombophilia and recurrent spontaneous abortion (RSAs), Deligiannidis et al. (59) reported favorable pregnancy outcomes in 29 women with inherited or acquired thrombophilia and a history of spontaneous preterm births on low dose aspirin and low dose heparin daily compared

to 23 controls. Among protein C, antithrombin, or protein S deficient women, anticoagulant treatment, including heparin was associated with a 0.07 fold reduction in the adjusted relative risk of fetal loss (60). Among women with recurrent pregnancy loss, phosphatidylserine (PS), antiphospholipid antibodies (APA)to cardiolipin (CL), delivery of viable infants was higher with aspirin and heparin treatment (76%) compared to those treated with aspirin alone (46%) (61).

2.4.4 Uptake of antihypertensive drugs to prevent preterm births

Almost 10% of normotensive women develop abnormally elevated blood pressure, which in turn increases the risk of fetal growth restriction 2.3-fold. To prevent first pregnancy preterm births, the provision of antihypertensive drugs is effective for at-risk women. While evaluating the Cochrane Pregnancy and Childbirth Group's Trials Register in 2007, Abalos et al.(62)reported a 2% and 5% lower risk of preterm births and neonatal deaths when women received a hypertensive drug for mild or moderate hypertension in pregnancy. provision of calcium channel blockers reduced the risk of preterm labor and adverse neonatal outcomes such as respiratory distress in a representative sample of 1029 women from Australia (63).

The provision of oral better blockers(64) and nitric oxide (65)have also been found to prevent the progression of hypertension and its associated adverse outcomes such as respiratory distress syndrome, small for gestation age (SGA), and PTB. Women with a history of preterm births and who are at risk of an HDP could benefit from such interventions under clinical guidance.

2.5 Conceptual framework

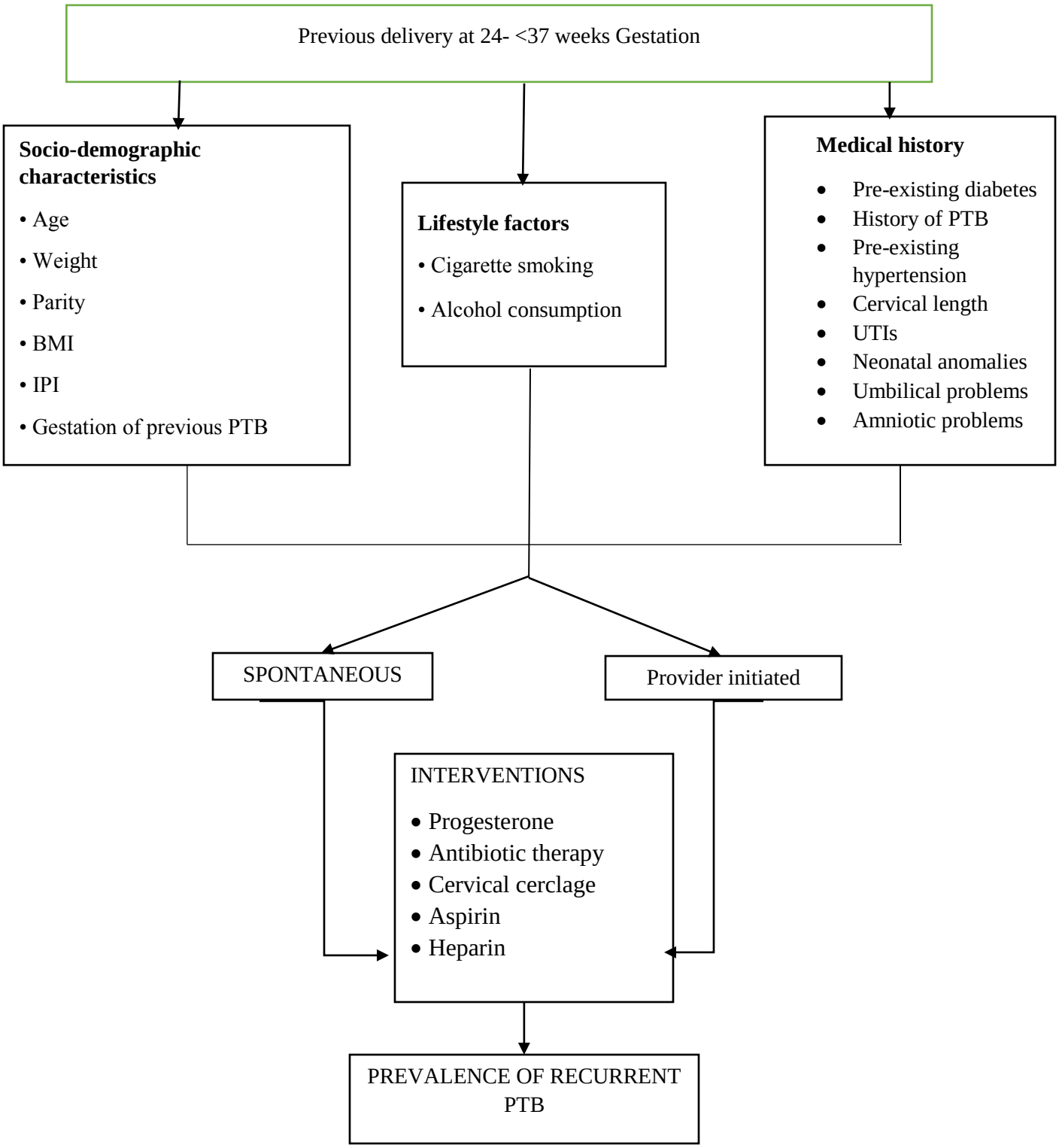

Figure2.1. Conceptual framework

2.5.1 Conceptual Framework Narrative

We intended to ascertain the prevalence, types, and uptake of interventions for preventing recurrent preterm births among women with a history of preterm births. Certain socio-demographic and medical factors, as well as lifestyle factors, predispose women at a gestation of 24-37 weeks to recurrent preterm births. The prevalence of recurrent preterm birth can also increase with increasing age, low IPI, low gestation of previous preterm birth, smoking and alcohol use, and pre-existing health conditions. As a result, these preterm births can be spontaneous or induced.

Treatment with anticoagulants and antihypertensive drugs such as aspirin, heparin, and progesterone, cerclage of the short cervix, or antibiotic therapy can lower the risk (both crude and adjusted) or prevalence of recurrent preterm delivery. By controlling the effects of each variable on the occurrence of preterm births, individual spontaneous and provider-initiated factors that predispose women with a history of preterm birth to recurrent preterm births could be established and used to guide management. The dependent variable (or outcome) with be the birth outcome of women, evaluated as a binary variable in two levels (live and preterm births).

2.6 Problem Statement

Preterm deliveries account for 16.3%-30.7%of all deliveries globally with the risk being higher among women of African origin compared to white women(5).81.1% of preterm births occur in Sub-Saharan Africa (10), with Kenya identified as a medium risk country (66). 10% of the mortalities among these infants are attributed to prematurity-related complications, the majority of which are preventable. However, there is no local data on the prevalence rates of recurrent preterm deliveries, causes of recurrent preterm births, and uptake of interventions for preventing

recurrent preterm births. There are also no local standard operating procedures regarding the management of recurrent preterm births. This study aims to bridge this gap as well as contribute to the identification of potential areas for further research.

2.7 Research question

What is the prevalence, underlying causes, and uptake of intervention measures for recurrent preterm births among multiparous postpartum women who delivered at Kenyatta National Hospital between December 2019 and December 2020?

2.8 Objectives

2.8.1 Broad objective

To determine the prevalence, underlying causes, and uptake of interventions for preventing recurrent preterm births at Kenyatta National Hospital between December 2019 and December 2020.

2.8.2 Specific objectives

Among multi-parous women with a previous history of at least one preterm birth who delivered at Kenyatta National Hospital between December 2019 and December 2020:

1. To determine the prevalence of recurrent preterm birth.
2. To describe the underlying causes of recurrent preterm births.
3. To evaluate the prevalence of uptake of interventions for preventing recurrent preterm births.

CHAPTER THREE

3 METHODOLOGY

3.1 Study design

The study design was descriptive cross-sectional. It was retrospective whereby records of multiparous women with a previous history of preterm birth who delivered from December 2019 to December 2020 were used to conduct the research. This was done at the KNH records department.

3.2 Study site

The study was conducted at Kenyatta National Hospital (KNH) – the largest referral hospital in Kenya– and the teaching hospital of the University of Nairobi, College of Health Sciences. Located in the upper hill Nairobi, 2km southwest of the Nairobi Central Business District, it not only serves residents of the Nairobi Metropolitan region but also receives special referral cases from other Counties. There are over 10000 deliveries annually in labor wards, occurring amongst mothers of all socio-economic status. Antenatal, intrapartum, and postnatal records of patients with a history of recurrent preterm births were used to collect data. These records were sourced from the KNH records department upon ethical and administrative approval. The site was selected because of its robust data archival system for mothers in which attributes such as birth outcomes, medical history of mothers, and maternal and neonatal outcomes in current and previous pregnancies are captured. The obstetrics and gynecology clinics and labor ward are also high-traffic areas that can grant researchers quick access to records of many qualified patients.

3.3 Study population

The study included records of postpartum women who delivered in KNH between December 2019 and December 2020, with a previous history of preterm birth at<37 weeks. Confirmation of gestation was done by use of the last normal menstrual period where the menstrual cycle is regular. In the case of irregular menstrual cycles, a first or second-trimester ultrasound was used for dating.

3.3.1 Inclusion criteria

1. Multiparous postpartum women
2. Previous history of at least one preterm birth at <37 weeks
3. Preterm delivery at Kenyatta National Hospital between December 2019 and December 2020
4. Complete medical records available at Kenyatta National Hospital

3.3.2 Exclusion criteria

1. Confirmed intrauterine fetal demise
2. Over 5% missing data from records

3.4 Sample size determination

Fisher's formula for the cross-sectional study was used to determine the sample size (n), assuming the prevalence of recurrent preterm delivery of 14.0 %and 5% margin of error.

Formula

$$n = \frac{Z^2 x p(1-p)}{d^2}$$

Assumptions

n: Sample size

P: The prevalence recurrent PTB (14.0%) based on Adams et al. (2002).

Z^2: Normal variate for alpha at 95% CI (1.96)

d: Precision (5%)

Sample size calculation

$$n = \frac{1.96^2 x 0.14(1-0.14)}{0.05^2} = 185$$

Assuming that 10% incomplete data, sample size (185) was adjusted upwards to204multiparous postpartum women with a history of at least one preterm birth at <37 weeks who subsequently delivered at the Kenyatta National Hospital between December 2019 and December 2020.

3.5 Sampling procedure

Consecutive sampling was used to recruit participants. Files of multiparous postpartum women who met our inclusion criteria were retrieved and participants were recruited from December 2020 backward until the sample size was reached.

3.5.1 Study tool

A questionnaire organized in four sections was used to collect data (Appendix 1). Section 1recorded the demographic characteristics of patients such as their age, educational level, and

marital status. Section 2recorded the medical and reproductive history of patients, including the gestation (in weeks), parity, presence of comorbidities such as human immunodeficiency virus (HIV), and the interpregnancy interval (IPI). Section 3 recorded the pregnancy outcomes of patients, which included the gestation at delivery and the type of birth (preterm or normal delivery). For patients with preterm delivery, the causes of the preterm delivery were recorded as either maternal, neonatal, or both. Maternal factors evaluated included bacterial infections, comorbidities such as diabetes, and gestational diabetes among others (Table 2). Neonatal factors included congenital anomalies, placental causes, asphyxia, trauma, umbilical problems, and amniotic or uterine factors among others. Before use, the tool was validated using Face Validity technique(67). To evaluate its suitability to answer the project's objectives, the protocol, and the tool was submitted to supervisors and reviewers at the department of obstetrics and gynecology for review and input. The additions, subtractions, or changes proposed after the review process was implemented before using the questionnaire to collect data for the definitive study.

Table 3.1.Study variables

Study objective	Variable (s)
Prevalence of recurrent preterm births	Birth outcome (preterm birth versus live birth) Recurrent preterm birth
Risk factors of recurrent preterm	Previous preterm delivery
	Age in years
	Education level
	Marital status
	Employment status
	BMI
	IPI
	Gestation of the previous preterm
	Smoking status
	Alcohol consumption
	Preexisting diabetes
	Preexisting hypertension
	Neonatal anomalies
	Umbilical problems
	Amniotic problems
	Substance use
	thyroid disease
	HIV
	Cervical insuficiency
	Fibroid
	Antibiotic use
Interventions for stopping recurrent preterm births	Progesterone administration
	Cervical cerclage
	Acetylsalicylic acid (aspirin)
	Preconception care
	Treatment of medical conditions

3.5.2 Data collection procedures

Data from files of patients identified during sampling were retrieved and recorded.

3.5.3 Quality assurance

To ensure quality was maintained, only experienced staff, including the Principal Investigator (PI) and a research assistant, handled data collection. The research assistant was a registered nurse with experience in medical research. Moreover, before deployment, the research assistants underwent mandatory training on data collection and abstraction of records and research ethics. Finally, they checked all questionnaires for completeness before filing and submission to a statistician for analysis. Double data entry was done to ensure accurate correct data capture. The changes to data were signed and dated by a research assistant and confirmed by the PI before filing.

3.6 Ethical considerations

3.6.1 Ethical approval

Ethical approval was sought from KNH/UoN Ethics review committee before data collection. The protocol, including the objectives, research questions, data collection procedures, and study tools were submitted for ethics review and used only after approval.

3.6.2 Institution approval

Approval was sought from the KNH administration before conducting the study. The protocol was submitted for review and approval. Approval was also sought from the records officer.

3.6.3 Confidentiality

During the data collection, analysis, and dissemination procedures, the confidentiality of all subjects was upheld. Personal identifiers such as hospital numbers, national identification numbers, and names were not be collected on questionnaires nor analyzed. Code numbers were used to link participants to the data in questionnaires instead of their identifiers.

3.6.4 Data management

After completion of the study, the questionnaires were filed in box files and stored in a locked cabinet. Only the PI had access to the questionnaires and did not provide them to any third party without written approval from the ERC. Digital data in Spreadsheets were archived as password-protected Zip files in computers. Data will be stored for 10 years from the date of completion.

3.7 Data analysis

The normality of continuous data was determined using the Shapiro-Wilk test and summary statistics computed as follows: means (±standard deviation for normally distributed data) and median with inter-quartile range for nonparametric data. Analysis per study objective is shown in table 12.

3.7.1 Data analysis per objective

Table 3.2. Data analysis per study objective

To determine the prevalence of recurrent preterm birth among multiparous postpartum women with a previous history of birth at <37 weeks who subsequently delivered at Kenyatta National Hospital between 2019 and 2020	The Exact Clopper Pearson method was used to compute the prevalence of recurrent preterm births and 95% confidence interval
To describe the underlying causes of recurrent preterm births among multiparous postpartum women with a previous history of preterm birth at <37 weeks who subsequently delivered at Kenyatta National Hospital between 2019 and 2020	Frequency distributions and percentages
To evaluate the prevalence of uptake of interventions for preventing recurrent preterm births among multiparous postpartum women with a previous history of preterm birth at <37 weeks who subsequently delivered at Kenyatta National Hospital between 2019 and 2020	Frequency distribution and percentages

3.8 Strengths and limitations

This was the first study at KNH evaluating the prevalence, underlying causes, and uptake of interventions for preventing recurrent preterm births – a public health problem that has attracted global attention recently. Due to its retrospective nature, the study was quick and easy to conduct and enabled us to evaluate a large sample of patients to improve the statistical power of assumptions we wanted to approve or disapprove. However, because secondary data was used, incomplete or missing data was common in variables, especially on demographic factors underlying causes of preterm births. To overcome this limitation, the sample size was adjusted upwards by a factor of 10% to cover missing data. Moreover, if it was possible, contact details were extracted from the files of participants.

3.9 Study dissemination plan

This project was conducted in partial fulfillment for the award of a Master of Science degree at the University of Nairobi. Therefore, upon completion, a dissertation has been developed and submitted to the Department of Obstetrics and Gynecology of the University of Nairobi. A manuscript will be written and sent to a peer-reviewed journal of Obstetrics and Gynecology and a presentation made in a local and or international conference of medicine.

3.10 Study closure plan

The study team was assembled and the study process, including the lessons learned and areas in need of improvement, discussed. The report will be shared with the study team and a study closure letter drafted to the KNH/UoN ERC following the laid down guidelines. Finally, all data collection tools, including questionnaires and consent forms, have been prepared for archiving in box files, digital files password-protected, and the final accounting done.

CHAPTER FOUR

4 RESULTS

4.1 Recruitment schema

During this period there were 12920 deliveries, we evaluated 6239 files of patients who delivered at Kenyatta National Hospital (KNH) between December 2019 and December 2020. 6028 were excluded for not having a preterm birth in the preceding pregnancy, leaving 211 qualified patients whose data was abstracted and analyzed.

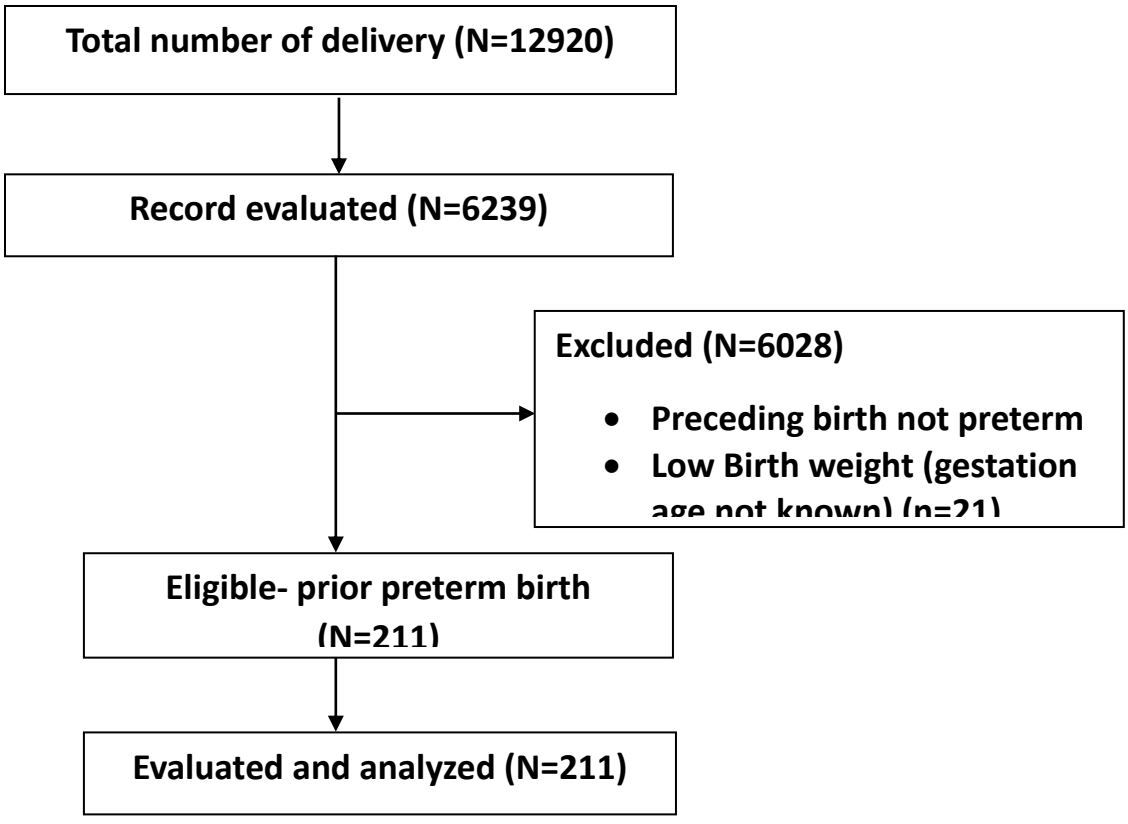

Figure 4.1. Participant's recruitment schema

4.2 Demographic, reproductive, and medical characteristics

Two hundred and eleven (211) women with a mean age of 29.4±5.8 years, age range 18-49 years were evaluated.Most were in age group <35 years (76.9%), married (88.0%), and unemployed (57.6%). Most had an IPI of 2-5 years (44.1%) and were multiparous (72.5%), non-smokers (99.5%) and did not use alcohol (99.1%) and substances such as bhang (98.6%) (table 4.1).

Table 4.1. Demographic, reproductive, and lifestyle factors of women who delivered in 2019-2020 with a history of preterm birth

		Frequency (N=211)
Age	Mean±SD	29.4±5.8
Age group	<35 years	160 (76.9)
	35+ years	48 (23.1)
	Unknown	3
Marital Status	Married	183 (88.0)
	Single	24 (11.5)
	Divorced/separated	1 (0.5)
	Unknown	3
Employment status	Employed	78 (42.4)
	Unemployed	106 (57.6)
	Unknown	27
Interpregnancy Interval	1 year	80 (37.9)
	2-5 years	93 (44.1)
	>5 years	38 (18.0)
Parity	Multiparous (2-4)	153 (72.5)
	Grand multiparous	58 (27.5)
Substance Use	Yes	3 (1.4)
	No/unknown	208 (98.6)
Smoking	Yes	1 (0.5)
	No/unknown	210 (99.5)
Alcohol use	Yes	2 (0.9)
	No/unknown	209 (99.1)

As shown in table 4.2, 28.4% had comorbidity, mostly preeclampsia, and eclampsia (75.0%). Twelves (5.7%) had a history of hypertension, while15.2%, 10%,2.4%, 2.4%, and 0.5%, had a

history of cervical insufficiency, UTI, fibroids, HIV, and thyroid disorders. Only three (1.4%) had congenital anomalies such as Dextacardia, bilateral cleft lip and pallet, and down syndrome.

Table 4.2. Medical factors of mothers with a history of preterm births

		Frequency (%)
Comorbidity present	Yes	60 (28.4)
	No/unknown	151 (71.6)
Preeclampsia/eclampsia		55 (75)
Diabetes mellitus		5 (8.3)
Renovascular disease (RVD)		3 (5.0)
Others*		7 (11.7)
hypertension	Yes	12 (5.7)
	No/unknown	199 (94.3)
diabetes	Yes	3 (1.4)
	No/unknown	208 (98.6)
HIV	Yes	5 (2.4)
	No/unknown	206 (97.6)
thyroid disorder	Yes	1 (0.5)
	No/unknown	210 (99.5)
fibroid	Yes	5 (2.4)
	No/unknown	206 (97.6)
cervical insuficiency	Yes	32 (15.2)
	No/unknown	179(84.8)
UTI	Yes	21 (10)
	No/unknown	190 (90.0)
neonatal congenital anomalies**	Yes	3 (1.4)
	No/unknown	208 (98.6)

**AKI, ESRD, ascites, pleural effusion, chronic hepatitis B, mitral valve stenosis, hyperthyroidism*
** Dextrocardia, Bilateral cleft lip, and pallet, Down syndrome, Umbilical herniation, Umbilical herniation, Unidentifiable sex, Holoprosephely

4.3 Prevalence of recurrent preterm birth

The prevalence of recurrent preterm birth was 40.3% (95% CI=33.6-47.2%) (Figure 4.2).

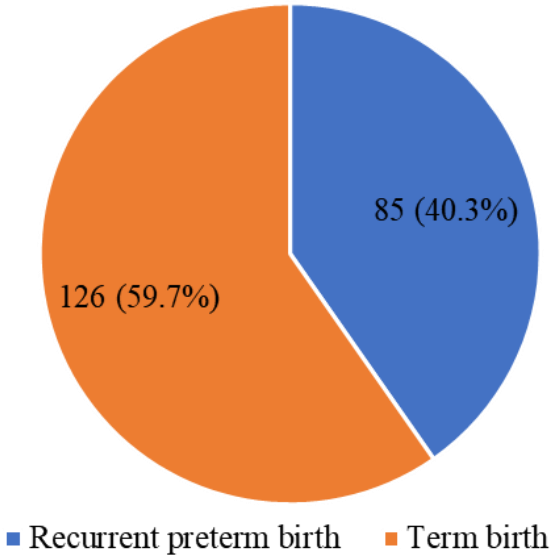

Figure 4.2. The proportion of women with a recurrent preterm birth at Kenyatta National Hospital

Of the 85, most cases[64.7% (95% CI=53.6-74.8)] were spontaneous(Table 4.3).

Table 4.3. Types of recurrent preterm births

Recurrent preterm birth type	Frequency(N=85)	95% confidence interval
Spontaneous	55 (64.7)	53.6-74.8
Provider induced	30 (35.3)	25.2-46.4

4.4 Underlying causes of recurrent preterm births

4.4.1 Socio-demographic and reproductive factors and recurrent preterm births

The socio-demographic and reproductive factors of mothers associated with recurrent preterm births are presented in table 4.5 below. Overall, most cases were in the age group<35 years (73.8%), married (89.2%), had an IPI of <1 year (45.9%), and had 2-4 pregnancies (69.4%). Patients who had spontaneous recurrent preterm births compared to provider-initiated were more likely to be age group 34+ years(27.3% versus 24.1%), married (90.6% versus 86.7%),

unemployed (59.9% versus 48.9%) and have <1-year (45.9% versus 45.5%)or >5-year(69.4% versus 67.3%) IPI.

Table 4.4. Socio-demographic and reproductive factors of mothers and recurrent preterm births

		Overall (85)	Spontaneous (55)	Provider initiated (30)
Age group	<35 years	62 (73.8)	40 (72.7)	22 (75.9)
	35+ years	22 (26.2)	15 (27.3)	7 (24.1)
	Unknown	1	0	1
Marital status	Married	74 (89.2)	48(90.6)	26 (86.7)
	Single	9 (10.8)	5 (9.1)	4 (13.3)
	Separated	0 (0)	0 (0)	0 (0)
	Unknown	2	2	0
Employment	Employed	31(40.1)	23 (51.1)	8 (29.6)
	Unemployed	41 (59.9)	22 (48.9)	19 (70.4)
	Unknown	13	10	3
IPI	1 year	39 (45.9)	25(45.5)	14 (46.7)
	2-5 years	31 (36.5)	24 (43.6)	7 (23.3)
	>5 years	15 (17.6)	6 (10.9)	9 (30.0)
Parity	2-4	59 (69.4)	37 (67.3)	22(73.3)
	5+	26 (30.6)	18 (32.7)	8 (26.7)
Substance Use	Yes	1 (1.2)	1 (1.8)	0 (0)
	No/unknown	84 (98.8)	54 (98.2)	30 (100)
Smoking	Yes	1 (1.2)	1 (1.8)	0 (0)
	No/unknown	84 (98.8)	54 (98.2)	30 (100)
Alcohol use	Yes	0 (0)	0 (0)	0 (0)
	No/unknown	85 (100)	55 (100)	30 (100)

4.4.2 Medical conditions of mothers and recurrent preterm birth

Thirty-eightcases(44.7%) had comorbidities. Around 1.2% had a history of diabetes, 10.6% hypertension, 2.4% HIV, 1.2% thyroid disorder, 3.5% fibroids, 1.7.5% cervical insufficiency, 8.2% UTI, and 1.2% congenital anomalies.Cases who had provider initiated recurrent preterm birth compared to spontaneous were more likely to have comorbidities (80.0% versus 25.5%) and history of diabetes (3.3% versus 0.0%), hypertension (16.7% versus 7.3%), thyroid disorders(3.3% versus 0.0%), and congenital anomalies(3.3% versus 0.0%).Cases who had spontaneous compared to provider initiated were more likely to have a history of HIV (3.6% versus 0.0%), fibroids (3.6% versus 3.3%), cervical insufficiency (21.8% vs0.0%), and UTIs (9.1% vs6.7%).

Table 4.5.Medial conditions of mothers and recurrent preterm births

		Overall (85)	Spontaneous (55)	Provider initiated (30)
Comorbidities	Yes	38 (44.7)	14 (25.5)	24 (80.0)
	No/unknown	47 (55.3)	41 (74.5)	6 (20.0)
Medical history				
Diabetes	Yes	1 (1.2)	0 (0)	1 (3.3)
	No/unknown	84 (98.8)	55 (100)	29 (96.7)
Hypertension	Yes	9 (10.6)	4 (7.3)	5 (16.7)
	No/unknown	76 (89.4)	51 (92.7)	25 (83.3)
HIV	Yes	2 (2.4)	2 (3.6)	0 (0)
	No/unknown	83 (97.6)	53 (96.4)	30 (100)
Thyroid disorder	Yes	1 (1.2)	0 (0)	1 (3.3)
	No/unknown	84 (98.8)	55 (100)	29 (96.7)
Fibroids	Yes	3 (3.5)	2 (3.6)	1 (3.3)
	No/unknown	82 (96.5)	53 (96.4)	29 (96.7)
Cervical insufficiency	Yes	15 (17.6)	12 (21.8)	0 (0.0)

	No/unknown	70 (82.4)	43 (78.2)	30 (100.0)
UTI	Yes	7 (8.2)	5 (9.1)	2 (6.7)
	No/unknown	78 (91.8)	50 (90.9)	28 (93.3)
Congenital anomalies	Yes	1 (1.2)	0 (0)	1 (3.3)
	No/unknown	84 (98.8)	55 (100)	29 (96.7)

4.5 Uptake of interventions uptake for preventing recurrent preterm births

The uptake of progesterone was 8.2%, bacterial vaginosis treatment was 14.3%, cervical cerclage was 14.1 heparin treatment was 1.2%, and aspirin treatment was 3.5%. Patients who had provider-initiated compared to spontaneous recurrent preterm birth were more likely to receive heparin treatment (3.3% versus 0.0%)and aspirin treatment (6.7% versus 1.9%).Patients who had spontaneous compared to provider-initiated recurrent preterm births were more likely receive progesterone treatment (12.7% versus (0.0%) and bacterial vaginosis treatment (1.9% versus 0.0%), and undergo cervical cerclage (21.8% versus 0.0%) (table 4.6)

Table 4.6. Uptake of interventions uptake for preventing recurrent preterm births

		Overall (85)	Spontaneous (55)	Provider initiated (30)
Progesterone	Yes	7 (8.2)	7 (12.7)	0 (0.0)
	No/unknown	78 (91.8)	48 (87.3)	30 (100)
Vaginosis treatment	Yes	1 (1.2)	1 (14.3)	0 (0.0)
	No/unknown	84 (98.8)	6 (98.8)	30 (100)
Cervical cerclage	Yes	12 (14.1)	12 (80.0)	0 (0)
	No/unknown	73 (85.9)	3 (20.0)	15 (100)
Heparin treatment	Yes	1 (1.2)	0 (0.0)	1 (3.3)
	No/unknown	84 (98.8)	55 (100)	29 (96.7)
Aspirin treatment	Yes	3 (3.5)	1 (1.9)	2 (6.7)
	No/unknown	82 (96.5)	54 (98.1)	28 (93.3)

CHAPTER FIVE

5 DISCUSSION, CONCLUSION, AND RECOMMENDATIONS

5.1 Discussion

We evaluated data of 211 women, most of whom were young (<35 years), married, unemployed, and had intermediate interpregnancy interval, defined as 2-5 years. Most had 2-4 pregnancies. All preceding pregnancies were preterm. Alcohol use, cigarette smoking, and substance abuse were not common. Close to a third had comorbidities, the commonest among them found to be cervical insufficiency, UTIs, and hypertension. The prevalence of recurrent preterm birth was high at 40.3%, mostly spontaneous recurrent preterm births (64.7%), peaking among young (<35 years), married, and unemployed women with a short IPI and 2-4 pregnancies. Comorbidities, mainly hypertension, and cervical insufficiency were other common predisposing factors, while lifestyle factors such as cigarette smoking and alcohol use contributed to a negligible degree (<2.0%). Cases mostly received cervical cerclage and progesterone to prevent recurrent preterm births. Uptake of heparin and aspirin was low at <5%. Cases with spontaneous preterm birth were more likely to receive progesterone or undergo cervical cerclage or bacterial vaginosis treatment. The cases with provider-initiated preterm births mostly received heparin and aspirin.

We evaluated the prevalence of recurrent preterm birth in a cohort of 211 Kenyan women with a history of preterm birth in an immediately preceding pregnancy. From findings, the subsequent pregnancy of 85 out of the 211 women evaluated was preterm, translating to a recurrence rate of40.3% (95% CI=33.6-47.2%). While this was within the higher end of prevalence rates reported globally (30.7%), it is significantly higher than individual study data reported from other East African countries. In Tanzania, for instance, a registry-based study reported a

prevalence of 17% in 2008, which was lower than in this study(9). A possible explanation for the difference is that hospitals in Tanzania might not have the same capacity or bulk of patients as Kenyatta National Hospital does. As currently constituted, KNH N is the last point of care for most women in Kenya and also receives referrals not only from Kenya but also from the larger East African region. In the USA, population studies have also reported a lower prevalence of between 9.6% to 18.4%, peaking at around 23.5% when gestation is narrowed down to 32-36 weeks of gestation (5,6,7). For this, we hypothesize that women in developed areas are likely to get better quality of care.

Women with a preceding preterm birth were more likely to have a spontaneous recurrent preterm birth than provider-initiated recurrent preterm birth. The prevalence of spontaneous recurrent preterm births was 64.7%, which is comparable to the findings of Faye-Petersen et al. in 2008 and Caughey et al. in 2008of 65-70%(18,19). Main factors of mothers associated with a high prevalence of recurrent preterm births in the population studied was being young (<35 years), married, unemployed, and having a short IPI. Moreover, its occurrence was higher when patients had comorbidities such as hypertension and diabetes and medical/gynecological problems such as cervical cerclage and urinary tract infections. However, stratified by the type of preterm birth, comorbidities such as hypertension, diabetes, and the presence of a congenital anomaly such as dextrocardia, bilateral cleft lip, and pallet, down syndrome, and umbilical herniation, et cetera, were common causes of provider-initiated recurrent preterm births. Spontaneous preterm births, on the other hand, were higher when patients presented with fibroids, cervical insufficiency, and UTI. These findings were in agreement with the findings of Yang et al. and Simonsen et al. that adverse reproductive factors such as a short IPI increase the odds of recurrent preterm births and that pre-existing medical conditions such as hypertension predispose women to provider-initiated

recurrent preterm birth (11,12). The finding was also similar to the findings of Laelago et al. and Mazaki-Tovi et al. that UTI and cervical insufficiency increase the risk of recurrent preterm births, mostly the spontaneous type, even though our prevalence values were somewhat lower (4, 28). Cervical length is not routinely measured at KNH, which could explain the lower rates.

The uptake of interventions for preventing recurrent preterm births was relatively low, especially for the provider-initiated type. Even though cervical cerclage was provided to 14.1 of patients who needed it, only 14.3% of women with UTIs received bacterial vaginosis treatment, while 8.2%, 1.2%, and 3.5% received progesterone, heparin, and aspirin treatment respectively. Stratified by types, cases with provider-initiated recurrent preterm birth were more likely to receive heparin and aspirin treatment compared to those with spontaneous recurrent preterm births. Cases with spontaneous recurrent preterm births were more likely to have progesterone, bacterial vaginosis treatment, or cervical cerclage compared to those with provider-initiated recurrent preterm births. This is inconsistent with findings from the USA (Stringer, 2016) and France (Marret, 2009) that progestogen and aspirin uptake was 47% and 21% respectively. Lack of awareness of suitable interventions, and lack of access to interventions are possible explanations for the differences.

5.2 Conclusions

- The recurrence rate of preterm births at Kenyatta National Hospital is high at 40.8%.
- Comorbidities such as hypertension, diabetes, and congenital anomalies are the common causes of provider-initiated recurrent preterm. Cervical insufficiency, fibroids, and UTI more common with spontaneous recurrent preterm birth
- The uptake of interventions for preventing recurrent preterm births is low.

- Women who had spontaneous recurrent preterm births were more likely to receive progesterone, bacterial vaginosis treatment, and cervical cerclage. Those who had provider-initiated recurrent preterm births were more likely to have heparin and aspirin.

5.3 Recommendations

- There is a need to identify high-risk groups during the prenatal period and antenatal care.
- There is a need to promote early comorbidity(hypertension, UTI, and cervical insufficiency) screening and management.
- There is a need to create awareness and promote interventions that prevent preterm births
- A prospective cohort study should be done to provide a better overview of this matter

5.4 Limitations

This was a retrospective study which is perceived to be inferior to experimental designs such as cohort and randomized control trials. The extensive level of missing data for several important variables might have impeded proper statistical analysis or lowered the statistical power of findings.

5.5 **STRENGTH**

- This was the first study at KNH evaluating the prevalence, underlying causes, and uptake of interventions for preventing recurrent preterm births.
- Due to its retrospective nature, the study was quick to conduct and enabled us to evaluate a large sample of patients to improve the statistical power of assumptions we wanted to approve or disapprove.

- It forms the foundation of other studies to further explore the area regarding recurrent preterm birth.

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APPENDICES

Appendix 1. Questionnaire

PREVALENCE, CAUSES, AND INTERVENTIONS FOR PREVENTING RECURRENT PRETERM DELIVERY AT KENYATTA NATIONAL HOSPITAL – A RETROSPECTIVE CROSS-SECTIONAL STUDY

(Fill all sections)

Study number…….. Date……..

Demographic characteristics

1. Age…….

2. Marital status
☐Married
☐Single
☐Divorced/separated
☐Unknown

3. Employment status
☐Employed
☐Unemployed
☐Unknown

4. Substance use
☐Yes
☐No
☐Unknown

If yes, specify……

5. Smoking
☐Yes
☐No
☐Unknown

6. Alcohol use
☐Yes

☐No
☐Unknown

7. Other (specify)……

8. Mother's weight……
   Unknown ☐

9. BMI…….
   Unknown ☐

Reproductive characteristics

10. Parity……

11. IPI from previous preterm birth……

12. Gestation of previous preterm…….

13. Gestation of current pregnancy…….

14. Number of pregnancies……

15. Number of preterm deliveries……..

Medical characteristics

16. Birth outcomes
☐Preterm
☐Normal

17. Recurrent preterm birth
☐Yes
☐No

18. Gestation……..

19. Comorbidities present
☐Yes
☐No

If yes,

a) Maternal

Preexisting diabetes
☐Yes
☐No

Preexisting hypertension
☐Yes
☐No

HIV
☐Yes
☐No

Thyroid disease
☐Yes
☐No

Fibroid
☐Yes
☐No

Cervical insuficiency
☐Yes
☐No

UTI that required admission
☐Yes
☐No
If yes, specify……..

UTI that did not require admission
☐Yes
☐No
If yes, specify……..

UTI that required admission
☐Yes

☐No
If yes, specify……..

Other (specify)…….

b) Neonatal

16. Neonatal anomalies present
☐Yes
☐No

If yes,

Umbilical anomalies
☐Yes
☐No
If yes, specify……..

Amniotic anomalies
☐Yes
☐No
If yes, specify…….
Congenital anomalies
☐Yes
☐No
If yes, specify…….

Others (specify)……..

20. Treatment modalities

a) Progesterone treatment
☐Yes
☐No
If yes, dose…….

b) Bacterial vaginosis treatment
☐Yes
☐No

If yes, antibiotic……

c) Cervical cerclage
☐Yes
☐No

d) Heparin treatment
☐Yes
☐No

e) Anti-hypertensive treatment
☐Yes
☐No
If yes, refer to question 21

Aspirin treatment
☐Yes
☐No

Other treatment
☐Yes
☐No

If yes, specify …….

21. Anti-hypertensive treatment…….

22. Comments

……

ERC APPRBAL LETTER

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Ref: KNH-ERC/A/144

26th April 2021

Code: 101

Dr. Justine Manani Otuke
Re. No.H58/88647/2016
Dept. of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Otuke

RESEARCH PROPOSAL – PREVALENCE, UNDERLYING CAUSES AND UPTAKE OF INTERVENTIONS FOR PREVENTING RECURRENT PRETERM BIRTHS AT KENYATTA NATIONAL HOSPITAL – A CROSS-SECTIONAL STUDY (P60/02/2021)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 26th April 2021 – 25th April 2022.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Obstetrics and Gynaecology, UoN
Supervisors: Dr.George Gwako, Dept. of Obstetrics and Gynaecology, UoN
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KNH APPROVAL

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KNH/HOD-OBS&GYN/07/VOL.11/ Date: 29th April, 2021

Dr. Manani Justine Otuke
Reg. No.H58/8864/2016
Dept. of Obstetrics & Gynaecology
School of Medicine
College of Health Sciences
University Of Nairobi

RE: RESEARCH PROPOSAL – FACTORS PREVALENCE, UNDERLYING AND UPTAKE OF INTERVENTIONS FOR PREVENTING RECURRENT PRETERM BIRTHS AT KNH – A CROSS-SECTIONAL STUDY (P60/02/2021)

This is to inform you that the department has given you permission to conduct the above study which has been approved by ERC.

Liaise with Senior Assistant Chief Nurse - Incharge Labour ward In-charge in Obstetrics and Gynaecology to facilitate your study.

You will be expected to disseminate your results to the department upon completion of your study.

Dr. Peter Michoma
Ag.HOD-OBSTETRICS & GYNAECOLOGY

Cc.

Incharge - Labour Ward
HOD – Health Information