FACTORS ASSOCIATED WITH PRETERM BIRTH IN KNH

A dissertation submitted in partial fulfillment for the award of degree of Master of Medicine in Obstetrics and Gynaecology of the University of Nairobi.

INVESTIGATOR:

DR. ENOCK O. ONDARI

SENIOR HOUSE OFFICER

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY
UNIVERSITY OF NAIROBI

DECLARATION

I hereby declare that this research work and dissertation is my original work and that it was done with the guidance of my supervisors. It has not been submitted to any other university for the award of a degree.

Signature:..... Date: 08/01/2010

Dr. Ondari E. Otieno
Student, Master of Medicine in Obstetrics and Gynaecology,
University of Nairobi.

CERTIFICATION OF SUPERVISION

This is to certify that this research work and dissertation was done under our guidance. It has been submitted for examination with our approval as the university supervisors.

1. Dr. Zahida Qureshi, MBChB, MMed,
   Senior Lecturer
   Department of Obstetrics and Gynaecology,
   University of Nairobi

   Signature: ..... Date: 8/1/2010

2. Dr. Gathari Ndirangu, MBChB, MMed
   Honorary Lecturer
   Department of Obstetrics and Gynaecology,
   University of Nairobi.

   Signature: ..... Date: 8/1/2010

CERTIFICATE OF AUTHENTICITY

This is to certify that this dissertation is the original work of Dr. Enock O. Ondari, Mmed student registration number H58/7508/06 in the Obstetrics and Gynecology department, University of Nairobi (2006-2010). The research was carried out in the department of Obstetrics and Gynaecology, School of Medicine, College of Health Sciences. It has not been presented in any other university for award of a degree.

Signature: _____

Date: 12/1/10

PROF. KOIGI KAMAU
ASSOCIATE PROFESSOR OF OBSTETRICS AND GYNAECOLOGY,
CONSULTANT OBSTETRICIAN AND GYNAECOLOGIST,
CHAIRMAN,
DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY,
UNIVERSITY OF NAIROBI.

DEDICATION

To my loving wife Judy Nyakerario and our children Angela Kwamboka and Dylan Omare, who have been supportive and a source of encouragement throughout this course.

To my parents, Mr. Caleb Otieno and Bathseba Kwamboka. Thank for your encouragement and never ending prayers.

To my elder brother, Victor Ombeka. Thank you for encouraging me and paying my fees through my undergraduate course.

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OPERATIONAL DEFINITIONS.

Anaemia -Hemoglobin concentration of less than 10g/dL during pregnancy or puerperium.[1]

Birth– Used interchangeably with delivery, is the complete expulsion or extraction from the mother of a fetus, irrespective of whether the umbilical cord has been cut or the placenta is attached. Fetuses weighing less than 500g are usually not considered as births, but are termed abortuses for purposes of vital statistics.[2]

Extremely Low Birth Weight: A newborn whose weight is less than 1000g.[3]

Expected Due Date (EDD): The calculated estimated date of delivery using Naegele's rule, i.e by adding 7 days to the date of the first day of the last normal menstrual period and counting back 3 months. [2]

Fundal height: The distance between the upper border of the pubic symphysis and the upper border of the uterine fundus measured in centimetres. This corresponds to the gestation in weeks upto 36 weeks gestation. A variation of $\pm$ cm is accepted as normal.[4]

Labour: A sequence of uterine contractions that results in demonstrable effacement and dilatation of the cervix. A cervical dilatation of 3-4cm with intact membranes is used to diagnose labour. [2, 5]

Last Menstrual Period (LMP): The first day of the last menstrual period. This precedes the conception day by approximately 14 days in a regular 28 day menstrual cycle. [3]

Low birthweight: A newborn whose weight is less than 2500g.[3]

Neonatal period: The period after birth of an infant weighing 500g or more and ending at 28 completed days after birth.[2]

Neonatal period I: period from birth through first 24 hours.[5]

Neonatal period II: birth through first 7 days.[5]

Perinatal period I: 28 weeks of completed gestation to the first 7 days of life.[5]

Preterm birth - Delivery that occurs between 28 weeks and 37 weeks of gestation.[2]

Quickening – The first perception of fetal movements by the pregnant woman. It is usually felt about the 18th week in primigravidae and about the 16th week in multiparae.[4]

Very Low Birth Weight: A newborn whose weight is less than 1500g.[3]

LIST OF APPREVIATIONS

ACOG – American College of Obstetricians and Gynaecologists

AIDS - Acquired Immune Deficiency Syndrome

ANC - Ante-Natal Care

BV - Bacterial Vaginosis

CPD - Cephalopelvic disproportion

EDD - Estimated Due date

ELBW- Extremely Low Birth Weight

FSB - Fresh Still Birth

HIV - Human Immunodeficiency Virus

HTN - Hypertension

IUFD – Intrauterine fetal Demise

KNH - Kenyatta National Hospital

LBW - Low Birth Weight

LMP - Last Menstrual Period

MSB - Macerated Still-Birth

NBU - New Born Unit

NRFS - Non-Reassuring Fetal Status

PROM – Prelabour Rupture of Membranes

PPROM- Preterm Prelabour Rupture of membranes

SGA - Small for Gestational age

SVD - Spontaneous vertex delivery.

UON - University of Nairobi

UTI- Urinary Tract infection

VLBW- Very Low Birth Weight

WHO - World Health Organization

ABSTRACT

Introduction: Preterm birth is an important cause of perinatal morbidity and mortality as well as increased cost of health care provision in our set-up. Preterm birth is the cause of at least 75% of neonatal deaths that are not attributable to congenital malformations, and causes long-term morbidity and disability for those who survive[1]. It is, therefore, important that risk factors be identified to help in preventive management of preterm birth in KNH.

Objective: To determine risk and outcome factors associated with spontaneous preterm birth among mothers delivering in KNH labour ward.

Design: This was a hospital-based comparative cross-sectional study.

Setting: Kenyatta National Hospital, Nairobi, Kenya.

Methods: Participants comprised of women delivering in KNH after spontaneous onset of labour. A structured, interviewer administered questionnaire was used to collect data. Data was collected over a three month period between June and August, 2009. There was no matching of the two groups.

Main Outcome Measures: Maternal risk characteristics and feto-maternal outcomes were compared between women who had preterm birth and those who delivered at term.

Study duration: 15th June and 29th August, 2009

Data analysis: this was done using SPSS version 13. Data entry was done into SPSS and data cleaning done by use of the questionnaires. Descriptive data was obtained and further analysis done. P-values, Odds ratios and 95% confidence intervals were calculated for the various variables under consideration.

Results: 200 women were recruited into the study, 101 in the preterm group and 99 in the term group. The prevalence of spontaneous preterm birth was 8.7%. There was no statistical difference between the two groups in socio-demographic characteristics. ANC attendance was 87.1% in the preterm group and 100% in the term group, which was statistically significant, p-value<0.005. Nineteen percent of the preterm mothers presented with IUFD as compared to 2% in the term group, p-value <0.005, OR0.09[95%CI 0.01-0.42] . There was a significant difference between the two groups in

terms of fetal outcomes. There was 100% mortality for infants born with a weight of less than 1000g.

Conclusion: Pregnant mothers should be encouraged to attend ANC, which may help in identifying and managing risk factors for preterm labour. There is need to develop cheap and simple biochemical markers to predict preterm labour.

INTRODUCTION

The length of human pregnancy is variable and ranges between 38 and 42 weeks (260-294 days). This is referred to as a term pregnancy. Pregnancies that extend up to and beyond 42 weeks (294 days) are termed as postterm pregnancies and those that end before 37 completed weeks are termed as preterm pregnancies.[2,3,6,7]

Under normal circumstances, pregnancy is expected to end in labour and delivery of a viable fetus at term. Labour can either be spontaneous or induced and delivery can be vaginal or through cesarean section.

Although the last menstrual period (LMP) has traditionally been used to calculate the estimated due date (EDD)-Naegele's rule-[2, 8], many inaccuracies exist using this method in women who have irregular menstrual cycles, have been on recent hormonal birth control, or who have first trimester bleeding[8,9]. Though ultrasonographic dating early in pregnancy can improve the reliability of the EDD, it is necessary to understand the margin of error reported at various times during each trimester. A calculated gestational age by composite biometry from a sonogram must be considered an estimate and must take into account the range of possibilities at that gestation[8].

The mechanisms that initiate labour are poorly understood[2,3]. Various theories have been put forward to explain the initiation of labour. These theories are oxytocin stimulation, change in fetal cortisol levels and fetal adrenal gland function, progesterone withdrawal and, finally, prostaglandin release.[3]

Anecdotally, the number of cases presenting with preterm labour and delivery in KNH appears to be increasing although the reasons are not clear. This was a prospective cohort study that investigated factors associated with preterm birth.

LITERATURE REVIEW

Preterm labour is defined as the occurrence of regular uterine activity which produces cervical effacement and dilatation before 37 completed weeks (259 days) of gestation, calculated from the last menstrual period, assuming that the last menses was followed by ovulation 2 weeks later. [2,3,6,7] The lower limit often differs from country to country[9]. While in most developed countries the lower limit of 20 weeks is used, others have adopted 24 weeks[4]. In most developing countries, a lower limit of 28 weeks is adopted, and this applies for Kenya[6,7]. However, WHO has recommended that all births over 500g should be registered to allow uniformity, as very few infants under this weight will survive. [9]

Underreporting of live births of very immature infants makes comparison of preterm birth rates between countries unreliable [9]. Because of these difficulties, much epidemiological work has used birth weight as a standard[10]. Low birth weight (LBW) is defined as less than 2501g, very low birth weight (VLBW) as less than 1501g, and extremely low birth weight (ELBW) as less than 1000g[3,9]. Using these definitions to describe outcome data leads to blurring of distinction between preterm babies and small for gestational age (SGA) babies, particularly in the low birth weight category, and also fails to differentiate the normally grown preterm neonate from the neonate who is both preterm and SGA [3,9] This is because neonatal morbidity and mortality are primarily influenced by gestational age and thus maturity, and less so by birth weight[2].

Preterm birth is the cause of at least 75% of neonatal deaths that are not attributable to congenital malformations [6,11], with neonatal mortality rising gradually between 36 and 28 weeks from 1 to 8%[2,3], and these figures could be higher in our set-up due to the relatively poor state of neonatal care available. This is because the baby is delivered before the homeostatic mechanisms are properly developed and so is prone to respiratory distress syndrome, hypothermia, hypoglycemia and jaundice [12]. Other adverse outcomes include retinopathy and hearing problems[3,12], with the risk of retinopathy of prematurity rising from less than 10% at 26 weeks to above 50% at 24 weeks. The fetal and neonatal brain is especially susceptible to injury between 20 and 32 weeks post-conception [3].

The prevalence of preterm labour and delivery ranges between 6% to 22 %, [2,3,12,13] being lower in developed and highest in developing countries[12,13]. In a cross-sectional study done in KNH in 2001[14], the prevalence of preterm labour was found to be 15.6%. This was lower than that found in India in 2005 of 22% [13], but quite similar to that found at Harare hospital in Zimbabwe in 1998 of 16%.[10] In the United Kingdom, the prevalence ranges between 6-10% [3].

The precise diagnosis of preterm labour is not easy. Uterine contractions of 4 in 20 minutes, cervical dilatation of more than 1 cm, and cervical effacement of 80% or more is diagnostic[2], but the only absolute proof is progressive dilatation of the cervix [12] The finding of fetal fibronectin in vaginal secretions is a sensitive screen for preterm labour[2,9,12], although it is of poor specificity with high false positive rate.[12] In one prospective study[15], it was found that women who are symptomatic for preterm labour, fetal fibronectin and bacterial vaginosis (BV) testing is a good pointer towards impending birth when both tests are positive than either alone. Hendler et al also concluded that women who tested positive for fetal fibronectin and BV, a resolution of BV is associated with a reduction in spontaneous preterm births before 34 weeks of gestation[16]. This test for fetal fibronectin is however not available for routine use.

Knowledge of cervical length, ultrasonographically determined, can also be a pointer towards impending labour and delivery. The shorter the cervical length, the higher the chances of impending labour[2,6]. The knowledge of cervical length and fetal fibronectin levels in cervical secretions have been shown to affect the management of women with threatened preterm labour. In one randomized trial, the knowledge of cervical length and fetal fibronectin was associated with a reduction in the length of evaluation in women with cervical length $\geq$30mm and in incidence of spontaneous preterm birth in all women with preterm labour[17].

Preterm births occur for many different reasons. Studies examining the clinical circumstances surrounding preterm delivery indicate that one-third of all patients present with preterm labour and intact membranes and one third with preterm rupture of membranes (PROM). The remaining third are as a result of indicated deliveries due to

maternal or fetal indications.[18] Risk factors for indicated preterm births tend to be different from those associated with spontaneous preterm birth.[19]

The aetiology of spontaneous preterm labour is multifactorial, but the association between genitourinary tract infection and spontaneous preterm labour is well established and thought to be responsible for up to 40% of cases[20,21]. Indeed, it is the only pathologic process for which a firm causal link with prematurity has been established. This is by causing a release of inflammatory cytokines, such as interleukin 1, 6 and 8 from endothelial cells and tumor necrosis factor from macrophages[18], which lead to inflammatory response in the cervix and lower uterine segment, thereby stimulating the cascade of prostaglandin production from the overlying fetal membranes, deciduas and from the cervix itself[3, 12]. One study has shown that intra-amniotic inflammation without infection is more common than intra-amniotic infection with or without inflammation[22]. In this study that was designed to determine the frequency and clinical significance of intra-amniotic inflammation in patients with preterm labour and intact membranes, amniocentesis was done in 206 patients with preterm labour and intact membranes. Intra-amniotic inflammation (negative amniotic fluid culture but elevated amniotic fluid interleukin-6) was more common than intra-amniotic infection (positive amniotic fluid culture regardless of amniotic fluid interleukin-6 concentration) in 21% as compared to 10% in a cohort of 206 women. The amniocentesis to delivery interval was significantly shorter in patients with intra-amniotic inflammation than in patients with a negative culture and without inflammation.

The commonest groups of organisms associated with intra-amniotic infection are streptococci, mycoplasmas and fusiform bacilli[12]. Fifty percent of patients with microbial invasion have more than one micro-organism isolated from the amniotic cavity, and the size of the inoculum varies considerably[18]. Bacterial vaginosis associated with a vaginal pH of more than 5.4 seems to promote preterm labour[13,20]. This is possibly by reducing the efficiency of the cervical barrier to infection, and also because women with BV are at an increased risk of urinary tract infections[23], which has been shown to be a risk for preterm labour[13]. The relationship between intrauterine infection and spontaneous preterm birth has been extensively studied to the extent that it has been suggested that the

existence of an association does not mean that infection causes preterm delivery. Indeed it has been argued that microbial invasion of the amniotic cavity is merely a consequence, and not the cause, of labour[18]. However, determining whether or not this relationship is causal is critical in that it has major clinical and therapeutic implications. The evidence supporting a causal role for infection follows the criteria outlined by Sir Bradford Hill in his presidential address before the Section of Occupational Medicine of the Royal Society of Medicine in 1965 and includes: (1) biological plausibility; (2) temporal relationship; (3) consistency and strength of association; (4) dose-response gradient; (5) specificity; and (6) human experimentation[12].

French and colleagues showed that first trimester bleeding is increased among patients with BV, *Trichomonas vaginalis, Chlamydia trachomatis*, and combinations of these infections[24]. Women with BV who also experienced first-trimester bleeding are at increased risk for preterm birth, with treatment of studied infections significantly reducing the risks of preterm birth among women without first-trimester bleeding. If and how gestational bleeding and common genitor-urinary tract infections are linked to each other and the risks of preterm birth have not been examined adequately. Early gestational bleeding has been ascribed traditionally to non-inflammatory factors such as presence of an abnormal conceptus, uterine anomaly, various hormonal deficiencies or disruption of the junction between the trophoblast and conceptus. Alternatively, several investigators suggest that ascending reproductive tract infections with presumed subclinical endometritis can adversely affect implantation, early placentation, and growth of the trophoblast and conceptus[18, 24].

Several other factors have been associated with preterm labour. They may be medical, obstetric, genetic, lifestyle related, maternal anthropometry, chorioamnionitis, cervical incompetence, several fetal factors, environmental, among others[2, 10].

In one cohort study, Simhan et al showed that regardless of maternal race, paternal black race is associated with increased odds of preterm birth, either through genetic or other biologic factors[25]. However, in a secondary analysis of four prospective studies, it was shown that black women have increased risks of prematurity that are associated with

prevalent reproductive tract infections during pregnancy[26]. Other studies have disputed these findings, citing social deprivation and reproductive tract infections that are more prevalent in the black race rather than genetic variation. In studies of populations where black and white women have similar lifestyles, levels of income and access to medical care, preterm delivery rates show a less marked ethnic variation[3].

Blood pressure dynamics in pregnancy also play a role in preterm labour[27]. In a secondary analysis of data from the WHO calcium supplementation for the prevention of eclampsia trial, it was shown that women experiencing early or late preterm birth had 10 mmHg and 3 mmHg higher rise , respectively, in systolic, diastolic and mean arterial blood pressure than women delivering at term in a dose response pattern. Another nested case control study [28] showed the presence of dyslipidemia in women with spontaneous preterm birth. This is closely related to the fact that women who deliver preterm infants may be at an increased risk for cardiovascular disease, perhaps related to dyslipidaemia. A large study found that wome who had delivered pregnancies before 37 weeks' gestation, not complicated by preeclampsia, had a 3-fold increased risk of cardiovascular death, independent of lifestyle or socioeconomic factors, after an average follow-up of 13 years[28, 29].

Preterm birth of twins has been shown to be associated with an increased risk of preterm delivery in a subsequent singleton pregnancy[30]. A population-based cohort study also showed that the risk of preterm birth and its recurrence increases with short inter-pregnancy intervals, even after adjustment for coexisting risk factors. This study highlights the importance of counseling women with either an initial term or preterm birth to wait at least 12 months between delivery and subsequent conception[31]. It is important to note that where the infant does not survive, the chances of a shorter inter-pregnancy interval are increased and health care providers need to counsel mothers appropriately.

HIV infection in relation to various aspects of preterm labour and delivery has been studied extensively. In one cohort study whose aim was to determine trends in low birthweight and preterm birth among infants born to HIV-infected women in USA[32], it

was found that the proportion of infants who had low birth weight or were born preterm declined during an era of increased antiretroviral therapies. These trends differed from the overall increases in both outcomes among the general population, where LBW and preterm birth still are markedly higher among infants who are born to HIV-infected women[32, 33]. In a study at Pumwani Maternity Hospital between 1989 and 1991, it was concluded that maternal HIV antibody was associated with preterm delivery[33]. This is possibly due to the high level of chorioamnionitis observed in these cases. In this case control study, the HIV seroprevalence in preterm group was 12.5% as compared to 6.9% in the controls. Moderate to severe choriamnionitis was found in 37% of HIV positive preterm placentas compared to 18% of matched HIV positive preterms vs 13% HIV negative term deliveries. The researchers concluded that maternal HIV antibody was associated with prematurity as is moderate to severe chorioamnionitis which was observed more in HIV positive than in HIV negative preterm and term deliveries.

While acknowledging that preterm delivery is associated with increased risks of vertical HIV transmission, another study looked at whether the risk of HIV infection for preterm infants is a consequence of intrauterine infection, or whether preterm infants are more vulnerable to infection[34]. The study showed that intrauterine infection is unlikely to precipitate preterm delivery. Rather, preterm infants appear to be more vulnerable to prolonged exposure to HIV at the time of delivery, as the association between preterm delivery and intrapartum transmission was found only among infants born following longer rupture of membranes. In another prospective study, Villamor and colleagues concluded that poor anthropometric status at the first prenatal visit and weight loss during pregnancy among HIV-1 infected women are strong risk factors for adverse pregnancy outcomes[35].

Maternal anaemia in pregnancy is also associated with spontaneous preterm labour. In a study done in KNH in 1992, it was shown that preterm deliveries are 1.5 times more likely to be associated with maternal anaemia than term deliveries[36]. This is due to various factors associated with anaemia in pregnancy, including low resistance to infections, chronic intrauterine hypoxia and even intrauterine fetal demise[2, 4, 36].

Smoking of cigarettes during pregnancy, alcohol consumption and coitus have also been associated with preterm birth by many researchers. Cigarette smoking has been heavily associated with preterm birth, among other pregnancy complications, especially when smoking is extended beyond 15 weeks' gestation[29]. Smoking is associated with decreased serum concentration of ascorbic acid. Cadmium in tobacco has also been found to increase the maternal binding of metallothionein in trophoblasts which may result in sequestration of copper. Coitus has been thought to increase preterm birth by orgasm which causes uterine contractions and also deposition of semen which is rich in prostaglandins which may then cause cervical changes and uterine contractions. Another theory is that it may be associated with introduction of microorganisms through the cervical mucus plug. [2, 4, 18].

The management of preterm labour, once diagnosed, is complex in view of the many associated causative factors. Prevention of preterm onset of labour and avoid delivery prior to 37 weeks, if possible, should be the ultimate goal of management[2,4]. Therefore, the causal factor needs to be known and possibly managed at the earliest opportunity. In primigravid women with no other significant risk factors for preterm delivery, there is no effective method for the prediction of preterm labour and therefore management can only be instituted at the time of acute presentation with contractions[3]. As the only absolute proof of preterm labour is progressive dilatation of the cervix, it follows that once this has happened, it may be too late to attempt preventive treatment[12].

The use of antimicrobials to delay preterm birth has been tried with very disappointing results[2, 3, 37]. Antibiotic use was advocated because preterm delivery is often associated with evidence of chorioamnionitis. But it is not yet clear whether infection or inflammation is the cause or an effect of preterm delivery[37]. Early screening and treatment of BV and asymptomatic bacteriuria may help to reduce occurrence of preterm labour later in pregnancy. Several studies have suggested various antibiotics to be used in the treatment of BV, but only metronidazole and clindamycin have shown positive results[37-40]. One multicentre, randomized, triple-blind, placebo-controlled trial[38], it was shown that early mid-trimester clindamycin treatment of women with asymptomatic abnormal vaginal flora or BV reduced the risk of late miscarriage or preterm birth by

66%. This study, however, showed no improvement in neonatal outcome. According to a meta-analysis of randomized, controlled trials, antibiotic treatment for BV in the late second trimester or early third trimester has no effect on preterm birth, or on any major neonatal morbidity[40]. Thus, treatment of BV should remain in the experimental realm. Verstraelen and colleagues[41], in a prospective cohort study, showed that accounting for atypical gram-positive bacteria and neutrophils on gram-stained vaginal smears may identify a larger proportion of women at risk of preterm birth compared to diagnosis of BV alone. They showed that the sensitivity of vaginal smear diagnosis for preterm birth increased from 25% with conventional scoring up to 70% with a modified criteria, which consists of a 4-category Gram-stained vaginal smear method, viz;- 'normal,' 'bacterial vaginosis-like,' 'grade I-like,' or 'purulent grade I.'

Cervical cerclage in cases of cervical incompetence, including emergency 'rescue' cerclage, has been shown to prolong pregnancy, improve birth weight and is not associated with increase in frequency of chorioamnionitis, maternal morbidity or perinatal mortality[2,3,9].

Suppression of uterine contractions would seem to be the obvious solution to the problem of preterm labour. However, tocolytic agents do not work effectively for longer than about 48 hours, probably because of tachyphylaxis[3, 12] a rapid decrease in response after repeated doses over a short period of time, probably by depletion of the neurotransmitter that is involved in the action of the drug. The major role of tocolytics is to postpone delivery to allow the administration of corticosteroids to the mother and so to the fetus to promote surfactant release in the fetal lung and reduce the incidence of neonatal respiratory distress syndrome, which it does by up to 50%.[12] It also allows for in-utero transfer to a tertiary centre in anticipation of preterm delivery for specialized neonatal care.

Many tocolytics are currently used. Sympathomimetics such as ritodrine and salbutamol and terbutaline are generally the safest choice for the mother and fetus, although they can cause tachycardia and pulmonary oedema if given in overdose.[2,12] Indomethacin can be used before 32 weeks as it may cause premature closure of the fetal ductus arteriosus if

used after 32 weeks' gestation, which can lead to pulmonary hypertension. Calcium channel blockers such as nifedipine work by reducing myometrial contractility, but they can cause significant hypotension. Magnesium sulphate has also been used, working possibly as a calcium antagonist. Nitric oxide donors such as glyceryl trinitrate are also being evaluated, but are not effective and not superior. They also lead to significant hypotension. [2-4, 12]

An oxytocin receptor antagonist, atosiban shows promise, as does nimesulide, a selective cyclo-oxygenase type 2 inhibitor.[2, 37] Romero and associates have shown benefits of atosiban after 28 weeks' gestation, with up to 7 days prolongation of pregnancy and fewer fetal and maternal effects that compare to placebo[42], but cost and unavailability, among other factors, have limited widespread use in Kenya.

Bed rest is an integral part of the management of a mother in preterm labour, but various studies are yet to show any benefit of this management,[2,11] with others arguing that it may increase chances of thromboembolic complications[1]. With bed rest traditionally prescribed as management, the argument has been whether to manage patients at home or in hospital. One randomized clinical trial showed that home care management is an efficient and acceptable alternative to hospital care for women experiencing preterm labour and with easy access to hospital in case labour was to progress further[43], although some proponents of hospital management have argued that it may be difficult for the woman to avoid coitus at home[2,44].

RATIONALE OF THE STUDY

Spontaneous preterm labour and delivery continues to be an important cause of perinatal mortality and morbidity, with dangers of both short-term and long term mental and physical handicap in the infants who survive, as well as emotional stress to the parents. It is the single largest contributor to perinatal mortality in the developing world[2,6,7]. Economic costs of caring for preterm infants and additional expenditures for developmental handicaps during the remainder of childhood are also considerably high[2].

Globally, the incidence of preterm labour continues to be high despite such advances as the development and use of tocolytic agents.[7] It is obvious, therefore, that the problem is bigger in the developing countries since such new drugs are not available for routine use.

It is, therefore, important that risk factors be identified to help in preventive management of preterm labour and delivery.

Previous studies done locally on the same topic of preterm labour and delivery[14,45] have not looked at medical conditions as a variables to be measured.
The only study done in KNH looking at the factors associated with delivery of preterm infants was a cross-sectional study done in 2001[14]. In this study, there was no control population and medical conditions were not considered as variables. The study found out no associated factor in 52% of the preterm deliveries while 26.6% were due to preterm PROM and 8.5% due to pre-eclampsia, among other factors. This study aimed at comparing mothers who presented with spontaneous preterm labour with those who presented with spontaneous labour at term. HIV status, among other medical conditions, was also included a variable. This study also aimed at comparing feto-maternal outcomes, mode of delivery and possible aetiologies of preterm birth.

This study was designed to compare socio-demographic, medical and obstetric factors and feto-maternal outcomes between mothers who had preterm delivery and those who delivered at term.

Research question
What risk and outcome factors are associated with spontaneous preterm birth in KNH?

Null Hypothesis
There are no significant differences between mothers who have preterm delivery and those who deliver at term

OBJECTIVES OF THE STUDY

Broad Objective

To determine risk and outcome factors associated with spontaneous preterm birth among patients delivering in KNH.

Specific Objectives

1. To determine the prevalence of spontaneous preterm delivery among mothers delivering in KNH
2. To determine socio-demographic, obstetric and medical factors associated with spontaneous preterm delivery.
3. To determine the fetal and maternal outcomes in subjects with preterm delivery.

Variables measured

1. Socio-demographic variables - age, marital status, level of education, occupation, residence, alcohol intake, cigarette smoking.
2. Obstetric variables – parity, previous preterm deliveries/ miscarriages, duration since last delivery, gestation at labour/ delivery, fetal and maternal outcomes, mode of delivery, ANC attendance.
3. Medical variables – Anaemia, genitor-urinary tract infections, chronic medical diseases.
4. Others – hospital stay, duration since last intercourse.

METHODOLOGY

Study design

This was a hospital based comparative cross-sectional, non-interventional study with an analytical, observational research design that compared characteristics of women who had preterm delivery as cases and those who delivered at term as controls.

The study area

The study area was Kenyatta National Hospital, which is a national referral and teaching hospital situated in Nairobi, 4 kilometres west of the central business district. It is also the main teaching hospital for the College of Health Sciences, University of Nairobi. The

hospital caters for patients from Nairobi and its environs as well as referrals from other hospitals in the country and the greater Eastern Africa region.

KNH has one Labour ward, the three antenatal/postnatal wards (GF A, GF B and 1A), a new born unit (NBU), neonatal intensive care unit (NICU) as well as an intensive care unit (ICU). Patients in pregnancy above 20 weeks gestation and those who are in immediate puerperium are admitted in the antenatal/postnatal wards. Patients in labour or with conditions requiring close monitoring, such as preterm labour, are admitted in labour ward. It also has a maternity theatre for caesarean sections and other obstetric procedures. On average, of 20 deliveries are conducted every day in the labour ward, either vaginally or through caesarian section.

The hospital is manned by several service providers, including consultants, senior registrars, residents, nurse midwives and medical and nursing students. It is also multidisciplinary with physicians, surgeons, obstetricians and gynaecologists and paediatricians, which helps to wholly manage patients.

While some patients who deliver at our labour ward are clinic attendees at KNH, hospital records suggest that majority do not attend ANC clinic at KNH. Most of them attend the city council of Nairobi clinics.

Study Participants

The study participants were women who were admitted to KNH labour wards for delivery during the study period. They were either at or before term and had spontaneous onset of labour. Gestation was confirmed by any three of the following criteria;

i) Last menstrual period (LMP) where the mother was very sure of her dates, was not on recent hormonal birth control for at least 3 cycles before the LMP, and did not have irregular menstrual cycles.

ii) Ultra-sound scan in the first trimester of the pregnancy or at least before 20 weeks of gestation.

iii) Fundal height recording in the antenatal clinic showing progressive increments in fundal height with gestation in weeks.

iv) Quickening. This was taken to occur at between 16-18 weeks for multigravid women and 18-20 weeks for primigravid women.

v) Positive pregnancy test after first missed menstrual period

vi) Fundal height recording that agrees with gestation by dates.

Exposure of interest

In this prospective cross-sectional study, the exposure of interest was preterm birth. Maternal characteristics and feto-maternal outcomes were compared between women who had preterm birth as cases and those who delivered at term as controls.

Sampling technique

This took place in the labour ward of KNH. As per the current management protocol, once a patient arrives, she is allocated to a primary nurse who takes her to into one of the "first stage" rooms. The registrar on duty then reviews the patient and management prescribed accordingly.

Two midwives in the labour ward were recruited as research assistants and trained on recruitment of cases and filling of the questionnaire.

All mothers admitted to KNH labour ward with an admission diagnosis of spontaneous preterm labour and spontaneous labour at term and who met the inclusion criteria were selected consecutively.

Those with an admission diagnosis of spontaneous preterm labour were recruited sequentially to the study arm of preterm birth. For every mother recruited to preterm arm, the next mother admitted with a diagnosis of spontaneous labour at term was recruited to the study arm of term birth.

The participants in the two arms of the study were followed up until discharge from the hospital or until 28 days from the time of recruitment, whichever came first. The neonates were also followed up in the same manner.

Inclusion criteria:

- Mothers who gave informed consent.
- Mothers with spontaneous onset of labour.
- Mothers at confirmed gestation between 28 weeks or below 41 completed weeks

Exclusion criteria:

To avoid bias, this study focused on women who presented with a diagnosis of spontaneous onset of labour. The following were therefore excluded;

- Patients who had labour induced or had elective delivery
- Mothers at confirmed gestation below 28 weeks or above 41 completed weeks
- Mothers who did not give informed consent.

Sample size estimation

Sample size was calculated using the formula below

Let p_i be the proportion of subjects in group i having the outcome of interest, $\bar{p} = (p_1 + p_2)/2$ and $\bar{q} = 1 - \bar{p}$.

$$H_0: p_1 - p_2 = 0$$

$$H_1: p_1 - p_2 = d$$

The sample size per group is

$$n' = \frac{\left[z_{\alpha}\sqrt{2\bar{p}\bar{q}} - z_{\beta}\sqrt{p_1q_1 + p_2q_2}\right]^2}{d^2}$$

$$n = n'/4\left(1 + \sqrt{1 + 4/n'|d|}\right)^2 \text{ "continuity correction".}$$

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Fleiss JL Statistical Methods for Rates and Proportions (2nd edition). Wiley:New York, 1981

Factor under consideration		"preterm delivery"
1ST GROUP		"Pre-Term delivery"
2ND GROUP		"Term delivery"
Parameter	**Symbol**	**Value**
Highest "probability" of preterm birth	p_1	22.0%
Lowest "probability" of preterm birth	p_2	7.0%
$p_1 - p_2$	d	0.15
Odds Ratio	OR	3.75
Proportion of participants expected in "Pre-Term delivery" group	m_1	50.0%
Proportion of participants expected in "Term delivery" group	m_2	50.0%
Ratio of ("Pre-Term delivery":"Term delivery") sizes	r	1.00
P corrected	p-bar	0.145
Power	1-β	80%
Where z is the abscissa of the normal curve	z-β	0.84
Confidence level	1-α	95%
	z-α	1.96
Where α is probability of type I error and β probability of type II error		
Number of subjects required for "Pre-Term delivery" group	n_1'	86
Number of subjects required for "Term delivery" group	n_2'	86
Continuity correction for n_1'	n_1	99
Continuity correction for n_2'	n_2	99
Sample size		**198**

The highest reported prevalence for preterm delivery is 22%[13] and the lowest is 6%[3]. This would give a sample size of 172. However, to be conservative an assumption of a lower prevalence of 7% was made; hence the sample size in our study was 198 with 99 in each arm.

Data collection procedure

Data was collected by the principal researcher and two assistants. A pre-tested structured questionnaire was used to collect data. The in-patient numbers were obtained from the admission and discharge registers in labour ward, maternity wards and maternity theatre. Mothers were interviewed and the information so given entered into a structured questionnaire. Labour and delivery records including case files, observation charts, infant notes, admission and discharge records and operating theatre notes were interrogated and information entered in a structured questionnaire.

Data collection instrument

A pretested, interviewer administered research questionnaire was used. It included both open-ended and closed-ended questions.

Data analysis

Data collected was cleaned, entered into a computer programme and analyzed using SPSS version 13 computer package. Results are presented in prose and tables. P-values, odds ratios and 95% confidence intervals were computed to test for significance.

Quality control of data

Two research assistants were trained on interviewing, information retrieval and filling the questionnaire. Recording of clinical findings in antepartum, intrapartum and postpartum period was entered after thorough scrutiny.

In order to avoid double participant recruitment, the participants' admission (in-patient) numbers were entered into a register upon recruitment for serialization. This register was counter-checked on a daily basis for any double entries and if it is so discovered, one of the questionnaires was withdrawn and discarded and the serialization rectified before recruitment continued.

Ethical considerations

Approval was sought from the KNH Ethics and Research Committee before the study was carried out. Informed consent of patients was obtained before participating in the study. Standard care was given to all mothers regardless of whether they consented or declined to participate in the study and subjects were not exposed to any risk by participating or declining to participate in the study. The records were coded and the patients' names were not used. The information so collected remained confidential and was used for the purposes of the study only. No incentives were given to the study subjects.

My study proposal was also presented to the department of Obstetrics and Gynaecology of the University of Nairobi and clearance to carry out the study was granted.

Study limitations

- The quality of recording clinical findings had a direct impact on the study, as some clinicians did not record status of membranes at the time of admission.

- Sincerity of mothers and their recall on socio-demographic data may have had an impact on the study.

Mitigation of study limitations

To overcome the above limitations, the following measures were taken

- Time was taken to retrieve the appropriate records and, where necessary, confirmation was sought from both the clinicians and the mother.

- It was emphasized to the mothers the importance of the study and the abounding benefits. They were encouraged to co-operate until discharge.

RESULTS.

Table 1: SOCIODEMOGRAPHIC DATA

	Preterm n=101	Term n=99	p-value
Age in years	**n(%)**	**n(%)**	
15-20	13(10.6)	11(11.1)	
21-25	29(27.6)	38(37.7)	0.339
26-30	31(32.2)	33(31.9)	
31-35	17(15.7)	12(13.3)	
>35	11(13.9)	5(5.9)	
Education level	**n(%)**	**n(%)**	
Primary	33(35.7)	35(34.1)	0.129
Secondary	55(54.4)	42(44.4)	
Tertiary	13(9.9)	22(21.5)	
Marital status	**n(%)**	**n(%)**	
Single	16(13.4)	17(13.9)	
Married	85(86.6)	80(84.1)	0.339
separated/widowed	0(0.0)	2(2.0)	
Occupation	**n(%)**	**n(%)**	
Unemployed	46(47.5)	42(46.2)	
self employed	35(36.7)	33(31.1)	0.509
salaried employed	20(15.8)	22(21.1)	
Student	0(0.0)	2(1.6)	

Table 1 shows that there were no statistically significant differences between the two groups in terms of sociodemographic characteristics. The mean age was 24.3 years, with a range of 16 to 39 years.

Table 2: PATIENT'S HABITS DURING PREGNANCY

	Preterm n=101	Term n=99	p-value	Odds ratio	95%CI
Alcohol intake	**n(%)**	**n(%)**			
No	90(89.1)	89(89.9)	0.855	0.92	0.34-2.47
Yes	11(10.9)	10(10.1)			
Cigarette smoking	**n(%)**	**n(%)**			
No	101(100)	99(100)	undefined	-	-
Yes	0(0)	0(0)			
sexual intercourse before delivery	**n(%)**	**n(%)**			
<1 week	33(32.7)	15(15.2)	<0.005	2.09	1.18-3.67
1-2 week	23(22.8)	22(22.2)	0.08	2.10	0.83-5.36
2-4 weeks	18(17.8)	31(31.3)	<0.005	3.79	1.51-9.66
> 4 Weeks	27(26.7)	31(31.3)	0.025	2.53	1.06-6.09

As shown in table 2, none of the participants smoked during the index pregnancy. There was a statistically significant difference between the two groups in terms of last sexual intercourse before onset of labour. Majority in the preterm group (57.5%) had intercourse within two weeks of admission as compared to the term group where majority (62.6%) had intercourse more than two weeks before admission. There was no statistically significant difference in terms of alcohol intake during pregnancy.

Table 3: PAST OBSTETRIC CHARACTERISTICS

	Preterm n=101	Term n=99	p-value	Odds ratio	95%CI
Parity(number of previous deliveries)	**n(%)**	**n(%)**			
1-2	62(57.0)	73(69.7)			
3-4	34(38.4)	24(27.7)	0.06	0.57	0.30-1.03
>5	4(3.5)	2(2.6)			
Previous preterm delivery	**n(%)**	**n(%)**			
0	75(78.8)	84(84.9)			
1	23(19.0)	13(13.1)	0.084	0.5	0.24-1.09
>2	3(2.2)	2(2.0)			
Inter-pregnancy interval	**n(%)**	**n(%)**			
<1 year	9(7.4)	4(3.6)			
1-2 years	16(16.7)	12(13.0)	0.30	1.86	0.66-5.14
>2 years	42(44.0)	36(38.3)			
n/a	34(31.9)	47(45.2)			

Table 3 shows that majority of participants in both groups were of low parity with 57% in the preterm group and 69.7% in the term group having had one or two previous deliveries. While the preterm group had more previous preterm deliveries (21.2% vs 15.1%), overall there was no statistically significant difference between the two groups in terms of past obstetric characteristics.

Table 4: ANTE-NATAL CHARACTERISTICS

	Preterm n=101	Term n=99	p-value	Odds ratio	95%CI
Attended ANC	**n(%)**	**n(%)**			
No	13(12.9)	0(0.0)	<0.005	undefined	Undefined
Yes	88(87.1)	99(100)			
Haemoglobin level	**n(%)**	**n(%)**			
<7 g/dl	0(0.0)	2(1.9)			
8-9 g/dl	13(10.7)	16(14.1)	0.0.95	1.03	0.45-2.47
>10 g/dl	59(60.9)	79(82.5)			
not indicated	28(28.4)	2(1.5)			
HIV status	**n(%)**	**n(%)**			
Negative	72(68.7)	91(93.3)			
Positive	8(6.9)	8(6.7)	0.65	0.79	0.25-2.46
not indicated	21(24.4)	0(0.0)			
VDRL	**n(%)**	**n(%)**			
Negative	76(74.5)	96(97.7)			
Positive	0(0.0)	1(0.8)	1.0	undefined	Undefined
not indicated	25(25.5)	2(1.5)			

As shown in table 4, ANC attendance was 87.1% in the preterm group as compared to 100% in the term group. This difference was statistically significant. There was no statistically significant difference in ante-natal profile between the two groups.

Table 5: ANTE-NATAL COMPLICATIONS

Antenatal complications	**Preterm n=101 n(%)**	**Term n=99 n(%)**	**p-value**	**Odds ratio**	**95%CI**
yes	38(37.6)	23(23.2)	0.044	0.98	0.42-1.69
no	63(62.4)	76(76.8)			
complications	**n=38 n(%)**	**n=23 n(%)**			
APH	3(7.9)	1(4.2)	0.781	0.99	0.24-4.15
HTN	11(30.4)	8(35.1)	0.964	0.98	0.59-1.61
UTI	11(30.4)	7(30.7)	0.857	1	0.56-1.83
PV discharge	2(5.2)	2(8.6)	0.739	0.99	0.41-2.46
False labour	3(7.9)	0(0.0)	0.003	-	-
Polyhyramnios	1(2.6)	0(0.0)	Undefined	-	-
Twin gestation	8(21.0)	2(8.7)	0.004	1.36	0.97-4.37
Other	1(2.6)	3(13.0)	1	undefined	Undefined

Table 5 shows that 37.6% of the participants in the preterm group had some form of ante-natal complication as compared to 23.2% in the term group. Significantly, false labour and twin gestation were statistically different between the two groups with p-value of < 0.005.

Table 6: MATERNAL OUTCOMES

	Preterm n=101	Term n=99	p-value	OR	95%CI
Mode of delivery	**n(%)**	**n(%)**			
SVD	73(72.3)	75(75.2)			
Caesarean	24(23.8)	20(20.7)	0.386	0.49	0.06-3.22
assisted vaginal delivery	0(0.0)	2(1.5)			
breech delivery	4(3.9)	2(2.6)			
Maternal complications after delivery	**n(%)**	**n(%)**			
No	88(89.6)	91(92.5)	0.269	0.60	0.21-1.63
Yes	13(10.4)	8(7.5)			
Complications	**N=13 n(%)**	**N=8 n(%)**			
PPH	3(23)	4(50)	0.451	0.56	0.12-1.35
Retained placenta	3(23)	0(0.0)	0.004	-	-
Puerperal sepsis	2(15.5)	2(25)	0.049	1.23	0.9-3.12
Other	5(38.5)	2(25)	0.008	0.39	0.12-2.22
Length of hospital stay	**n(%)**	**n(%)**			
<2 days	51(48.6)	68(68.0)	1	-	-
3-5 days	34(39.1)	29(30.0)	0.15	0.64	0.33-1.24
6-10 days	10(7.9)	1(0.8)	0.002	0.08	0.00-0.6
>10 days	6(4.5)	1(1.1)	0.005	0.13	0.01-1.10

Table 6 shows that majority of deliveries in the two groups was by spontaneous vertex delivery (SVD), 73.2% in the preterm group and 75.2% in the term group. There was a statistically significant difference between the two groups in terms of maternal complications after delivery, with23% of those who had complications in the preterm group having retained placenta and none in the term group, p value 0.004. Participants in the preterm group had a significantly longer hospital stay as compared to the term group, with a statistically significant difference being observed for hospital stay of over 5 days.

Table 7: INFANT OUTCOMES

	Preterm n=109	Term n=101	p-value	OR	95%CI
Status of fetus at admission	**n(%)**	**n(%)**			
Alive	71(81.2)	97(99.2)	<0.005	0.09	0.01-0.42
IUFD	21(18.8)	1(0.8)			
APGAR score at 5 minutes	**n(%)**	**n(%)**			
<5	35(29.3)	3(2.2)			
6-7	13(11.7)	6(7.2)	<0.005	0.13	0.06-0.29
>8	62(59.0)	91(90.6)			
Birth weight	**n(%)**	**n(%)**			
<1000g	10(8.4)	0(0.0)			
1001-1500g	40(32.3)	0(0.0)	<0.005	0.01	0.01-0.03
1501-2500g	44(39.7)	8(7.1)			
>2500g	16(19.6)	92(92.9)			
NBU admissions	**n(%) n=88**	**n(%) n=100**			
No	37(42.4)	85(85)	<0.005	7.6	3.73-15.68
Yes	51(57.6)	15(15)			
Length of stay in NBU	**n(%) n=51**	**n(%) n=15**			
1-4 days	23(45.6)	11(73.3)			
5-7 days	8(15.8)	4(26.7)			
8-10 days	8(15.8)	0(0.0)	0.08	0.31	0.09-1.14
>10 days	12(22.8)	0(0.0)			
Status of infant on discharge	**n(%) n=51**	**n(%) n=15**			
Alive	27(58.1)	14(95.0)	<0.005	0.07	0.032-0.19
Dead	24(41.9)	1(5.0)			

Table 7 shows infant outcomes. There were 109 preterm and 101 term babies delivered. 18.8% of the preterm and 0.8% of the term infants had been diagnosed with IUFD at admission. 41% of the preterm infants had an APGAR score of <7 at five minutes as compared to 9.4% in the term group. 57.6% of the preterm infants were admitted to NBU for various reasons as compared to 15% of the term infants. Of the NBU admissions, mortality rate was 41.9% in the preterm group with only 5% in the term group. Safe for length of NBU stay, there were statistically significant differences between the two groups in terms of neonatal outcomes.

Table 8: Gestation at delivery versus status of infant on discharge.

gestation at delivery (weeks)	status of infant on discharge		Total	p-value
	Alive n (%)	Dead n (%)		
28-30	6(20.7)	23(79.3)	29	
31-33	18(48.6)	19(51.4)	37	
34-36	26(74.3)	9(25.7)	35	
37	8(88.9)	1(11.1)	9	
38	21(95.5)	1(4.5)	22	0.002
39	28(93.3)	2(6.7)	30	
40	31(91.2)	3(8.8)	34	
41	14(100)	0(0.0)	14	
Total	**152(72.4)**	**58(27.6)**	**210**	

Of the infants, the highest mortality was at 28-30 weeks at 79.3% and was lowest at 41 weeks (0.0%) there's a gradual reduction of mortality from a high of 79.3% at28-30 weeks to only 4.5% at 38 weeks (table 8). There is a statistically significant difference at various gestations as far as mortality is concerned.

Table 9: Birth weight versus status of infant on discharge.

birth weight (g)	status of infant on discharge		Total	p-value
	Alive n(%)	Dead n(%)		
<1000g	0(0)	10(100)	10	
1001-1500g	11(27.5)	29(72.5)	40	
1501-2500g	38(73.1)	14(26.9)	52	<0.001
>2500g	103(95.4)	5(4.6)	108	
Total	**152(72.4)**	**58(27.6)**	**210**	

From table 9, there was 100% mortality for infants born with a weight of less than 1000g. As expected the lowest morality was for infants with a birth-weight of more than 2500g (4.6%). This difference was statistically significant.

DISCUSSION

During the study period, between 15th June and 29th August, a total of 1160 deliveries were recorded, with 8 sets of twins in the preterm group and 2 in the term group. Of these deliveries, 101 followed spontaneous preterm labour, giving a prevalence of spontaneous preterm delivery of 8.7%, which is much lower than that found by Irungu in 2001 of 15.7%[14]. This is possibly because in this study we looked at spontaneous preterm birth only as opposed to both spontaneous and induced preterm delivery considered by Irungu. The figure is however higher than that found in Denmark of 5.7% for primiparous women and 3.2% in multiparous women[44]. This difference could be due to the prevalent socioeconomic status in these two regions. Studies have linked low socioeconomic status with higher incidence of bacterial vaginosis[19, 46] that predisposes to preterm labour and delivery.

Majority of the participants in the preterm group (30.7%) were aged between 26 and 30 years and in the term group majority (38.4%) were aged between 21 and 25 years. In both groups, majority of the participants were aged between 21 and 30 years (59.4% in the preterm group and 71.7% in the term group). The range was between 16 – 39 years, with a mean age of 24.3 years, similar to that found by Irungu[14] of 24.3 years and also that of 23.7 years found by Mbatha[47] in her study in Kikuyu Mission Hospital. No studies have linked age as risk factor for preterm birth.

Majority had secondary education (54.5% in preterm and 42.4% in term group). More than 80% in both groups were married and majority (45.5% and 42.4%) were unemployed. There was no significant difference between the two groups in socio-demographic characteristics.

All the participants in the two arms of the study were non-smokers. This is in keeping with KDHS 2003[48] report that less than 1% of Kenya women smoke and less than 3% have ever used tobacco of any kind. Cigarette smoking has been heavily associated with preterm birth, especially when smoking is extended beyond 15 weeks' gestation[29].
In this study, majority in both groups (>89%), did not take alcohol during pregnancy. This is higher than 2% found by Irungu in his study at KNH[14]. Majority (57.5%) in the

preterm group had intercourse within 2 weeks of admission as compared to term group where majority (62.6%) had intercourse more than 2 weeks before admission. Significantly, 33.7% in the preterm group had intercourse within 1 week of admission as compared to 15.2 in the term group, p-value <0.005, OR 2.09, 95%CI[1.18-3.67]. It was observed that 17.8% in the preterm group had intercourse between 2 and 4 weeks prior to admission as compared to 31.3% in the term group, p-value<0.005, OR3.79, 95%CI [1.51-9.66]. It shows, therefore, that coitus could be a predisposing factor for preterm labour in our set-up. Coitus, especially through orgasm and introduction of infection, has been found to be associated with preterm labour[12], although the contribution of other factors that may be aggravated by coitus, like bacterial vaginosis, can not be ruled out. Awimbo, in her study in KNH, however, did not show the significance of coitus in preterm delivery[45].

In regard to past obstetric history, majority of the participants in both groups were of low parity, with 57% in the preterm group and 69.7% of the term group having only their first or second delivery. Notably, 38.4% of the preterm group had 3 or more previous births as compared to 27.7% in the term group. This however was not statistically significant. Mbatha showed that the lowest morbidity and mortality was found in para 1 and 2 and higher for para 3 or higher[47]. While the preterm group had more previous preterm births or miscarriages (21.2% vs 15.1%), overall there were no statistically significant differences between the two groups. Studies have shown that a history of previous preterm birth or miscarriage is a risk for preterm delivery[4].In terms of inter-pregnancy interval, there was no statistical difference between the two groups in this study. Other studies have, however, shown that a short inter-pregnancy interval is a risk factor for preterm birth and its recurrence[31]. This lack of difference in the two groups may be due to the small sample size in our study.

As for ANC attendance, the attendance rate was 87.1% in the preterm group and 100% in the term group. This compares with the national figures of 88% ANC attendance[48]. This difference was statistically significant, while there was no difference between the two groups in terms of number of visits made and gestation at first visit. Mbatha, however, showed that there was a significant difference in neonatal morbidity and mortality with

increasing number of clinic visits[47]. There is a strong direct relationship between ANC attendance and having term births, p-value <0.005. Therefore, mothers should be encouraged to attend ANC which may reduce chances of preterm birth.

Antenatal complications, either medical or obstetric, if not managed, are a major contributor to preterm birth[23, 27, 28, 40]. In this study, 37.6% of the preterm participants had some kind of pregnancy complication ante-natally as compared to 23.2% in the term group. HTN and UTI were the commonest complications in both groups with 30.4% each in the preterm group and 35.1% and 30.7% respectively in the term group. Notably, there was a statistically significant difference between the two groups in terms of false labour and twin gestation. False labour accounted for 7.9% of the preterm complications and 0.0% in the term group, p-value 0.003, while twin gestation accounted for 21% in the preterm group and 8.7% in the term group, p-value 0.004, OR 1.36[95%CI 0.97-4.37] Pre-eclampsia and UTI have been incriminated in various studies as being associated with preterm birth[14, 27, 47]. Patients with recurrent false labour before term have also been shown to be at an increased risk for preterm birth by some unknown mechanism, possibly some other underlying condition like UTI or BV[23]. Studies done locally have not found twin gestation or false labour as a risk factor for preterm birth[14,45], but twin gestation, just like polyhydramnios, may cause preterm labour due to overstretching of the uterus[2].

In terms ante-natal profile, haemoglobin level, HIV status and Syphilis status were considered. There was no difference statistically between the two groups. Only 1 participant tested positive for VDRL from the term group and she was treated for syphilis. Onwere showed that preterm deliveries are 1.5 times more likely to be associated with maternal anaemia than term deliveries[36]. In our study, no difference was observed between the two groups possibly because now mothers are given haematinics routinely, and syphilis is almost obsolete thanks to widespread use of effective antibiotics to treat cases.

In regard to maternal outcomes, we considered various aspects including mode of delivery, post-delivery complications and duration of hospital stay. Majority of deliveries

in the two groups was via SVD, 72.3% in the preterm group and 75.2% in the term group. Cesarean section rate was 23.8% in the preterm group and 20.7% in the term group.

Among the preterm group, 13% of the participants had some complication during or after delivery as compared to 8% in the term group. PPH and retained placenta (23%each) were the most prevalent complications in the preterm group while PPH (50%) was the most prevalent of complications in the term group. This difference between the two groups, however, was not statistically significant.

The mean duration of hospital stay for preterm group was 3.4 days while that of term group was 2.7 days, with a notable difference between the two groups in terms of hospital stay. The mothers with preterm delivery are more likely to stay in hospital for longer than 7 days compared to those who deliver at term, p-value <0.005. This could be explained by the fact that their newborn infants are likely to stay in NBU for longer, reflecting on the economic burden of preterm delivery.

There were 109 preterm and 101 term babies delivered, and18.8% of the preterm and 0.8% of the term infants had been diagnosed with IUFD at admission. Forty-one percent of the preterm infants had an APGAR score of <7 at five minutes as compared to 9.4% in the term group. 57.6% of the preterm infants were admitted to NBU for various reasons as compared to 15% of the term infants. Of the NBU admissions, mortality rate was 41.9% in the preterm group with only 5% in the term group. Safe for length of NBU stay, there were statistically significant differences between the two groups in terms of neonatal outcomes, p-values <0.005. This agrees with a finding that morbidity and mortality has continued to increase over time in the NBU of KNH[49,50].

The average length of NBU stay was 7.6 days in the preterm group and 3.5 days in the term group, again reflecting on the economic burden of caring for preterm infants. Overall mortality was 27.6%.

Analysis of perinatal mortality revealed a notable decrease of mortality from 28-30 weeks (79.3%) to 38 weeks (4.5%). There was also a substantial decrease of mortality from

<1000g birth-weight (100%) to >2500g birth-weight (4.6%). This mortality is much higher than that found by Mbatha[47] of 31.3% at 28-30 weeks and 11.4% at 34 weeks. The findings, however, agree with those found by Were et al[49], where there was 100% mortality for those weighing less than 1000 grams and 22% for those weighing 1500-1999 grams. This could be explained by the fact that KNH is a referral hospital for very sick and premature infants, and therefore numbers are bound to be higher due to possibility of neonatal sepsis.

CONCLUSIONS

Prevalence of spontaneous preterm delivery was 8.7%. There was no difference in sociodemographic characteristics of the two groups. Antenatal clinic attendance was 87% in the preterm group and 100% in the term group. This difference was statistically significant. There was no observed difference between the two groups in terms of parity, previous preterm delivery or inter-pregnancy interval. Urinary tract infections and Hypertension were the commonest primary complications in the preterm group, with false labour and twin gestation being statistically higher in the preterm group as compared to the term group. There were major statistical differences between the two groups in terms of infant outcome, with higher mortality, need for NBU admission and length of hospital stay in the preterm group than in the term group. This reflects on the cost and economic burden of preterm birth in our set-up.

RECOMMENDATIONS

1. There is need to develop cheap and simple biochemical markers to predict preterm labour.
2. Pregnant mothers should be encouraged to attend ANC, which may help in identifying and managing risk factors for preterm labour.
3. Efforts aimed at improving neonatal care to reduce mortality of low birth weight infants should be encouraged.
4. A study of the preterm perinatal outcome in KNH comparing mode of delivery, gestational age, birth weight and use of corticosteroids at different gestations for lung maturation should be undertaken.

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APPENDICES

APPENDIX I: CONSENT FORM

Dr. Enock Ondari is a post-graduate student in the department of obstetrics and gynaecology of the University of Nairobi carrying out a study on the "factors associated with preterm birth". My mobile phone contact is **0722362198**.

My supervisors are **Dr. Zahida Qureshi** of the Department of Obstetrics and Gynaecology, University of Nairobi and **Dr. Gathari Ndirangu** of the Department of Obstetrics and Gynaecology, Kenyatta National Hospital.

This study has been approved by the KNH Ethics and Research committee, and any questions or issues regarding the study could be addressed to:

The Chairman, KNH-ERC
P.O. Box 20723, Nairobi.
Tel. 2726300-9.

This study entails investigating the characteristics of patients who have preterm birth and comparing them with patients who deliver at term, involving asking questions and looking at your medical records. This information will be used to improve the future management of patients.

Participation is voluntary and the information obtained will be confidential. Declining to give consent or withdraw from participation will not influence your management in any way. The procedures that will be carried out will not harm you or your baby. If your HIV status is not known, you will be counseled and the test will be done if you consent to it.

Consent

I have been explained to about the study and I accept to participate. I have not been coerced or enticed in any way.

Participant's signature .....Date.....

Witness signature.....Date.....

APPENDIX II: QUESTIONNAIRE

FACTORS ASSOCIATED WITH PRETERM DELIVERY IN KNH

Date ____/_____/____ Serial No.....

SOCIODEMOGRAPHIC DATA OF THE WOMAN

1. Mothers Age _____years
2. Marital status [ ]
   a. single
   b. married/ cohabiting
   c. separated
   d. divorced
   e. widowed
3. Educational level [ ]
   a. none
   b. primary: standard_____
   c. secondary: form_____
   d. tertiary
4. Occupation
   a. unemployed (housewife)
   b. self employed
   c. salaried employment
   d. other (specify)_____
5. Spouse Occupation(if applicable)
   a. unemployed
   b. self employed
   c. salaried employment
   d. other (specify)_____
6. Did you take alcohol during the index pregnancy? [ ] a=Yes b=No
7. If yes, to what extent [ ]

a. occasionally

b. socially

c. daily

8. Did you smoke cigarettes during this pregnancy? [ ] a=Yes b=No

9. If yes, how many cigarette sticks per day?

a. 1-5

b. 6-10

c. >10

OBSTETRICS

1. Number of pregnancies, including the last pregnancy. [ ]

2. Number of previous term births excluding the last delivery [ ]

3. Number of previous miscarriages/preterm births. [ ]

4. When was the last menstrual period (LMP)?

a. ___ /___/___ b. Not known [ ]

5. When was the expected due date (EDD)?

a. ___ /____/____ b. Not known [ ]

6. What is the gestation by dates? a. _____ weeks b. Not known [ ]

7. What is the duration since the last delivery? [ ]

a. < 1 year

b.1-2 years

c.> 2 years

8. What was the mode of the last delivery? [ ]

a. SVD

b. Caesarean delivery

c. Assisted vaginal delivery

d. Breech delivery

e. Other (please specify)_____

9. Did you have any complications in previous pregnancies? [ ]

a. yes

b. no

10. If yes, specify_____

ANTE-NATAL CARE

1. Did you attend ANC during this pregnancy? [ ] a=Yes b=No
2. If yes, how many visits did you make? _____
3. What was the gestation at first ANC visit? _____ weeks
4. Have you had any complications during this pregnancy? [ ] a=Yes b=No
5. If yes, specify_____
6. Have you been admitted to hospital during this pregnancy? [ ] a= Yes b= No
7. If yes, why_____
8. When did you last have intercourse before this admission? [ ]

    a. <1 week

    b. 1 – 2 weeks

    c. 2 - 4 weeks

    d. More than 1 month

DRUGS

1. Was any of the following drugs prescribed; and if yes, what were the indications?

	Drugs	1= Yes 2= No	Indications
1	Haematinics		
2	Antibiotics		
3	Antifungals		
4	Analgesics		
5	Antacids		
6	Antihypertensives		
7	Antiretroviral Drugs		
8	Antimalarial Drugs		
9	Steroids		
10	Others		

LABORATORY

Were the following test results documented?

1= yes 2= no 9= not documented

1. Haemoglobin level ☐ Result _____
2. VDRL ☐ Result _____
3. HIV ☐ Result _____
4. Urinalysis ☐ Result _____
5. Blood Group (a.) ABO type ☐ Result _____
   (b) Rhesus status ☐ Result _____
6. Other tests done
   a) Ultrasound ☐
   If yes, indication _____
   b) Laboratory tests ☐
   If yes, specify _____

DELIVERY

1. Date of admission ___ / ____/ ____
2. Clinical findings at time of admission
   a. Show 1= Present 2= Absent 9= Not indicated ☐
   b. Membranes 1=Intact 2= Ruptured 9=Not indicated ☐
   c. Cervical dilatation _____cm
3. Date of delivery ___/____/____
4. Gestation at delivery _____ weeks
5. Mode of delivery ☐

   1= SVD 2= Caesarean Section 3= Assisted vaginal delivery 4= Breech delivery
6. If C/S, what was the indication _____
7. Did the mother experience any complications during or immediately after delivery?

   1= Yes 2 = No ☐
8. If yes, explain _____
9. What was the duration from admission to discharge? _____ days.

FETAL OUTCOME

1. Infant sex [ ]

1= male 2= female

2. What was the infant Apgar score at 5 minutes? [ ]

3. What was the infant birth weight? _____grammes.

4. Status at birth [ ] 1=Alive 2=FSB 3= MSB 9=Not documented

5. Was the infant admitted to NBU? [ ] 1=Yes 2= No

6. If yes, indication _____

7. If yes to 5 above, what was the length of stay in NBU _____days.

8. Status of infant on discharge [ ] 1=Alive 2= Dead

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

Ref: KNH/UON-ERC/ A/232

3rd June 2009

Dr. Enock O. Ondari
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Ondari

Research proposal "Factors associated with Preterm Birth in Kenyatta National Hospital" (P76/3/2009)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above revised research proposal for the period 3rd June 2009 - 2nd June 2010.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

DR. L. MUCHIRI
AG. SECRETARY, KNH/UON-ERC

c.c. Prof. K.M. Bhatt, Chairperson, KNH/UON-ERC
The Deputy Director CS
The Dean, School of Medicine, UON
The Chairman, Dept.of Obs/Gynae, UON
Supervisors: Dr.Zahida Qureshi, Dept.of Obs/Gynae, UON
Dr. Gathari Ndirangu, Dept.of Obs/Gynae, UON