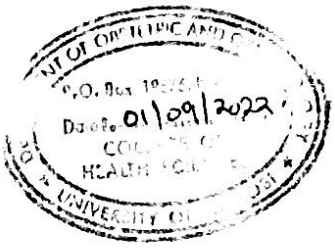

UNIVERSITY OF NAIROBI

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

To the Chair,

Department of Obstetrics & Gynecology

RE: RE-EVALUATION OF DISSERTATIONS

Student's name: DR. JULIET MUKAMI MUNENE

Registration number:H58/11109/2018

Study title: PREVALENCE, CLINICAL PRESENTATION AND INITIAL MANAGEMENT OF SUBCHORIONIC HEMATOMA AMONG WOMEN WITH PER VAGINAL BLEEDING IN THE FIRST TRIMESTER OF PREGNANCY AT KENYATTA NATIONAL HOSPITAL IN YEAR 2019-2020.

I have re-evaluated the above student's dissertation and do confirm that the comments given to the student have been addressed to my satisfaction.

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Internal Examiner's name	**Signature**	**Date**
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2. Prof. E. Chasakom		01/09/22

PREVALENCE, CLINICAL PRESENTATION AND INITIAL MANAGEMENT OF SUBCHORIONIC HEMATOMA AMONG WOMEN WITH PER VAGINAL BLEEDING IN THE FIRST TRIMESTER OF PREGNANCY AT KENYATTA NATIONAL HOSPITAL IN YEAR 2019-2020

Dr. Juliet Mukami Munene

H58/11109/2018

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS AND GYNECOLOGY OF THE UNIVERSITY OF NAIROBI.

2021

DECLARATION

This is the original work of Dr. Juliet Mukami Munene and has not been undertaken or presented for the award of a degree in another University.

29/8/2022

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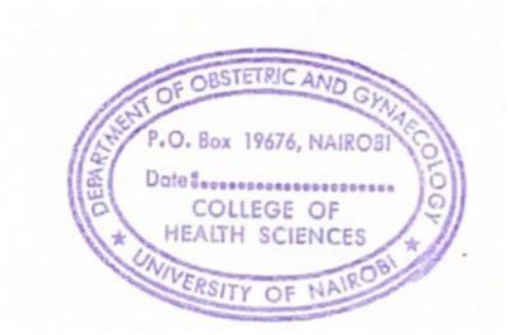

Signature…… Date ……01/09/2022…….

DEDICATION

I dedicate this dissertation to my family for their immense support and encouragement thorough out this project.

ACKNOWLEDGEMENTS

I wish to thank the Almighty for giving me strength and resilience to carry out this research to completion. My sincere gratitude to my supervisors Prof. Omondi Ogutu and Dr. George Gwako for their guidance and support throughout the study period. The records department Kenyatta National hospital for their assistance during data collection and finally to my colleagues for the encouragement offered as we worked toward a common goal.

LIST OF ABBREVEATIONS

ANC: Antenatal Clinic

APH: Antepartum Haemorrhage

BMI: Body Mass Index

CRL: Crown Rump Length

GA: Gestational Age

IPH: Intraplacental Hematomas

IUH: Intrauterine Hematomas

IVF: In Vitro Fertilization

KNH: Kenyatta National Hospital

RPH: Retroplacental Hematomas

SCH: Subchorionic Hematoma

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ABSTRACT

Background: Subchorionic Hematoma (SCH) refers to bleeding that occurs between the chorion and uterine wall and occurs usually in first trimester. The incidence of SCH based on studies done globally is between 3.5% to 39.5% It carries a risk of complicating pregnancy outcomes, including inducing miscarriages, preeclampsia, antepartum haemorrhage, preterm labour, placental insufficiency, fetal growth restriction, and stillbirths. Despite the common occurrence of SCH in pregnancy and the adverse pregnancy outcomes associated with it, there is limited data on its burden and effect on pregnancies in Kenya.

Objective: To determine the prevalence, sonographic features, clinical characteristics, and initial management of subchorionic hematoma at Kenyatta National Hospital (KNH).

Methodology: A retrospective cross-sectional study was conducted at KNH in 2021 where the data of 145 women who were seen with vaginal bleeding in early pregnancy at the gynaecology outpatient clinic and the accident and emergency unit between January 2019 and December 2020 was reviewed. Patient demographic, reproductive, and medical characteristics and their ultrasound findings were extracted from hospital files. The data was uploaded into a Statistical Package for Social Scientists software (version 25 for Windows) and cleaned. Demographic and reproductive data was summarized as means with standard deviations and as counts with percentages. The exact Clopper Pearson method was used to calculate the prevalence of SCH with 95% confidence interval estimates and sonographic, clinical characteristics, and the initial management of patients who were diagnosed with SCH assessed using counts and percentages. Comparative analyses of women with and without SCH were conducted using the Chi-square test or Fishers test at 95% confidence interval. A P value <0.05 was statistically significant.

Results: 145 participants were recruited. The mean age of participants was 29.3 years. Most were in age group <35 years (76.6%), married (64.8%), multigravida (72.4%), and did not have comorbidities such as HIV infection (97.2%), chronic kidney disease (CKD) (99.3%), and uterine anomalies (91.0%). The prevalence of SCH was 18.6% (27/145), 95% CI=12.6-25.9. Women with versus those without SCH were more likely to present with vomiting (11.1% versus 2.5%), but less likely to have lower abdominal pain (37.0% versus 60.2%) or dizziness (3.7% versus 11.0%). Most SCH were small (81.5%) at a mean gestation of 8.85 ±2.13 weeks and required treatment (81.5%), mostly progestin (90.9%). SCH resolved after treatment in approximately 38.9% of the cases who proceeded to deliver at term.

Conclusions: The prevalence of SCH among women who develop per vaginal bleeding in first trimester in Kenya is higher at 18.6% compared to studies from high income countries that have reported rates as low as 3.5%. Women with SCH were more likely to vomit but less likely to have lower abdominal pain or dizziness compared to those without SCH. Progestin was the most common initial treatment for SCH and most pregnancies proceeded to deliver at term.

Recommendations: Due to the high prevalence of SCH in our population it is important to create more awareness on the condition among pregnant women and educate health care providers to have a high index of suspicion and investigate for SCH whenever a pregnant woman presents with per vaginal bleeding in the first trimester of pregnancy.
There is need for a larger study to look at the risk factors associated with SCH and pregnancy outcomes in women with SCH in our population.

CHAPTER ONE

1 INTRODUCTION

1.1 Background

Subchorionic hematoma refers to bleeding that occurs between the chorionic membrane and the uterine wall(1). This sonographic abnormality is one of the most common types that occur in the presence of a live embryo in first trimester. It can occur during the first or second trimester of a pregnancy. Most symptomatic patients present with vaginal bleeding(2–4).

The incidence of subchorionic hematomas in first trimester based on the studies done globally is 3.5- 39.5% depending on the population size (5,6). Vaginal bleeding is seen among 25% of all pregnant women in first trimester of pregnancy (2). Ultrasound forms mainstay of diagnosis of subchorionic hematoma. They appear as hyperechogenic crescent shaped areas between the uterine wall and fetal membranes (chorion). This is the classical appearance of acute SCH. Sub-acute forms present as more echogenic areas (7,8). In most cases the hematoma extends towards the margin of the placenta (9,10).

The etiology of subchorionic hematomas has not been clearly established. The most accepted etiology is the partial separation of the chorionic membranes from uterine walls leading to haemorrhage and thus hematoma formation (11). The separation in early pregnancy has been attributed to shallow trophoblastic invasion and impaired angiogenesis, creating friable blood vessels or premature perfusion of the intervillous spaces before placenta adapts to cope with oxidative stress (7,12). A hematoma forms a line of weakness on the placenta leading to separation of placenta from uterine wall increasing risk of placenta abruptio. In early gestation detachment of a gestational sac from endometrium can lead to miscarriage (7). Reattachment of the gestational sac is however possible leading to pregnancy progression without adverse effects. However, it is believed to be associated with recurrent pregnancy losses, infections and

uterine malformations. Bleeding disorders, autoantibodies and use of anticoagulants also increase risk of SCH in pregnancy (13,14). Small hematomas are described as those whose sizes are 20% less the size of gestational sacs while large subchorionic hematomas are up to 50% of the size of the gestational sac. Large hematomas are usually symptomatic presenting as per vaginal bleeding (11). The frequency of subchorionc hematomas has been shown to be high among patients who have undergone in-vitro fertilization (22.4%) compared with those in non-IVF cycles (11%). Frozen thawed embryos, blastocyst transfer and parity of more than one are factors contributing to the risk in IVF patients (15,16).

Small SCH often resolve and the pregnancy progresses without complications. With vaginal bleeding, SCH increase the risk of abortion, preeclampsia, antepartum haemorrhage, placenta Abruptio, placental insufficiency, intrauterine growth restriction, preterm labour or stillbirths, which makes early diagnosis crucial. In Kenya, there is paucity of epidemiological data on SCH, which impedes early diagnosis and management of women. Its prevalence in referral health institutions such as the Kenyatta National Hospital has been shown to be substantial at around 10% (17), but its risk factors, clinical presentation, initial management and pregnancy outcomes are underexplored. To fill these gaps, the study evaluated the prevalence and clinical presentation and initial management of SCH at the Kenyatta National Hospital (KNH).

CHAPTER TWO

2 LITERATURE REVIEW

2.1 Definition

Mantoni et al (18), defined sub chorionic hematomas as a crescent shaped hypoechogenic area between the uterine wall and chorion. The exact cause of the hematoma is unknown. However, the most postulated cause is partial detachment of the membrane of the chorion from the uterine wall. Other suggested predisposing factors are history of recurrent pregnancy losses, infections (19) and uterine malformations. Patients with bleeding disorders, autoantibodies and those on anticoagulants are also at risk of developing SCH. SCH carries a risk of altering the progress or outcome of pregnancy. In a 2015 study in Pakistan, Ghazala et al., (20) demonstrated the great role ultrasound plays in detection and subsequent monitoring of SCH while evaluating sonographic SCH in the early first trimester. According to Ghazala et al., the site, size and echogenicity of the hematoma are crucial factors to consider while evaluating the risk status of patients for adverse pregnancy outcomes. Large hyperechogenic SCH in the lower uterine segment were associated with a higher risk of having a spontaneous abortion.

2.2 Classification of sub chorionic hematomas

Four grading systems for SCHs based on ultrasound examination exist. First classification is based on the size of hematoma (small, moderate and large hematomas). Second classification factors the size of hematomas as a fraction of the gestational sac size, expressed as a percentage (less or equal to 10%, 11-25%, 26-50% and more than 50%). Third classification uses the estimated fraction of a gestational sac with the hematoma and expressed as a percentage as listed in second classification. Fourth classification involves measurement of orthogonal diameters of SCHs. According to Howard et al., (21) estimation of SCH size as a fraction of the gestational sac (third classification) is most reliable as it has a statistically significant correlation with pregnancy outcomes in the first trimester (22,23).

2.3 Prevalence of sub chorionic hematoma

Sub chorionic hematoma (SCH) is a commonly observed clinical feature in early pregnancy, especially if patients present with vaginal bleeding. From studies, SCH seems to be a common health problem in sonographic and ultrasound examinations with prevalence rates of between 8.5% and 18.2% reported in Italy and parts of Asia. In a 1990 prevalence study of 342 Italian women diagnosed with vaginal bleeding at 9-20 weeks gestation, Pederson and Mantoni (24) reported a prevalence rate of 18% using sonography. In the study, the size of hematomas ranged from 2-15 ml with patients with large compared to small hematomas having a comparable risk of premature delivery. In a study by Mandruzzato et al. (25), SCH was diagnosed in 11% of Italian women with bleeding in early pregnancy and a live foetus. Wahid et al. (20), Sukur et al. (26), and Al-Nuaim et al. (27) reported a prevalence rate of 8.6%, 18.2%, and 8.5% in Afghanistan, Turkey, and Riyadh, Saudi Arabia in 2015, 2014, and in 1996 respectively.

High income countries such as Japan and the USA have a lower rate of SCH with vaginal bleeding in the first trimester of pregnancies, probably due to advanced healthcare systems. While evaluating characteristics of patients with subchorionic hematoma in Japan, Yamada et al. (28) reported a prevalence of 4.2% in a study of 47 pregnant Japanese women with vaginal bleeding in the first trimester. In Washington, USA, Tuuli et al., (29) reported an even lower prevalence of 1.7% in a retrospective study of 63,966 African American pregnant women before 22 weeks gestation. Like in the study by Yamada et al. and Mandruzzato et al., SCH predisposed women to adverse pregnancy outcomes such as abruption, preterm delivery, and preterm premature rupture of membranes, which makes it a condition of public health concern.

The highest rates of SCH have been reported in underprivileged countries in South America. In Venezuela, for instance, the prevalence of SCH was found to reach 33.5% in a study of 200 women who had viable intrauterine pregnancy at 6-13 weeks with and without vaginal bleeding

(30). Like South America, Africa is home to some of the most underprivileged countries in the world but the status of SCH in Africa is unclear. For example, the prevalence of SCH in first trimester in Kenya has previously not been described.

2.4 Risk factors for subchorionic hematomas

2.4.1 Demographic characteristics

Demographic characteristics such as maternal age does not seem to influence the occurrence of SCH in the first trimester of pregnancy. In Venezuela, maternal age did not vary statistically significantly between pregnant women with and without SCH in the first trimester (30). In another study, Sukur et al. (31) found no statistically significant difference in maternal age of Turkish women with SCH compared to those without SCH while evaluating the pregnancy outcomes of women with threatened abortion. In a 2017 Chinese study of 194 pregnancies, maternal age did not affect SCH development. However, several reproductive, medical, and behavioural characteristics of pregnant women are associated with an increased risk of SCH.

2.4.2 In Vitro Fertilisation

A significant correlation between in-vitro fertilisation (IVF) the development of subchorionic hematomas has been reported, with women who undergo IVF founds to be most at risk. While evaluating the association between SCH and IVF in 194 first trimester pregnancies in Japan in 2014, Asato et al. (32) reported the frequency of SCH to be statistically significantly higher in the IVF group (22.4%) compared to the non-IVF group (11.0%). Overall blastocysts transfer increases the risk of SCH by 3.75 (1.1-13.3) times, while free thawed embryos increased the risk of SCH by 6.18 (1.7-22.4) times. In another study on SCH among first trimester pregnant women who underwent IVF/ICSI treatment in China in 2017 by Zhou et al. (33), the risk of SCH development was 3.76 (2.28-5.90) times higher in fresh embryo transfer patients than in FET patients with prevalence rates of 16.6% and 5.1% respectively, reported. In a 2014 study

by Xiang et al. in China (22), pregnancies achieved through IVF embryo transfer were more likely to lead to subchorionic hematomas and associated complications such as placenta previa (OR=8.7, 95% CI = 3.4-22.2), oligohydraminos (OR=5.8, 95% CI=2.4-14.0), postpartum haemorrhage (OR=3.1, 95% CI = 1.8 -5.3), preeclampsia (OR=2.8, 95% CI= 1.5-5.0), and gestational hypertension (OR=2.6, 95% CI=1.5-4.6) after crude bivariate analyses.

2.4.3 Parity

The parity of women in the first trimester predisposes pregnant women to SCH although epidemiological data is limited. In 2014, Asato et al. (32) reported a higher risk of SCH among multiparous women in a comparative study of 194 Japanese women with SCH versus no SCH. From the data, high parity (>1) increased the risk of developing SCH statistically significantly.

2.4.4 Uterine malformations

Diagnostic and clinical studies of intrauterine hematomas have demonstrated a statistically significant relationship between uterine malformations and the onset of SCH. In a study of 62 intrauterine hematoma patients in Italy, Mandruzzato et al. (25) demonstrated a significantly higher incidence of SCH when placenta were on the posterior uterine wall. Having a myomas increased the risk of developing SCH by over two times in the population that was studied.

2.4.5 Medication

Medications such as aspirin have been associated with an increase in the risk of subchorionic hematoma in first trimester pregnancy. This was evident in a 2016 study in the USA by Truong et al. (34). In the prospective cohort study, taking low dose aspirin (ASA) in early pregnancy led to an increase in the risk of SCH during ultrasound examination. Overall, patients who were on ASA has a fourfold higher risk of having SCH compared to those who were not on ASA. Heparin, unlike low-dose aspirin, was not a significant risk factor SCH in that population.

2.4.6 Autoimmune diseases

A study on assessment of relationship between C4 levels, autoantibodies, and Intrauterine hematomas was done by Jaume et al. in 2003 (35). This study design was retrospective and involved 54 women with IUH and a poor obstetric history. Serum was analysed for DNA, anti-DNA antibodies, C4 complement, gamma globulin and compared with the control group. Antinuclear antibodies (ANA) and hypergammaglobunemia was evident in 50% of cases, while antiphospholipid antibodies were found in all (100%) cases. The study concluded that a poor obstetric history and autoantibodies – mostly antiphospholipid antibodies - might lead to the development of IUH in the presence of low C4 and or hypergammaglobunemia. In another study by in the USA in 2001, Tower et al. (36) reported similar results with the presence of antiphospholipid antibodies found to be more common among patients with IUH.

2.4.7 Thrombophilia

Vaginal bleeding is a reliable prognostic indicator for subchorionic hematoma from published literature. In a case series of three patient with SCH published by Debra et al in the journal of paediatric and developmental pathology in 2003, thrombophilia was a strong and statistically significant prognostic factor for SCH (37). Two of the studied patients had protein deficiency, while one had mutations on the methylene-tetrahydrofolate reductase gene C677T. In another study on the prognostic factors for subchorionic ecolucencies in pregnant women from New York, USA, in 2003, Sharma et al. (38) reported the prevalence of antepartum haemorrhage to be 16.8% - 22.6% with preterm delivery and 7% without APH.

2.4.8 Bacterial infections

Etiological analysis of vaginal haemorrhage by Queck and Berle (23) and Yamada et al. (8) have reported an association between expression patterns of different groups of bacteria and

the odds of developing SCH. The incidence of coagulase negative staphylococcus, Gardenella and negative lactobacillus were shown to be higher in patients with SCH than those without.

2.5 Conceptual framework

2.5.1 Narrative

From the review of literature, demographic and reproductive factors such as the age of patients, their parity, gestational age, and the presence of comorbidities such as HIV have been shown to influence the odds or risk of developing SCH in pregnancy. A higher parity, for instance, was a statistically significant prognostic factor for SCH in a 2014 retrospective study of first trimester Japanese women (32). The presence of bacterial infections (8), thrombocytopenia (37), autoimmune disease that compromised autoantibody production (35), and undergoing an invitro fertilization (32) have also been shown to be prognostic factors for SCH predominantly in studies conducted in America and Europe. Data from Africa can add to the existing evidence.

2.5.2 Schematic

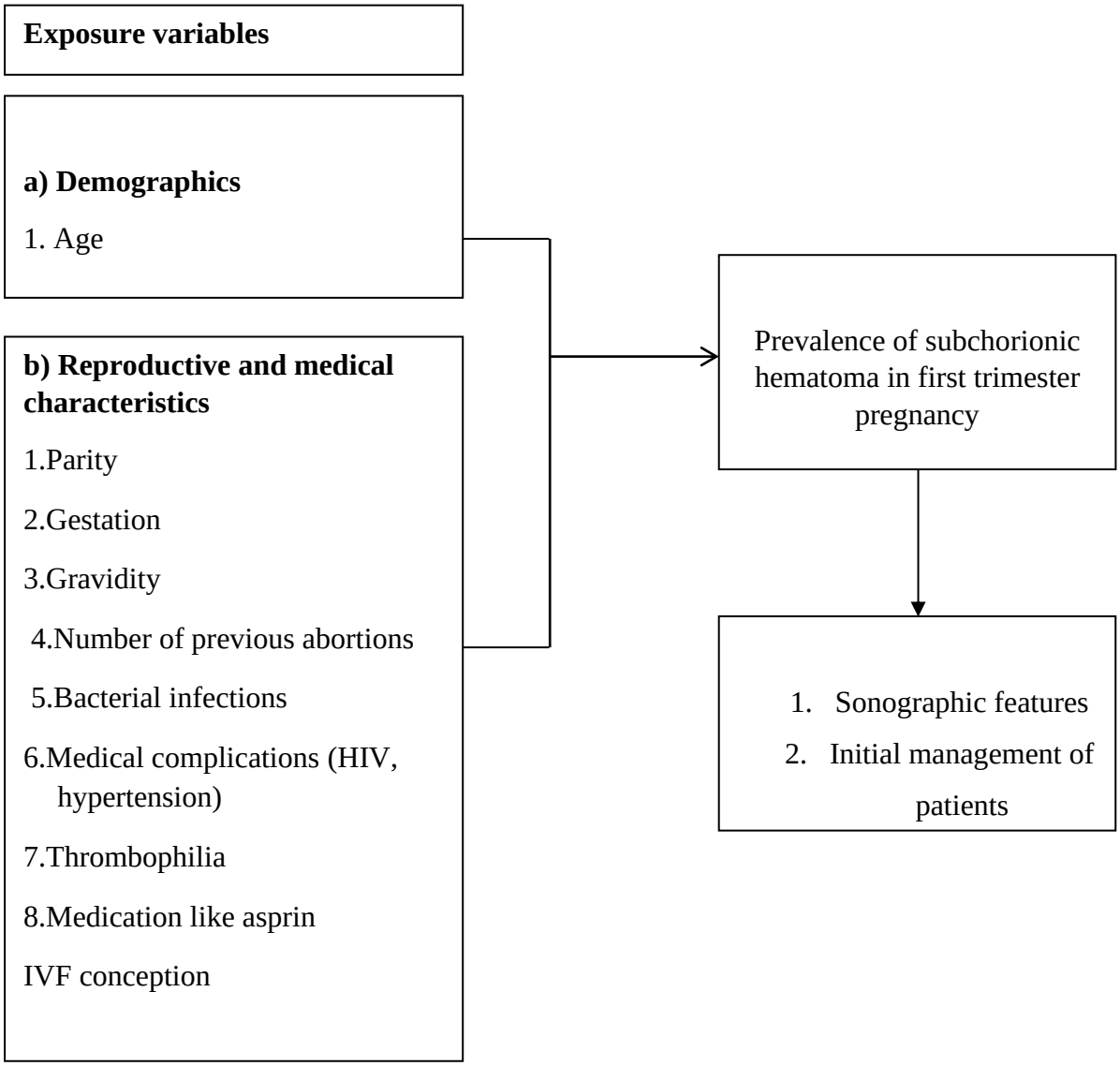

Figure 2.1. Schematic presentation of conceptual framework

2.6 Justification

Subchorionic Hematomas are hypoechogenic abnormalities between the chorion and uterine wall, estimated to afflict about 1.7-33% of women of a reproductive age globally (20,24–27). While a majority of cases have an unknown aetiology, uterine malformations such as partial detachment of the chronic membrane from the uterine wall has been reported (18), predisposing parturients to adverse pregnancy outcomes such as a high risk of abortion (27), premature labour (19), and high risk of caesarean section delivery (39). Successful diagnosis and

management of SCH requires accurate epidemiological data, which is insufficient in Kenya. in Kenya, for instance, the prevalence of SCH in referral health institutions of health such as the KNH has not been described in depth. Moreover, factors that predispose patients to SCH and how an SCH diagnosis influences the management of cases have not been studied in depth in this setting. Its prevalence at KNH was substantial at around 10% in a 2014 study (17), but clinical presentation and initial management are underexplored. To fill these gaps, the study evaluated the prevalence of SCH at the Kenyatta National Hospital in Kenya and determined demographic, medical, and reproductive factors that are associated with the development of SCH. The sonographic features of patients who were diagnosed with SCH and the initial management practices were also evaluated.

2.7 Research question

What is the prevalence, sonographic features, clinical characteristics, and initial management of subchorionic hematoma at Kenyatta National Hospital?

2.8 Broad objective

To determine the prevalence, sonographic features, clinical characteristics, and initial management of subchorionic hematoma among women with per vaginal bleeding in first trimester at Kenyatta National Hospital in 2019-2020.

2.8.1 Specific objectives

Among pregnant women with per vaginal bleeding in first trimester at KNH, to

1. determine the Prevalence of subchorionic hematoma
2. Evaluate clinical characteristics of those with subchorionic hematomas
3. describe Sonographic features of subchorionic hematomas
4. determine Initial management of women with subchorionic hematomas

2.8.2 Secondary Objectives:

1. To compare the demographic characteristics between patients with and those without subchorionic hematomas.
2. To describe the pregnancy outcomes of patients with subchorionic hematomas

CHAPTER THREE

3 METHODOLOGY

3.1 Study design

This was a cross-sectional study in which the files of pregnant women presenting with per vaginal bleeding in the first trimester between January 2019 and December 2020 were retrieved and data extracted retrospectively from each month until sample size achieved. Since the condition is not common in pregnancy, a retrospective data collection method was used to evaluate the prevalence of SCH, sonographic findings, and initial management of the cases. The data was abstracted from hospital files and from radiological records of the participants. The hospital files of these patients were also reviewed to assess the pregnancy outcomes in these patients who continued with antenatal care or follow-up at KNH.

3.2 Study site and setting

The study setting was at Kenyatta National Hospital, the main referral hospital in Kenya and the East African Region. Located in the upper hill area of Nairobi, six kilometres from the Central Business District (CBD); it serves around 1500 patients every day – primarily from the Nairobi Metropolitan Area – and is the teaching hospital of the University of Nairobi, College of Health Sciences, and the Kenya Medical Training College (KMTC). The study site was the Accidents and Emergency Unit – a department within KNH that receives around 200-250 patients every day and antenatal clinic 18. The Accidents and Emergency Unit provides medical treatment for emergency patients. It also responds to casualty incidents and national disasters and provides obstetric services such as triaging of patients, medical examinations, and treatment without limits. The accident and emergency unit has a sample collection and analysis laboratory. Ultrasound investigations are also conducted when needed. Incidental SCH diagnoses from the accidents and emergency unit are followed up at antenatal clinic 18. In accidents and emergency (A&E) there is a gynaecology room (room 5) where all patients with

early pregnancy bleeding are reviewed by the gynaecology resident on duty for the day. Ultrasounds are then carried out in the radiology department by the sonographers or residents in radiology. The ultrasound results are then reviewed by the gynaecology resident and initial management commenced. Patient who require follow up after initial visit at the A&E are seen at the antenatal clinics (clinic 18) if still pregnant or the gynaecological clinics for other care if not pregnant (Gynae clinic 18).

3.3 Study population

The files of patients seen at the accident and emergency unit with per vaginal bleeding in first trimester and were referred for an ultrasound to confirm the diagnosis were retrieved from the study sites and the health records department. The files were checked for completeness and patients who met the inclusion criteria were recruited until the sample size was reached.

3.3.1 Inclusion criteria

- Women with per vaginal bleeding in first trimester of pregnancy.

3.3.2 Exclusion criteria

- Other causes of per vaginal bleeding such as cervix trauma.
- Molar pregnancy, complete abortion, anembryonic pregnancy, incomplete abortion

3.4 Sample size and sampling procedure

Sample size was calculated using the formula by Fisher (1981) as follows:

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

Al-Nuaim et al. (27) reported the prevalence of SCH with vaginal bleeding to be 8.5% in Saudi Arabia. This rate was used to calculate sample size (n) at 5% margin of error as follows:

n= sample size

Z= normal variate for alpha at 95% CI = 1.96

P = Prevalence of sub chorionic hematoma with bleeding (8.5%)

d= Estimated error (5%)

Substituting this in the formula gave a sample size of 119 as shown below.

$$n = \frac{1.96^2 \text{x} 0.085(1 - 0.085)}{0.05^2} = 119$$

After adjustment by 10% to cover missing data, 130 participants were required.

Consecutive sampling was used to select the hospital files of 145 patients seen at the accident and emergency unit and at clinic 18 with per vaginal bleeding in the first trimester between January 2019 and December 2020. The files were checked for completeness and selected consecutively from December 2020 going backwards until the sample size was reached.

3.5 Data collection and management

3.5.1 Study tool

The study questionnaire in *Appendix 1* was used to collect secondary data retrospectively from hospital files or from the records of patients seen at KNH antenatal clinics and the accidents and emergency department. Demographic characteristics such as marital status, age, education level, and the employment status of patients were recorded. Reproductive and medical data such as BMI, gravidity, parity, gestation age at diagnosis, size of hematoma (if positive), gravidity, multiple pregnancies, uterine anomalies such as fibroids, and comorbidities like hypertension and HIV were also be recorded as presented in *Table 3.1*. The questionnaire was pretested on 13 patients (10% of the sample size) using the test-retest method (40).

Table 3.1. Study variables.

Objective	Exposure	Categories	Outcome
Prevalence of subchorionic hematoma			SCH diagnosis
Clinical characteristics of those with or without subchorionic hematomas			SCH diagnosis
	Age in years		
	Education level	Primary	
		Secondary	
		Tertiary	
	Marital status	Married	
		Single	
		Widowed/Divorced	
	Parity	Primiparous	
		Multiparous	
		Grand multiparous	
	Gravidity	Nulligravida	
		Primigravida	
		Multigravida	
	Multiple pregnancies	Yes	
		No	
	IVF pregnancy	Yes	
		No	
	Number of previous abortions		
	Systolic blood pressure		
	Diastolic blood pressure		
	Hypertension	Yes	
		No	
	CKD	Yes	
		No	
	HIV	Yes	
		No	
	Uterine anomalies	Yes	
		No	
	Smoking or alcohol	Yes	
		No	
	Drugs like asprin	Yes	
		No	
Sonographic features of subchorionic hematomas	SCH diagnosis		Large hematomas
			Small hematomas
Initial management	SCH diagnosis		Progestin
			Analgesics

3.5.2 Data collection procedures

Data was extracted from patient files containing clinical and ultrasound reports. The files of patients who were seen at accident and emergency between January 2019 and December 2020 were retrieved from archives and evaluated. The file numbers of patients seen with per vaginal were recorded and ultrasound findings, if present, tracked from the accident and emergency unit. Only the files of patients seen with per vaginal bleeding and had complete ultrasound findings were used, while those of patients seen with per vaginal bleeding but did not undergo ultrasound evaluation at KNH were excluded. Hospital files of all patients who were selected for the study were retrieved from the health records department. Ultrasound reports were retrieved from computers in the ultrasound room, data abstracted and abstraction tools filled.

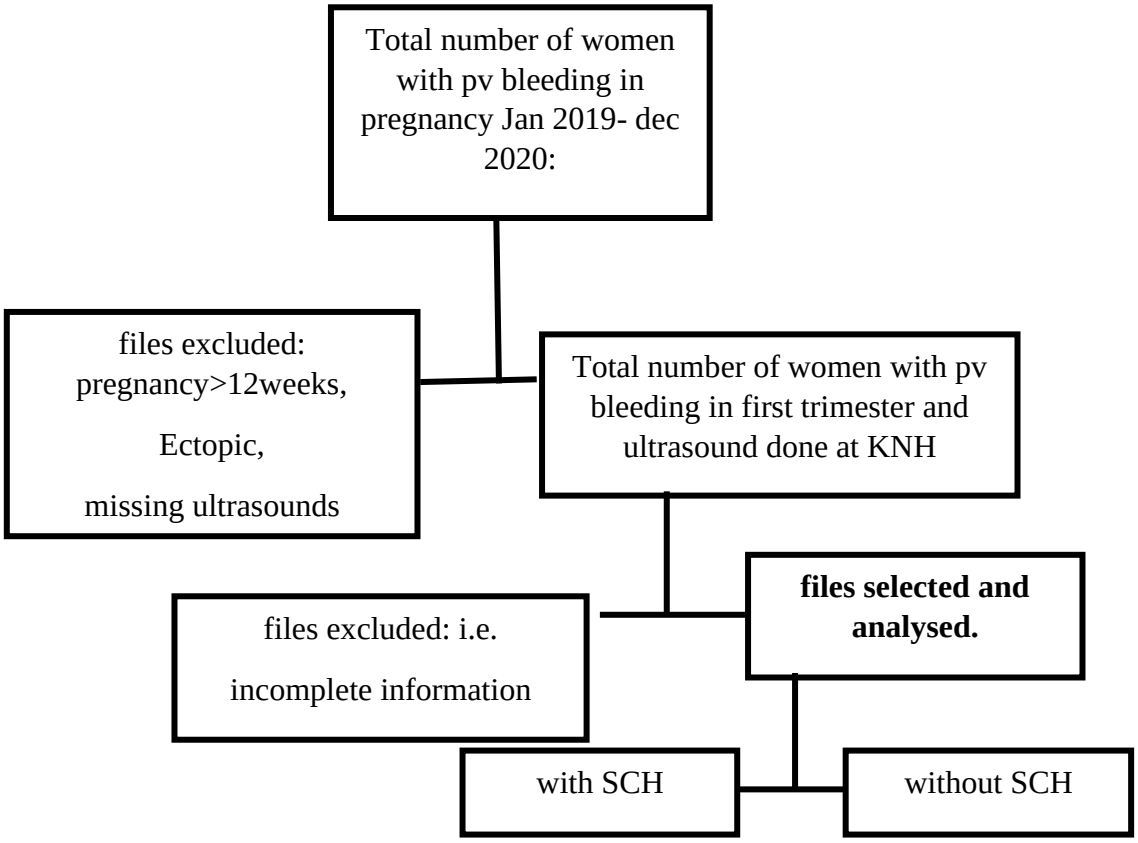

Figure 3.1. Recruitment and data collection strategy

3.5.3 Quality assurance

Data obtained from files was counter checked using the ultrasound number to confirm patient details. Counter checking was done for all files retrieved to ensure data accuracy. This was

done by the research assistants or data collection persons. Training of study staff was done over a period of two weeks on how to identify and retrieve files and data until they were competent to do it on their own. Data was stored in password-protected computers, hard drives and flash drives to ensure confidentiality. Data access was accessible to the primary investigator, the supervisors, and statistician. Pretesting of questionnaire was done after ethics approval. Single entry of data with visual verification was conducted to check for entry errors.

3.6 Data analysis methods

Data was uploaded and cleaned using SPSS (version 25). Demographic and reproductive characteristics were summarised and presented as means with standard deviations or as frequencies with percentages. Clopper Pearson method was used to calculate the prevalence of SCH with 95% confidence interval estimates and the sonographic, clinical characteristics, and the management of patients with SCH evaluated using counts and percentages. Comparative analyses of women with and without SCH were conducted using the Chi-square test or Fishers test at 95% confidence interval. A P value <0.05 was statistically significant.

3.7 Research ethics

The study protocol was approved by the Kenyatta National Hospital - University of Nairobi Ethics Review Committee (KNH/UON ERC) before commencement. Approval number: (P252/04/2021).Permission was also sought from the Department of Obstetrics and Gynaecology, University of Nairobi and the KNH administration prior to commencement of data collection. Request for waiver of written informed consent was made to the KNH/UoN ERC during ethical approval since this was a retrospective study that utilised already collected patient data.

There was no direct contact with the patients. The study procedures did not pose any risk to the study participants. Confidentiality was maintained throughout the study. Names and other

personal identifiers such as identification numbers were not abstracted. Instead, unique study generated numbers were used to identify patients and were not be linked to personal data of patients. A waiver of written informed consent was sought from the ERC.

3.8 Study limitations

- Reports were from multiple radiologists /sonographers and this could have brought variations in the reporting.
- Transvaginal ultrasound (US) was not done routinely. Most US were transabdominal. Transvaginal ultrasound is more accurate in diagnosis during first trimester before 8 weeks of gestation as compared to transabdominal ultrasounds hence small hematomas may have been missed.
- Missing information – this was mitigated by adjusting the sample size upwards thus increasing it from 119 to 145.

CHAPTER FOUR

4 RESULTS

4.1 Recruitment schema

The number of women seen at Kenyatta National Hospital with per vaginal bleeding in pregnancy between January 2019 and December 2020 was 1242. Of these, 312 met the inclusion criteria of having per vaginal bleeding in first trimester and a pelvic ultrasound done at KNH to confirm the diagnosis. The other 930 were excluded for various reasons as shown in figure 4.1 Of the 312 who met the inclusion criteria of the study 167 files had missing information hence incomplete and was further excluded. A total of 145 files that met the criteria and had complete information were then selected and analysed. Twenty-seven patients were diagnosed with subchorionic hematoma (SCH) while 118 did not have SCH (Figure 4.1).

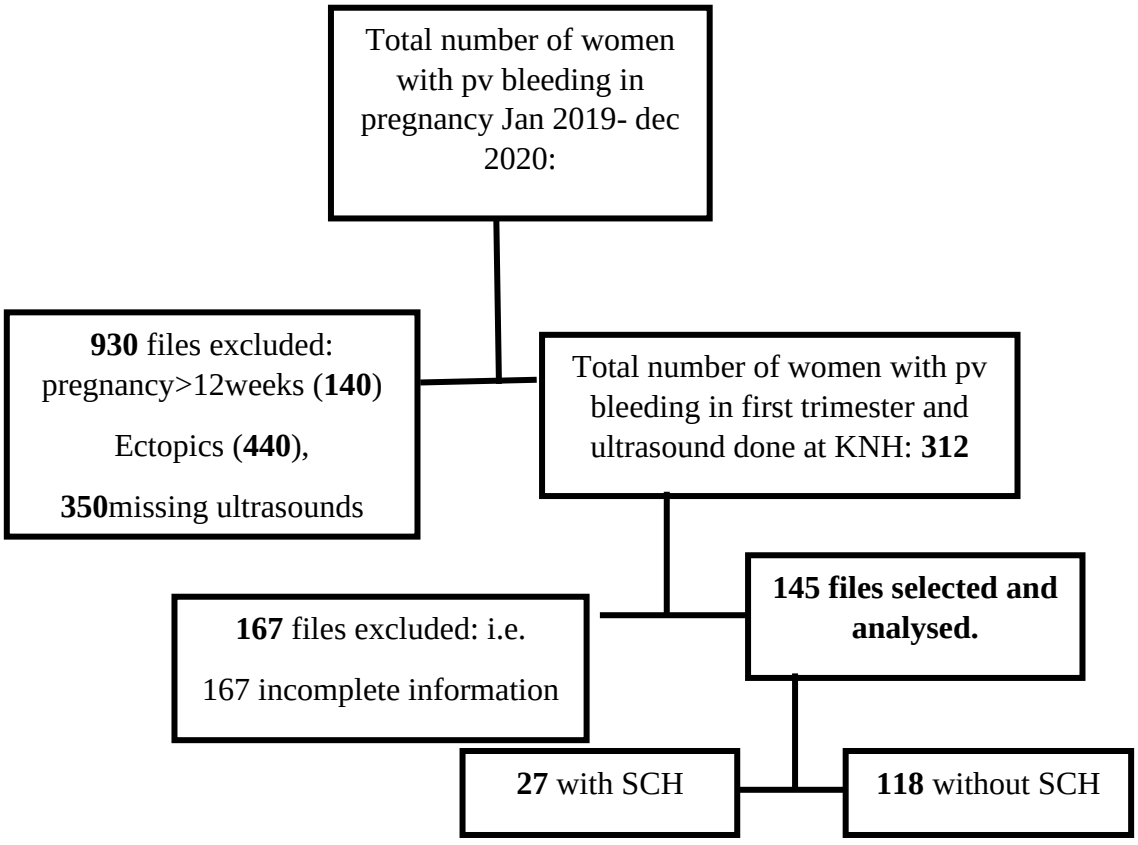

Figure 4.1. Recruitment schema for patient files of women with per vaginal bleeding in first trimester at KNH between 2019 and 2020

4.2 Demographic and obstetrics characteristics

Participants had a mean age of 29.3years, age range of 18-42 years (Table 4.1). Most (76.6%) were in the age group of <35 years, had a secondary level of education (48.3%), and were married (64.8%). The majority were multiparous (46.2%), non-smokers (99.3%), multigravida (72.4%) and did not have a history of abortions (64.1%). About 3.4%, 2.8%, and 9.0% had a history of hypertension, HIV, and uterine anomalies, mostly fibroids (84.6%) (table 4.1).

Table 4.1. Demographic characteristics of women with per vaginal bleeding in the first trimester at KNH between 2019 and 2020

		Frequency (N=145)	Percent
Age group	<35	111	76.6
	35+	35	23.4
Education Level	Primary	11	7.6
	Secondary	70	48.3
	Tertiary	64	44.1
Marital Status	Married	94	64.8
	Single	40	27.6
	Widowed/divorced	11	7.6
Cigarette smoking	Yes	1	0.7
	No	144	99.3
Alcohol consumption	Yes	7	4.8
	No	138	95.2
Parity	Primiparous	37	25.5
	Nulliparous	39	26.9
	Multiparous	67	46.2
	Grand multiparous	2	1.4
Gravidity	Primigravida	40	27.6
	Multigravida	105	72.4
Multiple Pregnancies	Yes	2	1.4
	No	143	98.6
History of abortions	Yes	51	35.2
	No	93	64.1
Hypertension	Yes	5	3.4
	No	140	96.6
HIV	Yes	4	2.8
	No	141	97.2
Uterine Anomalies	Yes	13	9.0
	No	132	91.0

4.3 Prevalence of subchorionic hematoma

The prevalence of subchorionic hematoma was 18.6% (95% CI=12.6-25.9), table 4.2.

Table 4.2. Prevalence of subchorionic hematoma among women with per vaginal bleeding in the first trimester at KNH between 2019 and 2020

		Frequency	Percent (95% CI)
SCH Diagnosis	Present	27	18.6 (12.6-25.9)
	Absent	118	81.4 (74.1-87.4)

4.3.1 Clinical characteristics of patients with per vaginal bleeding with and without subchorionic hematomas

Most participants presented with Lower abdominal pains (LAPS) (37.0%), while 11.1% and 3.7% respectively experienced vomiting and were dizzy. Most patients without SCH presented with LAPS (60.2%), while 11% and 5.9 were dizzy and had a headache (Table 4.3)

Table 4.3. Clinical presentations of women with and without SCH at KNH between 2019 and 2020

Clinical presentation		**SCH (N=27)**	**Without SCH (N=118)**
Vomiting	Yes	3 (11.1)	3 (2.5)
	No	24 (88.9)	115 (97.5)
LAPS	Yes	10 (37.0)	71 (60.2)
	No	17(63.0)	47 (39.8)
Dizziness	Yes	1 (3.7)	13 (11.0)
	No	26 (96.3)	105 (89.0)
Syncope	Yes	0 (0.0)	1 (0.8)
	No	27 (100)	117 (99.2)
Headache	Yes	0 (0.0)	7 (5.9)
	No	27 (100)	111 (94.1)
Dysuria	Yes	0 (0.0)	2 (1.7)
	No	27 (100)	116 (98.3)
Palpitations	Yes	0 (0.0)	2 (1.7)
	No	27 (100)	116 (98.3)
Malaise	Yes	0 (0.0)	1 (0.8)
	No	27 (100)	117 (99.2)
Blurred Vision	Yes	0 (0.0)	1 (0.8)
	No	27 (100)	117 (99.2)

4.4 Sonographic features of subchorionic hematomas

Women who had SCH compared to those who did not have SCH were more likely to have small hematomas (81.5%) at 8.85±2.13 weeks gestation, range of 6-12 weeks (table 4.4).

Table 4.4. Sonographic features of subchorionic hematomas at KNH between 2019 and 2020

		Frequency (N=27)	**Percent**
Hematoma size	Large hematoma (>50% of gestational sac involved)	5	18.5
	Small hematoma (<20% of gestational sac involved)	22	81.5
Gestation in weeks	Mean±SD, range	8.85±2.13, 6-12	

4.5 Initial management of subchorionic hematomas

The majority of women who were diagnosed with SCH were put on treatment (81.5%), mainly progestin (90.9%). 50% were put on haematinic supplementation and 22.7% (Table 4.5).

Table 4.5. Initial management of subchorionic hematomas at KNH between 2019 and 2020

		Frequency (N=27)	**Percent**
Initial management	Not prescribed	5	18.5
	Prescribed	22	81.5
Treatment modality	Progestin	20	90.9
	Analgesics	5	22.7
	Haematinic supplementation	22	50.0
	Antibiotics	2	9.1
	Bedrest	2	9.1
	Tranexamicacid	2	9.1
	Junior asprin	1	4.5
	Nosic(doxylamine and vitamin B6)	1	4.5
	Antiemetics (unspecified)	2	9.1
	Ranitidine	1	4.5

4.6 Secondary objectives

Even though the study was not powered enough to evaluate associations between demographic characteristics and pregnancy outcomes of patients with SCH the following was noted.

4.6.1 Comparison of demographics of patients with and without SCH

The odds of SCH was 3.25 times higher (95% CI=1.23-8.17) among patients who had a tertiary education compared to secondary education (**p=0.014)**; 6.42 times higher (95% CI=1.58-29.1) among multiparous patients compared to primiparous (**p=0.008**); and 2.81 times higher (OR= 1.19-6.24) higher among patients with a history of abortions (**p=0.015**). The two groups were similar with regards to age, marital status, gravidity, parity, and uterine anomalies (table 4.6).

Table 4.6. Comparison of demographic characteristics of patients with per vaginal bleeding in first trimester with and without SCH between 2019 and 2020 at Kenyatta National Hospital

		SCH Diagnosis			
		Yes (N=27)	**No (N=118)**	**OR (95% CI)**	**P value**
Age group	<35	17 (15.3)	94 (84.7)	Reference	
	35+	10 (29.4)	24 (70.6)	2.30 (0.90-5.78)	0.065
Education	Primary	3 (27.3)	8 (72.7)	3.37 (0.80-13.7)	0.131
	Secondary	7 (10.0)	63 (90.6)	Reference	
	Tertiary	17 (26.6)	47 (73.4)	3.25 (1.23-8.17)	**0.014**
Marital Status	Married	23 (24.5)	71 (75.5)	2.91 (1.01-8.24)	0.056
	Single	4 (10.0)	36 (90.0)	Reference	
	Widowed/divorced	0 (0.0)	11 (100)	-	-
Smoking	Yes	0 (0.0)	1 (100)	-	-
	No	27 (18.8)	117 (81.3)	Reference	
Alcohol use	Yes	1 (14.3)	6 (85.7)	0.72 (0.06-4.80)	1.000
	No	26 (18.8)	112 (81.2)	Reference	
Parity	Primiparous	2 (5.4)	35 (94.6)	Reference	
	Nulliparous	5 (12.8)	34 (87.2)	2.57 (0.48-13.5)	0.432
	Multiparous	18 (26.9)	49 (73.1)	6.42 (1.58-29.1)	**0.008**
	Grand multiparous	2 (100)	0 (0.0)	-	-
Gravidity	Primigravida	5 (12.5)	35 (87.5)	Reference	
	Multigravida	22 (21.0)	83 (79.0)	1.85 (0.64-4.77)	0.243
Multiple Pregnancies	Yes	1 (50.0)	1 (50.0)	4.50 (0.22-86.0)	0.339
	No	26 (18.2)	117 (81.8)	Reference	
History of abortions	Yes	15 (29.4)	36 (70.6)	2.81 (1.19-6.24)	**0.015**
	No	12 (12.9)	81 (87.1)	Reference	
Uterine Anomalies	Yes	2 (15.4)	11 (84.6)	0.77 (0.16-3.14)	1.000
	No	25 (18.9)	107 (81.1)	Reference	

4.6.2 Outcomes of patients with subchorionic hematoma

Most patients (50.0%) had SCH resolve and progress to delivery at term. Approximately 27.8% had second trimester pregnancy losses,11.1% had first trimester pregnancy loss and 11.1% had a preterm birth at 32weeks gestation. Data for nine patients was unavailable (Table 4.7).

Table 4.7. Outcomes of women with subchorionic hematomas with per vaginal bleeding in the first trimester at KNH between 2019 and 2020

	Frequency	**Percent**
Resolved - progressed to delivery (n=18)	9	50.0
Discharged but had pregnancy losses in second trimester(n=18)	5	27.8
Discharged for follow up but had pregnancy loss 2weeks later(n=18)	2	11.1
Admitted for bedrest, resolved but developed a retroplacental bleed and preterm birth at 32weeks (n=18)	2	11.1
Unknown (n=27)	9	33.3

CHAPTER FIVE

5 DISCUSSION, CONCLUSION, AND RECOMMENDATIONS

5.1 Discussion

The data of 145 women with a mean age of 29.35 years was reviewed. Participants were well educated, mostly married and nulliparous. Risky social behaviours such as cigarette smoking and alcohol consumption were not common but the history of abortions was high at about 35.9%. The prevalence of other comorbidities such as HIV, CKD, hypertension, and uterine anomalies were low (<10%). The prevalence of SCH was 18.6%. Women who had SCH were more likely to vomit but less likely to develop LAPS and dizziness compared to women who did not have SCH, and were also more likely to have small hematomas at 8 weeks of gestation and be put on progestin. SCH was most likely to resolve and proceed to delivery at term.

The first objective was to determine the prevalence of SCH in women seen with per vaginal bleeding in the first trimester of pregnancy. The data showed that SCH was a common health problem between 2019 and 2020 at KNH, with a prevalence of 18.6% (12.6-25.9%) reported. From the data approximately one in every five pregnant women with per vaginal bleeding in a first trimester of a pregnancy was found to have us diagnosis of SCH. A comparable finding was reported in a cross-sectional study of 342 Italian women with per vaginal bleeding at 9-20 weeks of gestation where the prevalence of SCH was 18.0% (24). Mandruzzato *et al*. (25) reported a prevalence of 11% in another cross-sectional study in Italy, while Sukur *et al*. (26), Wahid *et al*.(20) and Al-Nuaim *et al.* (27) reported a prevalence of 18.2% in Turkey, 8.6% in Afghanistan, and 8.5% in Saudi Arabia respectively. Developed countries such as America and Japan have reported a significantly lower SCH prevalence in a similar cohort of between 1.7% and 4.2% (28)(29). The highest burden of SCH has been reported in South America with a prevalence of 33.5% reported in Venezuela at 6-13 weeks of gestation (30). A possible explanation for the variability in prevalence reported herein is that women who deliver in high

income countries might be receiving better level of care whilst pregnant compared to those who deliver in low-income countries. Traditionally, residents of developed compared to developing countries are thought to get better level of care. High level of care impacts SCH prevalence as high risk patients can receive preconception care and also care early in pregnancy which can help prevent SCH recurrence.

We compared the clinical characteristics of women with and without SCH with per vaginal bleeding. Before controlling the demographic characteristics of patients, our data showed a statistically significant association between vomiting and SCH. Patients with SCH with per vaginal bleeding were eight times more likely to vomit compared to women who did not have SCH. Other clinical characteristics, which included LAPS and dizziness were less common among women with SCH compared to without SCH but the difference was not statistically significant. After controlling demographic characteristics of patients such as age and parity, clinical characteristics of women with per vaginal bleeding with and without SCH were similar. However, no studies have compared these clinical characteristics among patients with SCH.

The sonographic findings of women with per vaginal bleeding and a SCH in the first trimester of a pregnancy mirrored the findings of Mantoni et al. (18). On imaging, SCHs were more likely to be small at a mean gestation of about 8.85 [2.13] weeks. After treatment, SCH was likely to resolve with cases proceeding to delivery. Having small SCH seemed to bear a lower risk to pregnancy as previously reported by Wahid et al. (20). This may be explained by the little effect of the small hematoma on the growing foetus as compared to large hematoma. The small hematoma can resolve easily without interfering with the foetus or pregnancy in general. A majority of SCH in our population were treated with progestin as the initial management (90.9%). This compares with study done by Pelinescu et al (33) in Romania where 100 women with subchorionic hematoma were treated with oral dydrogesterone as initial management with

93 of these patients having a favourable pregnancy with resolution of the SCH. It is thought that progestins have immunomodulatory effect which helps in maintaining a T-helper 2 cytokine balance, hence reducing chances of miscarriage or pregnancy loss.

5.2 Conclusion

The prevalence of SCH among women with per vaginal bleeding in the first trimester was high at 18.6%. Clinical characteristics of women with SCH were similar to those of women without SCH. SCH were likely to be small at a mean gestation of 8.85 ±2.13 weeks. Treatment with progestin was the preferred initial management for SCH with most cases being likely to resolve after treatment and pregnancies proceeding to delivery.

5.3 Recommendation

- Due to the high prevalence of SCH in our population it is important to create more awareness on the condition among pregnant women and educate health care providers to have a high index of suspicion and investigate for SCH whenever a pregnant woman presents with per vaginal bleeding in the first trimester of pregnancy.
- There is need for a larger study to look at the risk factors associated with SCH and pregnancy outcomes in women with SCH in our population.

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APPENDICES

Appendix 1. Questionnaire

PREVALENCE, CLINICAL PRESENTATION AND INITIAL MANANGEMENT OF SUBCHORIONIC HEMATOMA IN FIRST TRIMESTER OF PREGNANCY AT KENYATTA NATIONAL HOSPITAL IN YEAR 2019-2020

Study questionnaire

Answer all questions accurately

Study number…… Date…….

1. Age in years…….

2. Education level

☐Primary

☐Secondary

☐Tertiary

3. Marital status

☐Married

☐Single

4. Parity……..

5. Gravidity…….

6.Previous abortions……

7. Multiple pregnancies in current pregnancy

☐Yes

☐No

8. Systolic blood pressure…….

9. Diastolic blood pressure……

10. Hypertension

☐Yes

☐No

If yes, type

☐Gestation

☐Chronic

☐Preeclampsia

☐Eclampsia

☐Superimposed preeclampsia

11. CKD

☐Yes

☐No

12. HIV

☐Yes

☐No

13. Other comorbidity (specify)……

14. History of recreational drug use……

15. Uterine anomalies

☐Yes

☐No

16. Sub chorionic haematoma diagnosis

☐Positive

☐Negative

17. Size of hematoma and sonographic findings: ……

18.initial management……

19. Comments

……

……

……

End

Appendix 2. KNH-ERC approval certificate

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15th July, 2021

KENYATTA NATIONAL HOSPITAL APPROVED 15 JUL 2021 KNH/UoN-ERC P. O. BOX 20723 • 00202 NAIROBI

Dr. Juliet Mukami Munene
Reg. No.H58/11109/2018
Dept. of Obstetrics and Gynaecology
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Dear Dr. Munene

RESEARCH PROPOSAL: PREVALENCE, CHARACTERISTICS AND INITIAL MANAGEMENT OF SUBCHORIONIC HEMATOMA AMONG WOMEN WITH PER VAGINAL BLEEDING IN THE FIRST TRIMESTER OF PREGNANCY AT KENYATTA NATIONAL HOSPITAL IN YEAR 2019-2020 (P252/04/2021)

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 15th July, 2021 – 14th July, 2022.

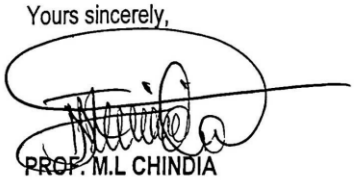
This approval is subject to compliance with the following requirements:

i. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
ii. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
iii. 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.
iv. 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.
v. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
vi. 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).
vii. 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 Chair, KNH- UoN ERC
The Dean, School of Medicine, UoN
The Chair, Dept. of Obs/Gynae, UoN
Supervisors: Prof. Omondi Ogutu, Dept. of Obs/Gynae, UoN
Dr.George Gwako, Dept.of Obs/Gynae,UoN

Appendix 3. Kenyatta National Hospital approval

KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723, 00202 Nairobi

Tel.: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

OFFICE OF HEAD OF DEPARTMENT, OBSTETRICS & GYNAECOLOGY
EXT.43370

KNH/HOD-OBS&GYN/07/VOL.11/ Date: 10th August, 2021

Dr Juliet Mukami Munene
Reg. No.H58/11109/2018
Dept. of Obstetrics & Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

RE: RESEARCH PROPOSAL – PREVALENCE, CHARACTERISTICS AND INITIAL MANAGEMENT OF SUBCHORIONIC HEMATOMA AMONG WOMEN WITH PER VAGINAL BLEEDING IN FIRST TRIMESTER OF PREGNACY AT KENYATTA NATIONAL HOSPITAL IN YEAR 2019-2020 (P252/04/2021)

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 In Incharge Clinic 18 to facilitate your study.

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

Dr. [illegible] for HOD.

Dr. Maureen Owiti
HOD-OBSTETRICS & GYNAECOLOGY

Cc.

In charge Clinic 18

Appendix 4. Study Timelines

	2019		2020		2021					
Study activity	**Nov**	**Dec**	**Oct**	**Nov**	**Feb**	**Mar**	**Apr-July**	**Aug**	**Sept**	**Oct**
Concept note development										
Proposal development										
Internal marking										
Proposal presentation										
Ethics submission										
Data collection										
Data analysis										
Presentation of findings										

Appendix 5. Study Budget

Item	**Cost in Kshs.**
Charges for KNH/UON ERC proposal review	3,000
Research assistants: 2 for 15 days at 1000 per diem per day	30,000
Data entry	5,000
Statistician	30,000
Photocopying/printing and publishing	20,000
Contingency fund	10,000
Total	**98,000**