FACTORS ASSOCIATED WITH THROMBOCYTOPENIA AMONG PREGNANT WOMEN SEEKING ANTENATAL CARE SERVICES IN HOMABAY TEACHING AND REFERRAL HOSPITAL IN HOMABAY COUNTY, KENYA

BY

SEBUWUFU PIUS

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MASENO UNIVERSITY

DECLARATION

This thesis is my original work and has not been presented for any award in any University.

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DEDICATION

I dedicate this thesis to my two daughters Luyiga Mary Precious and Namwanje Joy Paula who always give me a reason to work harder.

ABSTRACT

Thrombocytopenia has been defined as a bleeding disorder characterized by the circulation of lower than normal amounts of platelets in the blood. Globally, thrombocytopenia is considered to be the most common hematological abnormality among pregnant women. In Kenya, the prevalence of thrombocytopenia among pregnant women has not been documented, however, records at the Homabay County Teaching and Referral Hospital (HTRH) show that between the year 2019 and 2021, there was an increase in the number of cases of thrombocytopenia among pregnant women attending the facility compared to the data for the same period in the neighboring Counties. Several factors have been associated with thrombocytopenia among pregnant women include; bone marrow disorder such as leukemia, side effects of taking certain medications, hereditary, gestational related thrombocytopenia, infections such as malaria, HIV, and diseases such as aplastic anemia. However, the majority of the studies done so far have focused on pediatric hematological cases, leaving information gap on factors associated with thrombocytopenia among pregnant women. Anodal information remotely relate malaria in pregnancy history, HIV infections and even familial characteristics with thrombocytopenia occurrence among pregnant women but this needs to confirmed by a formal study. The overall objective of this study therefore was to investigate the factors associated with thrombocytopenia among pregnant women seeking antenatal care services (ANC) in Homabay County, Kenya. The specific objectives were to determine the association between familial characteristics, malaria, and HIV/AIDS and thrombocytopenia among pregnant women. The study adopted cross-sectional design with a sample size of 161 pregnant women seeking ANC services at HTRH. Consecutive sampling method was used to select the participants. This approach was complemented with retrospective assessment of disease events to capture other information. The data collection tools were a structured questionnaire and a medical record abstraction form. The data analysis involved univariable, bi-variable and multivariable techniques. Inferential analysis was done using a binomial logit model, with statistical significance established at *P*-values less than 0.05. Ethical clearance was obtained from the MUERC, HTRH, and NACOSTI. Consent was also sought from each of the participants as a show of one's own discretion to participate in the study. The prevalence of thrombocytopenia among pregnant women in Homabay County was 14%; the odds of having thrombocytopenia were less by 94% among pregnant women to whom the person with thrombocytopenia history in their family was their first or second degree relative (aOR = 0.056 [95% CI = 0.003 - 0.923], P = 0.044). The odds of having thrombocytopenia in the current pregnancy were 8 times higher among pregnant women who had malaria in pregnancy (aOR = 8.199 (95% CI = 2.466 - 27.263], P = 0.001). None of the HIV related characteristics had a statistically significant association with thrombocytopenia in pregnancy. Thrombocytopenia is a reality among pregnant women in Homabay and substantially prevalent, going by global and regional prevalence. In addition, the findings of this study may be a basis for policy amendment to accord the disease due attention as a maternal mortality risk confounder and thrombocytopenia should be assessed among pregnant women.

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LIST OF ACRONYMS

ART	Active Antiretroviral Therapy
AZT	Zidovudine
BSS	Bernard-Soulier syndrome
CD4	Cluster of Differentiation 4
CVDs	Cardiovascular Diseases
DIC	Disseminated Intravascular Coagulation
FMS	Free Maternity Service
HAART	Highly Active Antiretroviral Therapy
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HIV	Human Immunodeficiency Virus
HTRH	Homa-Bay Teaching and Referral Hospital
IEBC	Independent Electoral and Boundaries Commission
IT	Idiopathic Thrombocytopenia
IT	Inherited Thrombocytopenias
ITP	Idiopathic thrombocytopenic Purpura
MPV	Mean Platelet Volume
MUSERC	Maseno University Scientific and Ethical Review Committee
NACOSTI	National Commission for Science, Technology and Innovation
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
SDG	Sustainable Development Goal
VITT	Vaccine-Induced Immune Thrombotic Thrombocytopenia
WHO	World Health Organization

DEFINITION OF TERMS

Factors associated with thrombocytopenia	This was used to refer to a set of three characteristics that will be found to have statistically significant associations with gestational thrombocytopenia
Familial characteristics	This term referred to characteristics related to the family from which the pregnant woman hails, in terms of heredity, history of thrombocytopenia, history of gestational thrombocytopenia etc.
HIV characteristics	This term referred to the status, viral load, clinical stage and duration characteristics of HIV in pregnancy
Malaria characteristics	This term referred to the manifestation, severity and frequency characteristics of malaria in pregnancy
Pregnant women	This term was used to refer to a woman carrying a pregnancy that is in its third trimester, whilst seeking antenatal care services from Homabay county teaching and referral hospital only.
Thrombocytopenia	This term was used to refer to a gestational health condition in which a pregnant woman has a platelet count that is less than 150×10^9 per liter of blood. It was a binary variable whose other category was the possession of a platelet count that exceeds 150×10^9 per liter of blood

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CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

This chapter entails the background information to the study, statement of the problem, study objectives, hypotheses, significance, and scope of the study.

Thrombocytopenia has been defined as a bleeding disorder characterized by the circulation of lower than normal amounts of platelets in the blood consequent due to sub optimal production or heightened destruction (Provan and Semple, 2022; Vera-Aguilera et al., 2022; Kruse et al., 2021). Clinically, thrombocytopenia is defined by blood platelet counts being less than 150×10^9 /L, with severe thrombocytopenia being defined as a blood platelet count of $< 50 \times 10^9$ /L(Kosiyo et al., 2021; Jinna et al., 2021). Among the various hematological disorders, thrombocytopenia is one of the most concerning (Zitek et al., 2022; Bahadoram et al., 2022) particularly when incident during pregnancy (Zitek et al., 2022). That makes thrombocytopenia important in the achievement of maternal mortality reduction (SDG target 3.1). Perhaps of most concern, thrombocytopenia is a known risk factor for postpartum hemorrhage (Govindappagari et al., 2020), the leading cause of maternal deaths (WHO, 2022) and severe maternal morbidity. Historically, thrombocytopenia is an ancient medical condition and the reference to the first classic case stretches back to the year 1735 (Blanchette & Freedman, 1998). Some 70 years later, Robert Willan distinguished four types of thrombocytopenia with a common symptom of severe bleeding of irregular duration from the mucus membranes. In 1883, Guilio described the existence, structure and fundamental role of platelets (piastrine), concluding that the platelets directly influenced coagulation and thrombosis (Blanchette & Freedman, 1998). Theoretically, several propositions have been put forward to explain the development of severe thrombocytopenia in patients. For example, Mega karyocyte theory postulates that platelets are produced in the pulmonary circulation by the physical fragmentation of megakaryocyte cytoplasm and anomalies may arise due to a variety of factors (Trowbridge EA, et al; 1984).

Operationally, major factors associated with thrombocytopenia among pregnant women have been documented as; bone marrow disorder such as leukemia, side effects of taking certain medications, hereditary or familial line, gestational or pregnancy related thrombocytopenia(Jain et al., 2021). Others include infections such as malaria, HIV, folate deficiency and diseases such

as leukemia and aplastic anaemia (Verma, 2019; DeLoughery, 2018). These factors may reduce the number of circulating platelets by trapping in the spleen or destruction. Association between malaria and thrombocytopenia in pregnancy remains unclear. This is because, the type of thrombocytopenia as well as its severity is still unknown. A study Kosiyo and colleagues determined association between thrombocytopenia and malaria (Kosiyo et al.,2021) however, this did not consider the pregnant women. As an inherited condition, the prevalence of inherited (familial line) thrombocytopenia as an epidemiological concern is underexplored. It is also unclear where thrombocytopenia in HIV/AIDS could be associated, the pathogenesis involved in HIV infection or weather thrombocytopenia could be attributed to medication used during HIV infection. Knowledge on prevalence thrombocytopenia in relation to its etiology would be of major public health significance since these would help in mitigation of its occurrence among pregnant women. From epidemiological perspective, it is important to know prevalence and risk factors associated with thrombocytopenia as a haematological abnormality in pregnant women attending ANC services. As such, the current study will determine the factors associated with thrombocytopenia among pregnant women seeking ANC services HTRH in Homabay County, Kenya.

Globally, thrombocytopenia is considered to be the most common hematological abnormality among pregnant women (Mangla et al., 2022). It was estimated to occur between 7 to 11% of pregnant women (Mangla et al., 2022), with less than 1% of the pregnant women having platelets whose count goes below 100 x 10^9/L (Fogerty, 2018). However, other global estimates have put its incidence within a range of 7 to 12% (Subtil et al., 2020), implying that 1 in 10 pregnant women may develop it (Care et al., 2018). However, an earlier estimate had it that thrombocytopenia occurs in about 6% to 12% of all pregnant women (Mohseni et al., 2019).

In Sub-Saharan Africa, the prevalence of gestational thrombocytopenia has been reported to be 10.2% (Getawa et al., 2022). Quite a number of studies have found thrombocytopenia to be associated with HIV and Malaria, among women in Africa (Gebreweld et al., 2021; Bisetegn & Ebrahim, 2021; Pretorius, 2021; Duguma et al., 2021; Ruiru et al., 2021; Mohammed et al., 2020; Punnath et al., 2019; Naing and Whittaker, 2018; Mikre and Zerdo, 2016; Kotepui et al., 2014). The implication to this effect is that indeed thrombocytopenia is prevalent during pregnancy, on the African continent, although its magnitude is not widely documented. In

Kenya, thrombocytopenia and hematological disorders in general have garnered research interest over the years (Kosiyo et al., 2021; Gerardin et al., 2018; Mboya et al., 2016; Ongondi et al., 2016); however, none of them covered pregnant women. Majority of the studies done (Kosiyo et al., 2021; Gerardin et al., 2018) mainly focused on pediatric hematological cases, leaving information gap on factors associated with thrombocytopenia among pregnant women. Moreover, these previous studies were conducted in other areas and considering Homabay County's uniqueness with regards to socio-economic issues, especially its high level of illiteracy and poverty (KENBS, 2021) that may significantly influence access to maternal healthcare, and prevalence of the disease among pregnant women therein, dynamics of thrombocytopenia may be different in the county. Available information remotely relates malaria in pregnancy history, HIV infections and even familial characteristics with thrombocytopenia disease occurrence among pregnant patients (Hospital records, 2021, unpublished) but this association needs to be confirmed by a formal study. What is also clear from the literature reviewed is that previous studies (Gebreweld et al., 2021; Joshi et al., 2021; Gebreweld et al., 2021; Almazni et al., 2019; Belury et al., 2017; Hileman & Funderburg, 2017) generated descriptive evidence that needs testing by analytical study methods. The disease could be substantially prevalent among pregnant women in Homabay County as evidenced by the fact that between 150 and 170 cases of gestational thrombocytopenia are diagnosed every year at Homabay hospital. However, its actual prevalence is not known by far and neither are its contextual associated factors, whose identification may aid prevention. There is therefore need to assess the factors associated with thrombocytopenia among pregnant women in the county. Therefore, the proposed study is aimed at determining the association between the implicated factors and thrombocytopenia disease among pregnant women in Homabay County, Kenya.

1.2 Statement of the Problem

Records at the Homabay County Teaching and Referral Hospital shows that between in the years 2019 and 2021, there was an increase in the number of cases of thrombocytopenia in pregnant women attending the facility. Clinical data indicate that; in 2019, out of the 1568 mothers who attended ANC, 168 (10.7%) had thrombocytopenia. In 2020, out of 1285 mothers who attended ANC, 148 (11.5%) had thrombocytopenia. In 2021, out of 1363 mothers who attended ANC, 178 (13%) had thrombocytopenia. These figures are high compared to the data for the same period in Counties like Kisumu and Siaya. Available has scanty information which remotely relate malaria

in pregnancy history, HIV infections and even familial characteristics with thrombocytopenia occurrence among pregnant women but this needs to be confirmed by a formal study. This creates a gap in knowledge, since no study has been conducted to determine the factors associated with thrombocytopenia among pregnant women in Homabay County, Kenya and thrombocytopenia can be a predisposing factor to postpartum hemorrhage. Therefore, the present study was aimed at determining the factors associated with thrombocytopenia among pregnant women seeking ANC services in HTRH in Homabay County, Kenya.

1.3 Objectives of the study

1.3.1 General objective

To determine the factors associated with thrombocytopenia among pregnant women in Homabay County, Kenya.

1.3.2 Specific objective

i. To determine the association between familial characteristics and thrombocytopenia among pregnant women in Homabay County.
ii. To assess the association between Malaria and thrombocytopenia among pregnant women in Homabay County.
iii. To determine the association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County.

1.4 Study Hypotheses

1.4.1 Null hypotheses

i. H_{01}: There is no association between familial characteristics and thrombocytopenia among pregnant women in Homabay County
ii. H_{02}: There is no association between Malaria and thrombocytopenia among pregnant women in Homabay County
iii. H_{03}: There is no association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County

1.5 Significance of the study

The current study has unveiled important findings that could be very crucial in preventing the occurrence of thrombocytopenia. Furthermore, the findings of the current study is of a major

utility to policy makers in terms of unveiling information on prevalence of thrombocytopenia in pregnancy as well as its associated factors with respect to family history, malaria infection and HIV in pregnancy. This information is useful in developing policies geared toward prevention of thrombocytopenia. The administration of Homabay county teaching and referral hospital will also benefit from this study, given that all the study findings are reflective of the dynamics of pregnant women who seek and receive antenatal care from the hospital. The administration of the hospital may appreciate the implications of familial characteristics, malaria and HIV/AIDS on the incidence of thrombocytopenia during pregnancy and perhaps intensify preventive interventions for malaria and HIV/AIDS. Given that this study has analyzed the influence of family characteristics, malaria and HIV/AIDS on the incidence of thrombocytopenia among pregnant women, all of which (factors) are within the control of the women, we believe that the study will be of significance to pregnant women at an individual level. It is possible that the women will be in position to appreciate the consequences of familial characteristics, malaria and HIV/AIDS, following which they will be endeavor to adopt preventive behavior for malaria and HIV/AIDS. For those that were found to be already infected, the evidence adduced in this study may trigger behavior change in as regards adherence to medication meant to treat the disease so as to suppress their contributory effects on thrombocytopenia.

With the rising interest in the study of hematological disorders in Kenya, coupled with the fact that the study of gestational thrombocytopenia is still a grey area in the country, we anticipate that the study and its findings may stimulate more interest and guidance in the study of factors associated with thrombocytopenia during pregnancy in Kenya, perhaps in different parts of the country. Besides the interest, the findings of this study will also be used as in-country literature in all those studies that may be conducted in future.

1.6 Scope of the study

The study was conducted among pregnant women seeking antenatal care services from only Homabay County Teaching and Referral Hospital, located in Homabay County. The hospital was purposively sampled because of the considerable number of gestational thrombocytopenia cases clinically diagnosed among pregnant women at the hospital. The hospital is located Homabay County in what was formerly called the Nyanza province, and it currently has a population of 1,131,950, distributed within 8 sub-counties and 40 wards (Independent Electoral and

Boundaries Commission [IEBC], 2020). The study did not assess thrombocytopenia based on type (immune or non-immune), given time and resource limitations, only platelet count was assessed.

CHAPTER TWO
LITERATURE REVIEW

2.1 Introduction

This chapter presents a review of literature related to the study, and hence organized per specific objective. The literature was sourced from data bases mainly including PubMed, CINHAL, Science direct, and Springer link. The chapter further presents the conceptual framework for the study.

2.2 Thrombocytopenia

Thrombocytopenia is a hematological abnormality characterized by reduced platelet to below the reference range ($<150\times10^9$/L) (Sandfeld-Paulsen et al., 2022). It has been demonstrated to be common conundrum in malaria infection (Murewanhema et al., 2022) and may also occur in other conditions. Thrombocytopenia has been shown to be a predisposing factor to excessive bleeding when an injury occurs to a blood vessel. Several mechanisms have been postulated to cause thrombocytopenia. These mechanisms may include immune destruction of platelets(Liu et al., 2023), drug induced (Danese et al., 2020), platelet sequestration (Amini et al., 2023)and impaired production and maturation (Song et al., 2023).

2.3 Association between familial characteristics and thrombocytopenia among pregnant women

Thrombocytopenia has been associated with family related characteristics and genetics (Marchionatti and Parisi, 2021). The first identification of Immuno Thrombocytopenia (IT) was done in 1948 during which a bleeding disorder referred to as Bernard-Soulier syndrome (BSS), was named (Noris and Pecci, 2017). It is over the last decade that gene sequencing has been used to identify genes link to thrombocytopenia (Nurden & Nurden, 2020). Although inheritable thrombocytopenia is in some cases referred to as rare, some estimates have insinuated it as being substantially prevalent (Mikaelsdottir et al., 2021).

Globally, there is growing evidence that thrombocytopenia is highly heritable (Donato, 2021; Chojnowski et al., 2020; Almazni et al., 2019; Noris & Pecci, 2017; Johnson et al., 2016), at which point it is referred to as Inherited Thrombocytopenias (IT) (Chojnowski et al., 2020). A study by Zhao et al. (2021) reported that some of the children they studied had variants they had

inherited from their parents. Some children are reportedly born with normal sized platelets but with severe thrombocytopenia because they have no mature bone marrow megakaryocytes (Nurden & Nurden, 2020). Wang and Zhao (2020) on the other hand reported that congenital thrombotic thrombocytopenic purpura (TTP) is one of the inheritable autosomal recessive diseases disorder misdiagnosed, and identified as Immune Thrombocytopenia (ITP). Tan et al. (2020) also reported that Thrombocytopenia 2 (THC2) a highly inheritable form of thrombocytopenia, while Pujol-Moix et al. (2018) reported that Immune thrombocytopenia (ITP) was sporadic and not familial. It is therefore evident that thrombocytopenia has family links, however, even though the above mentioned studies have asserted the existence of such links, none of them made inferential analysis to that effect. Secondly, there hasn't been evidence of familial links with gestational thrombocytopenia generated.

2.4 Association between Malaria and thrombocytopenia among pregnant women

Malaria has been severally linked with the incidence of thrombocytopenia (Gebreweld et al., 2021; Joshi et al., 2021; Gebreweld et al., 2021; Mahittikorn et al., 2021; Santos et al., 2021; Ansah et al., 2021; Kosiyo et al., 2021; Eisa et al, 2021; Mboya et al., 2016)., However, a review of those studies reveals that few of them have numerically established relationships between malaria and thrombocytopenia in pregnancy. Gebreweld et al. (2021) reported that malaria increases both the rates of destruction and consumption of platelets and also suppresses thrombopoiesis. According to a study in Kenya, prevalence of thrombocytopenia among malaria patients was found to be 20.6% (Kosiyo et al., 2021). It has been suggested that the increments in consumption of platelets during a malaria episode occurs due to immune-mediated destruction, disseminated intravascular coagulation (DIC), reticulo-endothelial system pooling, microcirculation sequestration, and apoptosis (McMorran, 2019; Srivastava et al., 2017; Foote et al., 2017). The mechanism behind thrombocytopenia in pregnancy remains unclear.

Globally and from epidemiological perspective it is now known that individuals with severe non *P. falciparum* and *P. vivax,* infection are likely to develop thrombocytopenia (Mahittikorn et al. 2021 & Santos et al. 2021) however how this is compounded in pregnancy is unknown. The same was found to be in studies by Naing and Whittaker (2018) and Punnath et al. (2019). Thrombocytopenia has therefore been shown to be a marker of malaria, (Arif et al. (2016), although such evidence may clearly vary between settings and may require clear differentiation

from other mechanisms and factors that may cause thrombocytopenia in pregnancy as a public health concern. Since the severity of malaria may determine the rate of consumption of platelets, yet in some settings, malaria may be endemic with very few cases that are severe, it is possible that malaria may be a significant predictor in a given setting but not others. It suffices to mention therefore, that whereas some studies inferentially established links between malaria and thrombocytopenia during pregnancy, the link may not be significant in some settings.

In Sub Saharan Africa, studies by Gebreweld et al. (2021) showed that most malaria cases increased the rates of destruction and consumption of platelets, and also suppressed thrombopoiesis. A study by Erhabor et al. (2014) in West Africa reported decrease in platelet count among malaria patients (Children). Studies have concluded that thrombocytopenia was a marker of malaria (Plasmodium infection), in Sub Saharan Africa (Awoke and Arota, 2019), Mikre and Zerdo 2016 and Kotepui et al. 2014). However, the studies by Awoke and Arota (2019), Mikre and Zerdo (2016) and Kotepui et al. (2014) included general populations of persons, and not pregnant women, making them largely non-generalizable to pregnant women.

In Kenya, Mboya et al. (2016) reported that there was a decrease in platelet count among malaria patients (Children). However, one study by Kosiyo et al. (2021) in western Kenya, didn't find thrombocytopenia to be one of the markers of P. falciparum malaria infection in children in Kenya. As can be noted from the findings reviewed above, the links established between malaria and thrombocytopenia are largely physiological and whereas they are rightly true and evidence based, their cause, malaria, may not explicitly translate into significant prediction of thrombocytopenia in a large population. It is also evident that even that the findings from the reviewed studies are not contextualized to pregnant women. The shown relationships between malaria and Thrombocytopenia may not therefore be generalizable to a population of pregnant women. It is also evident that even the studies that attempted to assess the effect of malaria on thrombocytopenia only considered a malaria diagnosis as the independent variable. None of them included the frequency of incidence of the disease as an exposure variable, making a literature gap.

2.5 Association between HIV/AIDS and thrombocytopenia among pregnant women

Like malaria, many studies have also described the role of platelets in immune system activation, vascular dysfunction and inflammation in cases of chronic HIV infection (Liang et al, 2017; Belury et al., 2017; Hileman & Funderburg, 2017; Nou et al., 2016; Longenecker et al., 2016; Liang et al., 2015). Others have shown that among HIV-1 infected patients reduction in platelet count is very frequent (Deressa et al., 2018; Gunda et al., 2017). Saha et al. (2015) and Kathuria et al. (2016) reported prevalence's of thrombocytopenia ranging from 7% to 21% among HIV infected patients. Getawa et al (2021) reported a prevalence of thrombocytopenia among HIV patients to be in the same range (17%), similar to Bisetegn & Ebrahim (2021) (9.69%). However, Talargia et al. (2021) reported a higher prevalence of thrombocytopenia among HIV patients, at 22.7%. Bisetegn and Ebrahim (2021) also gave a somewhat different range of 5.9% to 26%. Further still, it has been reported that cytopenias related to anemia (Woldeamanuel et al., 2021; Negesse et al., 2018; Assefa et al., 2015; Wankah et al., 2014) frequently happen among HIV-1 patients, before and after initiation of HAART. Cytopenia in general has been reported to be a common occurrence among patients living with HIV, and it is one of the risk factors for progression of disease to AIDS, anemia and hospitalization. Globally, Dai et al. (2016) studied antiretroviral treatment-naive HIV patients in China, and reported that their thrombocytopenia prevalence to be 4.5%, similar to findings by Fan et al. (2015). Those findings indicate a prevalence of thrombocytopenia in the context of HIV, although the findings were descriptive. However, Getawa et al. (2021) reported that they had found a strong significant relationship between HIV and thrombocytopenia; similar to what has been reported by Altayri et al. (2017) and Sebitloane et al. (2016). In agreement, Mohammed et al. (2020) also reported that Mean platelet volume (MPV) was a characteristic indicator that got affected following diagnosis with HIV. They added that people living with HIV had lower amounts of platelet counts and high Mean Platelet Volumes (MPV). Huibers et al. (2020) also reported that HIV affected the bone marrow, causing thrombocytopenia and anemia. In support, Pretorius (2021) reported that envelope proteins in HIV-1 and inflammatory molecules in circulation cause platelet complex formation and hence hyper-coagulation, which can then lead to platelet depletion and thus thrombocytopenia. As can be noted in the aforementioned findings, all the reviewed studies reported the prevalence of thrombocytopenia among people living with HIV, and didn't establish relationships between HIV and thrombocytopenia. Therefore, they didn't establish associations

between the two conditions, which is a gap, and in addition, they didn't include pregnant women populations.

In Sub Saharan Africa, many studies have linked thrombocytopenia to HIV infection (Woldeamanuel et al., 2021; Duguma et al., 2021; Ruiru et al., 2021; Mohammed et al., 2020; Fan et al., 2020; Negesse et al., 2018; Tamir et al., 2018; Lv et al., 2018; Altayri et al., 2017; Dai et al., 2016). A study by Duguma et al. (2021) that included 308 HIV-positive adults on ART also noted that the patients had hematological abnormalities after being initiated on treatment. The same findings were reported by Fan *et al.* (2020) who found the prevalence of cytopenia to be 19.1%, implying that some of the patients had thrombocytopenia. However, the authors didn't analyze the effect of HIV on thrombocytopenia. Nonetheless, they analyzed risk factors for cytopenia, reporting that there was higher risk of cytopenia, among patients who were HAART-naïve, those who had a CD4 cell count<200 cells/μL, those whose WHO stage was IV, those who had a co-infection with the hepatitis B virus (HBV), and those with a viral load exceeding ≥100,000 copies/ml. They also found higher cytopenia among patients who were taking AZT (Zidovudine). In agreement, Talargia & Getacher (2021) and Shen et al. (2015) also found that thrombocytopenia risk was higher among HIV patients who had CD4 counts that were less that 200 cells/μL, and those who were taking zidovudine based therapy. From the foregoing literature, contrary to other studies that only descriptively assessed thrombocytopenia and HIV, most of the studies conducted have established relationship between HIV and thrombocytopenia (ldeamanuel et al., 2021; Duguma et al., 2021; Ruiru et al., 2021; Mohammed et al., 2020; Fan et al., 2020).

In Kenya no literature is available; however, HIV has a number of characteristics that could be linked to thrombocytopenia incidence, for instance viral load, duration on ART etc.

2.6 Prevention strategies of thrombocytopenia

From public health perspective, prevention of thrombocytopenia would involve prevention of any of its etiological factors such a malaria infection or any other infection that would impair bone marrow activity (Kosiyo *et al.*, 2021). Furthermore, use of certain medication that are known to cause thrombocytopenia should as well be minimized (Danese et al., 2020). Foods high in certain vitamins and minerals, including vitamins B12 and C, folate, and iron, may help

increase your platelet count. Some foods and beverages, including alcohol, may lower platelet count should be avoided. Pregnant women should avoid contact with toxic chemicals such as pesticides, arsenic, and benzene which can slow the production of platelets.

2.7 Literature gap

Factors associated with thrombocytopenia have been widely studied in many African countries (e.g., Gebreweld et al., 2021; Santos et al., 2021; Ansah et al., 2021; Eisa et al., 2021; Ruiru et al., 2021; Mohammed et al., 2020), however, virtually none have done so in the context of pregnancy. In Kenya, thrombocytopenia and hematological disorders in general have garnered research interest over the years (Kosiyo et al., 2021; Gerardin et al., 2018; Mboya et al., 2016; Ongondi et al., 2016); however, none of them covered pregnant women. The majority focused on pediatric hematological cases; leaving information gap in as far as the factors associated with thrombocytopenia among pregnant women. Moreover, these studies were conducted in other areas and considering the fact that Homabay County has its unique socio-economic issues that may directly or indirectly influence the occurrence of the disease, there is need for a study. What is also clear from the literature reviewed is that previous studies generated descriptive evidence that needs testing by analytical study methods**.** This study being analytical, aimed at bringing out clearly the evidence of the causal – response relationship between the disease (thrombocytopenia) and risk factors (family characteristics, Malaria, and HIV).

2.8 Conceptual framework

The study had one dependent variable, gestational thrombocytopenia, which was indicated by platelet count less than 150×10^9 /L of blood. It was a binary variable whose other category was the possession of a platelet count equal to or exceeding 150×10^9 /L of blood (Normal). The study had three independent variables whose choice was supported by the interactional model of client health behavior. That is in addition to evidence from previous studies as well (Gebreweld et al., 2021; Srivastava et al., 2017; McMorran, 2019; Foote et al., 2017; Santos et al., 2021; Ansah et al., 2021; Eisa et al., 2021; Mellors et al., 2019; Ruiru et al., 2021; Pretorius 2021; Duguma et al., 2021). The independent variables was; family characteristics (Family history of thrombocytopenia and family history of gestational thrombocytopenia), malaria (malaria in pregnancy and frequency of malaria), and HIV (Sero status, Duration since diagnosis, Current viral load, CD4, Opportunistic infections, Line of ART, Adherence to medication). The

association between the three independent variables and the dependent variable has been conceptualized as possibly being confounded by a number of characteristics, that were adjusted for during multivariable analysis (Figure 2.1).

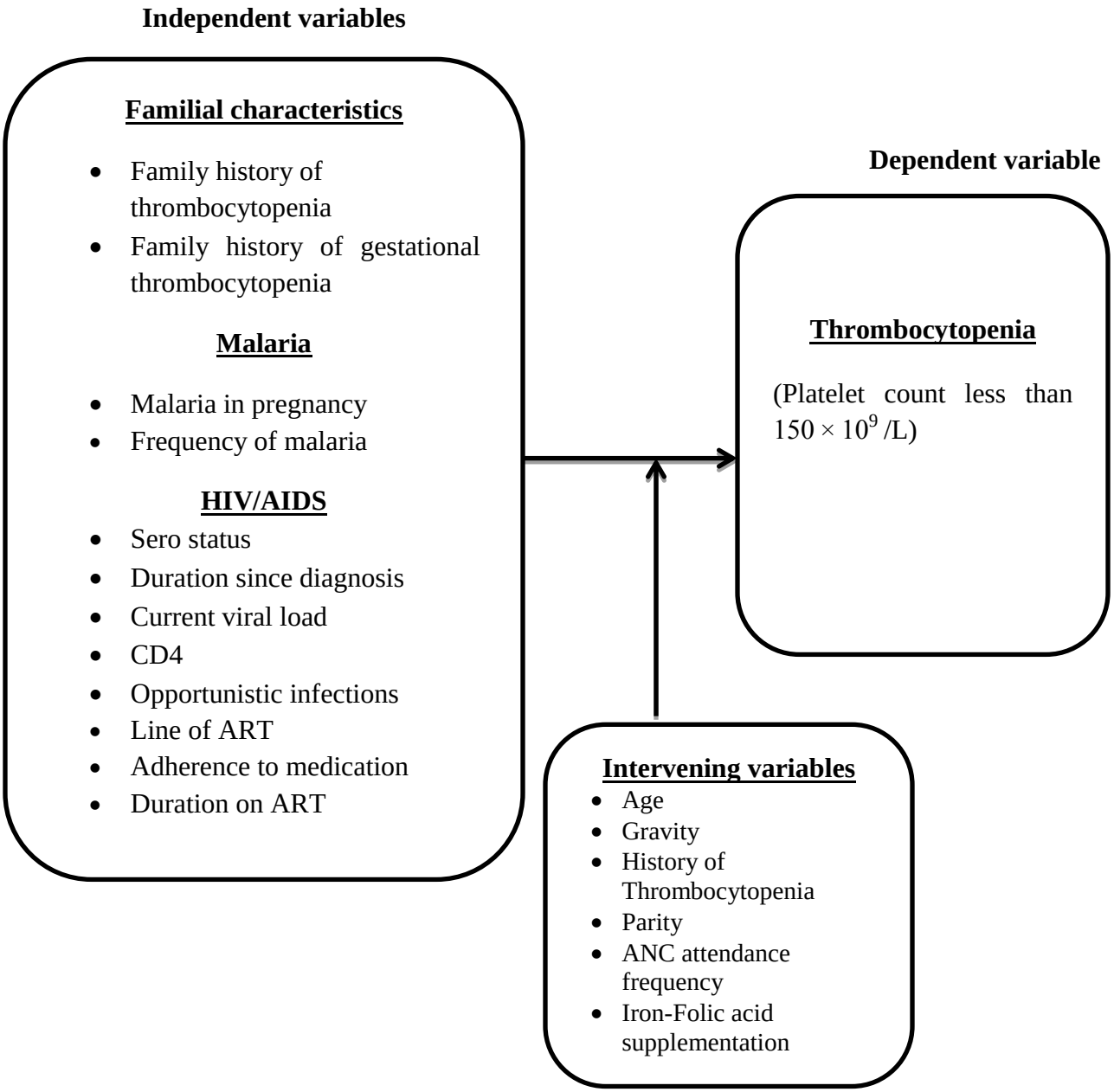

Figure 2.1: Conceptual framework

CHAPTER THREE
METHODOLOGY

3.1 Introduction

This chapter presents the study methodology. It is organized in eleven sections including study area, study design, study population, sample size determination, sampling procedure, data collection methods, data collection tools, quality control, data management and analysis plan and ethical considerations.

3.2 Study Area

The study was conducted at Homabay County Teaching and Referral Hospital, a Government health facility which provides comprehensive medical and surgical services, located in Homabay Township Sub-location, Homabay location, Asego, Western Kenya. Homabay County has an area of 3,154.7km2 and a population of 1,131,950 (2019 census). It has 262,036 households with an average of 4.3 people per household. The county has a population density of 359 people per square kilometer. Lake Victoria is the major source of livelihood for Homabay County. The hospital currently serves as the referral hospital for the residents from the 8 sub counties of Homabay County as well as the surrounding counties and receives approximately 118 mothers every month for antenatal care. The hospital catchment area is in the Lake Victoria region and manages high numbers of malaria patients. The hospital registers a considerable number of gestational thrombocytopenia cases. The number of cases of thrombocytopenia among pregnant women at the hospital could even be more than those clinically diagnosed, going by symptoms and signs registered in records. Perhaps most importantly, despite the evidently high number of cases of thrombocytopenia among pregnant women at the hospital, there have not been studies conducted thereat to assess the factors associated with thrombocytopenia among pregnant women who seek and receive antenatal care services from the hospital.

3.3 Study design

This study adopted a cross-sectional study design over a period of 2 months, in which a section of respondents was sampled, studied at one instance each and not followed up (Setia, 2016). This approach was complemented with retrospective assessment (6 months for Malaria and whole duration for HIV/AIDS), to capture all relevant information. The choice of a cross sectional design as the most suitable for this study was premised on the fact that (i) it is a positivist design

(Strang, 2015) which implies that it centers on the collection of only quantitative data (Setia, 2016; Strang, 2015) that is used to make deductions, as was required to achieve all the three objectives (ii) it allows for the concurrent assessment of both the exposure (independent) and outcome (dependent) variables, as was required in this study since thrombocytopenia had to be assessed at the same time among all sampled pregnant women, without need for follow up (Setia, 2016).

3.4 Study population

The study targeted 236 pregnant women seeking antenatal care services from Homabay Teaching and Referral Hospital. However, the study population was particularly 161 adult pregnant women in their third trimester given that thrombocytopenia is most prevalent at that gestational time period. In addition, such a time frame also allowed for a more valid retrospective assessment of earlier thrombocytopenia incidence in the same pregnancy, since there were up to 8 months over which prevalence could be assessed. It should be noted that by targeting the third trimester, there was little to no more room for future incidence of thrombocytopenia, making the retrospective assessment of thrombocytopenia over the previous 7 or 8 months more credible.

3.5 Inclusion and exclusion criteria

3.5.1 Inclusion criteria

1. Pregnant women (18years and above), given the need to include only women who are legally adults and can personally consent to participate in the study, that included phlebotomy. Secondly, younger women (< 18 years) usually experience more pregnancy complications compared to older women, with the implication that those below 18 years may not be in position to sustain a 40-minute interview, leading to a lot of item non-response.

2. Pregnant women in third trimester who was willing to have phlebotomy done on them for purposes of conducting blood tests for malaria, and HIV, given that those tests was important for providing data that will constitute two of the study independent variables.

3.5.2 Exclusion criteria

1. Pregnant women whose antenatal records could not be accessible at the time they were sampled, given that the study had to rely on both real-time tests for platelet count,

malaria, HIV and a historic assessment of them same in the current pregnancy, so as not to miss out on incidence.

2. Pregnant women who due to obstetric or non-obstetric complications were in a lethargic state, given that those could not be able to sustain a 40-minute interview.

3.6 Sample size determination

Sample size calculation for this study was done using a formula by Daniel (1999). That is because the mean number of pregnant women who seek antenatal care on a monthly basis, within which data collection is expected to be done, is known. The formula that was used is by Daniel (1999), given by;

$$n = \frac{X.N}{X + (N - 1)}$$

Where

n = Sample size

X = Maximum sample size at a probability of 50%, provided as 384, by the Kish Leslie (1995)

N = Population size = mean number of pregnant women who seek antenatal care during the two months of data collection, from Homabay County Teaching and Referral Hospital = 236(Hospital Records, 2021, unpublished).

Therefore, $n = \frac{384 \times 236}{384 + (236 - 1)}$

$$n = \frac{271,872}{384 + 235}$$

$$n = \frac{90,624}{619}$$

n = 146 Pregnant women +10% non-response

n = 161 pregnant women

3.7 Sampling procedures

On each day of data collection, all pregnant women who had sought antenatal care at the hospital were generally briefed about the study and intentions of the principal investigator whilst they were in the waiting area. That was then followed by the use of consecutive sampling to sample all the eligible ones that will have sought ANC on a given day. Consecutive sampling was the method of choice for the pregnant women, premised on evidence that the sample size required constitutes more than half of the population size, which made the use of random sampling inappropriate since it involved probability sampling and the elimination of some units. With consecutive sampling on the other hand, it was possible to approach every available pregnant woman at the hospital, assess them for eligibility and include them if found to be eligible (Setia, 2016b). That was done until 161 pregnant women had been sampled, over a two months period.

3.8 Study variable description

Table 1 below shows the variables that the study had included for analysis, three of which were independent variables including malaria, HIV, and malaria characteristics, which were measured as either scale or nominal variables, and analyzed at multivariable level. The dependent variable was thrombocytopenia, which was indicated by a platelet count platelet count less than150×10^9/L, and was measured as scale variable. Data related to this variable was determined using the complete blood count. The study also had intervening variables that were used for adjustment during multivariable analysis, all of which were collected using structured interviews (Table 3.1).

Table 3.1: Description of the study variables

Variable	Category	Data collection method	Measurement scale	Data analysis plan
Independent variables				
Familial characteristics	Family history of thrombocytopenia	Structured interviews	Nominal	Multivariable analysis
	Family history of gestational thrombocytopenia	Structured interviews	Nominal	Multivariable analysis
Malaria characteristics	Malaria in pregnancy	Medical record abstraction	Nominal	Multivariable analysis
	Frequency of malaria	Medical record abstraction	Scale	Multivariable analysis
HIV/AIDS characteristic	• Current viral load	Medical record abstraction	Scale	Multivariable analysis
	• Sero status	Medical record abstraction	Nominal	Multivariable analysis
	• CD4 level baseline	Medical record abstraction	Scale	Multivariable analysis
	• Duration since diagnosis	Structured interviews	Scale	Multivariable analysis
	• Opportunistic infections	Structured interviews	Nominal	Multivariable analysis
	• Line of ART	Medical record abstraction	Nominal	Multivariable analysis
	• Duration on ART	Structured interview	Scale	Multivariable analysis
	• Adherence to medication	Structured interview	Nominal	Multivariable analysis
Dependent variable			Scale	
Thrombocytopenia	• Platelet count less than 150×10^9 /L	Complete blood count diagnostic	Scale	Descriptive
	• Platelet count equal to or more 150×10^9 /L(Normal)		Scale	Descriptive
Intervening variables				
	Age	Structured interview	Scale	Multivariable analysis
	Gravidity	Structured interview	Scale	Multivariable analysis
	History of Thrombocytopenia	Structured interview	Nominal	Multivariable analysis
	Iron-Folic acid supplementation	Structured interview	Nominal	Multivariable analysis
	Parity	Structured interview	Scale	Multivariable analysis
	ANC attendance frequency	Structured interview	Scale	Multivariable analysis

3.9 Data collection methods

3.9.1 For the dependent variable (Prevalence of thrombocytopenia)

Whereas the establishment of the prevalence of thrombocytopenia is not part of the study objectives, it had to be determined since it was the dependent variable of the study, without

which the associations between familial, malaria, and HIV characteristics couldn't be established. To diagnose and/or assess thrombocytopenia, a laboratory diagnostic approach was used, that is, the complete blood count (Jinna and Khandhar, 2023). The complete blood count was conducted to assess platelet count and it was done following the drawing of venous blood from each respondent, whichwas then sent to the laboratory for analysis. A platelet count lower than 150 x 10^9 /l of blood indicated thrombocytopenia.

3.9.2 First objective (To determine the association between familial characteristics and thrombocytopenia among pregnant women in Homabay County)

Family characteristics were assessed using structured interviews given that such characteristics had to be self-reported, entirely.

3.9.3 Second objective (To assess the association between Malaria and thrombocytopenia among pregnant women in Homabay County)

The second objective involved the diagnosis of malaria as part of the independent variables for the objective. That was done using a Rapid Diagnostic Test (RDT) for malaria; an RDT is done using a test kit, on which a small sample of blood is placed, and a diagnosis made when two red lines show. A rapid test was used because of its low cost, yet closely similar accuracy with microscopy when it comes to detecting parasites (WHO, 2022), although without differentiation of the type of parasites. Capillary blood was used, and that was drawn following finger pricking with a sterile lancet that is appropriately gauged. The results from the RDT were entered into the data sheet. However, medical record abstraction also was used as data collection method for that objective to determine whether sampled pregnant women will have had any history of malaria diagnosis in the current pregnancy and the frequency. Medical record abstraction is a data collection method used to collect already captured and hence retrospective patient data, through abstraction of required patient data (Zozus et al., 2015).

3.9.4 Third objective (To determine the association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County)

For the third objective, HIV status was also assessed using a rapid diagnostic test, given the need to obtain real-time data. The diagnostic test for HIV was carried out among pregnant women for whom no antenatal record of antenatal HIV testing over the past three months was available.

However, in addition, to lab testing, questionnaire and medical record abstraction were also used for this objective since there was need to assess other HIV related clinical characteristics like viral load, which was obtained from records and put into the data sheet.

3.9.5 Data collection tools

The study used a structured questionnaire as the data collection tool, since it is designed with close ended questions that can hence capture close ended responses was one of the data capture tool. The Questionnaire (Appendix B) was designed with three sections, for which PART A had questions soliciting for socio demographic characteristics, PART B had questions designed to capture responses related to family characteristics, and PART C had some self-reported data on HIV. Diagnostic test kits were used for all lab tests, the data they provide was captured on the Data Sheet (Appendix C). Medical record abstraction was also be used and data captured onto the data sheet. The Data sheet had three parts, Part I to capture platelet count, PART II had questions designed to capture data for malaria characteristics and PART III ha questions designed to capture data related to HIV characteristics.

3.10 Quality control

Research Assistants recruitment and training, Pretest, Validity testing and Reliability testing were the Quality control steps taken in the study.

3.10.1 Research Assistants recruitment and training

Three quality control techniques were used, the first one being research assistant's recruitment and training. The need for research assistants is motivated by the fact that the hospital usually has a substantial volume of pregnant women, all of whom may not be interviewed concurrently by the principal investigator. The assistants therefore served to interview a section of the women available as the principal investigator engages the rest. The assistants were two in number and all were Diploma holding Nurses, fluent in both Swahili and English and with experience in data collection. They were oriented and non-didactically trained on issues related to the study and its procedures. The training was conducted within a span of 7 hours, in two sessions, with the focus being on the objectives of the study, the study population and its eligibility criteria, how the women were to be sampled, and how data was collected, plus all ethics to be observed. Particular emphasis was put on how malaria in pregnancy had to be assessed, using RDTs, or medical

record abstraction and as well as how HIV history was to be assessed. Role plays were also done in order to ascertain impact of the training.

3.10.2 Pretest

A pretest of the study tool was also be done at Sori Lakeside Hospital, which like Homabay Teaching and Referral Hospital, has had antenatal clinical records suggestive of considerable prevalence of thrombocytopenia. The pretest was done among 10 pregnant women at the hospital, and it allowed for the ascertainment of the comprehensibility of the items of the tool by the pregnant women, identification of any errors in the items within the tool and whether or not there was need for any additional questions. After the pretest, the data captured was used in reliability testing (Section 3.9.4), and in addition, the pretest experience was used to inform some few amendments in the data collection tool, including the expunging of two questions from Section B of the tool, due to their impracticality.

3.10.3 Validity testing

The third quality control technique was content validity testing, which was done using the content validity index approach, because with it, it is possible to determine whether the tool has all necessary items to achieve the study objectives (Sürücü & Maslakçı, 2020). A group of four experts in the area of epidemiology, maternal health and data analysis was chosen and each given the objectives and a rating scale. The scale was; 4 for very relevant, 3 for relevant, 2 for somehow relevant, and 1 for not relevant. Their ratings of questions as 4 or 3were as follows; 20, 22, 19, and 22, respectively. Therefore, mean number of items rated as 4 or 3was calculated to be 21 and then the content validity index was computed using the formula below;

$$\textbf{CVI} = \frac{\text{Number of items rated 3 or 4}}{\text{Total number of items in the tool}} = \frac{21}{24} = 0.875$$

Therefore, since the CVI was found to be 0.875 and hence between 0.7 and 0.99, it was considered valid (Lawshe, 1975)

3.10.4 Reliability testing

Reliability was also done in order to determine the ability of the study tool to be used in other settings and still produce near-consistent findings (Sürücü & Maslakçı, 2020). Reliability testing

was done using the Cronbac alpha test, in Statistical Package for the Social Sciences version 26. Pretest data was entered in the SPSS data screen, and scale statistics analyzed, using the alpha test. Reliability was established when the alpha is found to be between 0.7 and 0.99, and since the alpha for the tool was found to be 0.727, the tool was considered to be reliable.

Reliability Statistics

Cronbach's Alpha	N of Items
0.727	24

3.11 Data management and analysis

All questionnaires were scrutinized for completeness and accuracy. The data was then entered directly into a prepared data sheet in SPSS software version 26, then screened for any code entry errors and duplication for rectification. Data was then summarized using descriptive statistics such as means, range, standard deviation and proportions, among others. Analytical statistics such as binomial regression analysis and multivariate analysis were applied to determine association between the dependent variable (thrombocytopenia) and implicated factors such malaria, HIV/AIDS and familial characteristics.

Objective I (To determine the association between familial characteristics and thrombocytopenia among pregnant women in Homabay County)

The analysis of data obtained was done at univariate, bivariable and multivariable analysis. Univariate analysis was done for each familial characteristic, first, using frequency distributions and cross tabulations and the relationship between the independent (familial characteristics) and dependent variables (thrombocytopenia) were analyzed using a binomial logit model. Significance level was set to 5%, and the findings were reported in terms of crude odds ratios, along with their confidence intervals. However, inclusion into the multivariable model was set an alpha of 20%, with variables having p values that are less than 0.2 considered for multivariable analysis. However, after adjustment for confounders, the alpha for statistical significance was set at 5%, with all p-values less than 0.05 considered statistically significant. The findings at this stage were reported using adjusted odds ratios at 95% confidence.

Objective II (To assess the association between Malaria and thrombocytopenia among pregnant women in Homabay County)

The analysis of data obtained for objective 2 was also done at univariate, bivariable and multivariable analysis, with univariate analysis done using frequency distributions and cross tabulations. The association between the independent (malaria characteristics) and dependent variables (thrombocytopenia) were analyzed using a binomial logit model. Significance level was set to 5%, and the findings were reported in terms of crude odds ratios, along with their confidence intervals, at bivariable level. However, inclusion into the multivariable model was set an alpha of 20%, with variables having p values that are less than 0.2 considered for multivariable analysis. However, after adjustment for confounders, the alpha for statistical significance was set at 5%, with all p-values less than 0.05 considered statistically significant. The findings at this stage were reported using adjusted odds ratios at 95% confidence

Objective III (To determine the association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County)

The analysis of data obtained for objective 2 was also done at univariate, bivariable and multivariable analysis, with univariate analysis done using frequency distributions and cross tabulations. The association between the independent (HIV/AIDS characteristics) and dependent variables (thrombocytopenia) were analyzed using a binomial logit model. Significance level was set to 5%, and the findings were reported in terms of crude odds ratios, along with their confidence intervals, at bivariable level. However, inclusion into the multivariable model was set an alpha of 20%, with variables having p values that are less than 0.2 considered for multivariable analysis. However, after adjustment for confounders, the alpha for statistical significance was set at 5%, with all p-values less than 0.05 considered statistically significant. The findings at this stage were reported using adjusted odds ratios at 95% confidence

3.12 Ethical Consideration

Ethical approval was obtained from the Maseno University Scientific and Ethical Review Committee (APPENDIX D).Permission to collect data was obtained from National Commission for Science, Technology and Innovation (NACOSTI) issued a research permit (APPENDIX F). Permission to carry out the research in the hospital was sought from the hospital administration. Each study participant was asked to participate voluntarily and were equally free to withdraw from the study without any dire consequences. Furthermore, participants voluntarily provided written informed consent to participate in the study through signing of the informed consent form

(appendix G). Anonymity of data was ensured through the use of unique identifiers or cods other than use of names. Benefits from the study which included further referral for management of thrombocytopenia were equally explained to the participants.

3.13 Expected output

This study will have two outputs, one of which was a thesis (report) detailing the study findings and the second was a manuscript which was meant for publication in one of the high impact health journals that was identified.

3.14 Study limitations

One of the limitations of this study is that whereas data for HIV status and malaria in pregnancy was obtained using diagnostic testing or medical record review, that for family history will have to be inevitably obtained based on self-reports. That may allow for some exaggeration or denial of thrombocytopenia family history to occur, hence affecting data quality. To prevent that, the consenting process was made more rigorous to include assurance of confidentiality, anonymity and beneficence of the study to the women sampled, so that they feel free divulge accurate information on family history.

For the case of malaria, some women that test negative for it, may not have accessible medical records to confirm that they will have never had malaria in the current pregnancy. For such women, thorough probing was made to ascertain history.

CHAPTER FOUR

RESULTS

4.1 Socio-demographic characteristics

Of all 161 participants included in the study, 100% responded and all the relevant information or data required from them were obtained during data collection process from the 1st July 2023 to 31st August 2023covering a duration of 2 months. The majority of the pregnant women sampled 89(55.3%) were aged between 18 and 25 years, and married 131(81.4%). More than a third of the respondents were affiliated to the Seventh Day Adventist faith 56(34.8%), while almost all of them 160(99.4%) were formally educated although the majority attained secondary level of education 84(52.2%). Almost a third of the pregnant women was carrying their second pregnancies 53(32.9%), and had at the time attended more than 4 ANC visits 82(50.9%). Almost all the pregnant women who participated in this study 154(95.7%) had received and taken iron and folic acid since conception **(Table 4.1).**

Table 4.1: Socio-demographic characteristics of the pregnant women sampled

Variable	Categories	n(%)
Current age in full years		
	18 - 25 years	**89(55.3)**
	26 -33 years	**57(35.4)**
	34 - 41 years	**15(9.3)**
Current marital status		
	Married	**131(81.4)**
	Single	**30(18.6)**
Religious denomination		
	Catholic	**31(19.3)**
	Anglican	**10(6.2)**
	Born again	**15(9.3)**
	Muslim	**3(1.9)**
	SDA	**56(34.8)**
	Others	**46(28.6)**
Formally educated		
	Yes	**160(99.4)**
	No	**1(.6)**
Level of education		
	Primary	**35(21.7)**
	Secondary	**84(52.2)**
	Post-secondary	**42(26.1)**
Gravidity		
	One	**46(28.6)**
	Two	**53(32.9)**
	Three	**30(18.6)**
	More than three	**32(19.9)**
ANC frequency		
	Less than 4	**79(49.1)**
	More than 4	**82 (50.9)**
Received and taken iron and folic acid since conception		
	Yes	**154(95.7)**
	No	**7(4.3)**

4.2 Thrombocytopenia

While this section does not directly address any of the three study objectives, the assessment of the prevalence of thrombocytopenia among pregnant women in Homabay County was important for the measurement of the dependent variable of the study, which was to be later used in multivariable analysis for the three objectives of the study. The findings in the figure above show that the prevalence of thrombocytopenia among pregnant women in Homabay County was 14% (Figure 4.1).

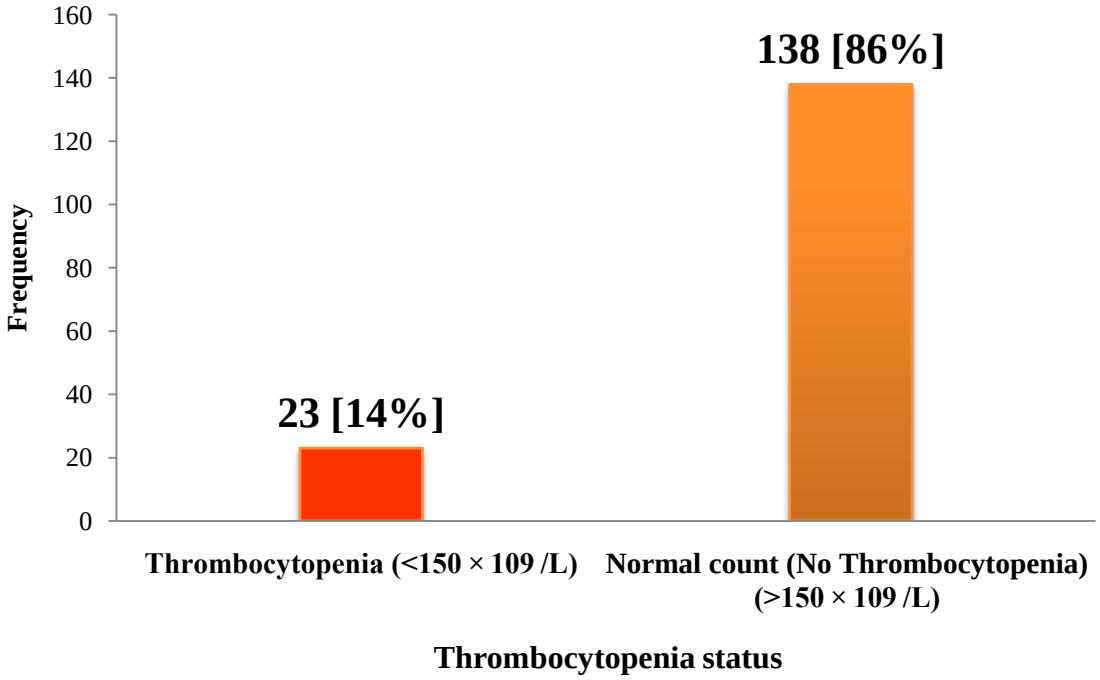

Figure 4.1: Prevalence of thrombocytopenia among pregnant women in Homabay County

4.3 Familial characteristics and thrombocytopenia

Descriptively, the findings in table 2 above show that more than three quarters of the pregnant women sampled 130(80.7%) had not had anyone in their family that had ever been diagnosed with too much bleeding, easy bruising or red spots visible under the skin. However, among the pregnant women who had a family member with thrombocytopenia history, more than three quarters of them had those family members as their first or second degree relatives 27(87.1%). Nearly three quarters of the pregnant women 23(74.2%) who had a family member with a history of thrombocytopenia reported that those family members were not pregnant More than three

quarters of the family members reported to have thrombocytopenia history were aged between 16 and 30 years 26(83.9%).

At bivariable analysis, only one familial characteristic showed statistical significance; and that was the relationship that the pregnant women sampled had with the person they reported to have thrombocytopenia history. The findings showed that pregnant women to whom the person with thrombocytopenia history was the first or second degree relative were less likely to have thrombocytopenia, with a margin of less than 92% (cOR = 0.080[95% CI = 0.007 - 0.911], p = 0.042). When adjusted for confounders, the variable remained statistically significant; the odds of having thrombocytopenia were less by 94% among pregnant women to whom the person with thrombocytopenia history in their family was their first or second degree relative (aOR = 0.056 [95% CI = 0.003 - 0.923], P = 0.044) compared to pregnant women to whom the person with a history of thrombocytopenia was a distant relative (Table 4.2).

Table 4.2: The association between familial characteristics and thrombocytopenia among pregnant women in Homabay County

Variable	n (%)	Thrombocytopenia status		cOR 95% CI	P value	aOR 95% CI	P value
		Thrombocytopenia [23]	No Thrombocytopenic [138]				
Any one in family ever been diagnosed with too much bleeding, easy bruising or red spots visible under the skin							
Yes	31(19.3)	4(12.9%)	27(87.1%)	0.865(0.272 -2.754)	0.807		
No	130(80.7)	19(14.6%)	111(85.4%)	1.000			
Relationship with the person(s)							
First or second degree relative	27(87.1)	2(7.4%)	25(92.6%)	0.080(0.007 -0.911)	**0.042***	0.056 (0.003 - 0.923)	**0.044***
Distant relative	4(12.9)	2(50.0%)	2(50.0%)	1.000		1.000	
Person(s) was pregnant?							
Yes	8(25.8)	1(12.5%)	7(87.5%)	0.952(0.085 10.725)	0.968		
No	23(74.2)	3(13.0%)	20(87.0%)	1.000			
Age of the person							
16 - 30 Years	26(83.9)	4(15.4%)	22(84.6%)				
31 - 45 years	5(16.1)	0(0.0%)	5(100.0%)				

4.4 Malaria and thrombocytopenia

More than three quarters of the pregnant women sampled 146(90.7%) had no malaria in pregnancy. In terms of having ever had a diagnosis of malaria made earlier in the current pregnancy, only 118(73.3%) had a diagnosis of malaria made earlier in the current pregnancy. One of the two malaria characteristics showed statistical significance; and that was malaria in pregnancy. The odds of having thrombocytopenia in the current pregnancy were 8 times higher among pregnant women who had malaria in pregnancy (aOR = 8.199 (95% CI = 2.466 - 27.263], P = 0.001) compared to those who were not currently having malaria in pregnancy (Table 4.3).

Table 4.3: To assess the association between Malaria and thrombocytopenia among pregnant women in Homabay County

Variable	n (%)	Thrombocytopenia status		cOR 95% CI	P value	aOR 95% CI	P value
		Thrombocytopenia [23]	No Thrombocytopenic [138]				
Malaria in pregnancy							
Positive	15(9.3)	7(46.7%)	8(53.3%)	7.109(2.275 -22.220)	**0.001***	8.199(2.466-27.263)	0.001
Negative	146(90.7)	16(11.0%)	130(89.0%)	1.000		1.000	
Had a diagnosis of malaria made earlier, in current pregnancy							
Yes	43(26.7)	6(14.0%)	37(86.0%)	0.963(0.352.629)	0.942		
No	118((73.3)	17(14.4%)	101(85.6%)	1.000			

4.5HIV/AIDS and thrombocytopenia

The majority of the pregnant women sampled were HIV Negative 132(82.0%)although for those that were positive, more than half had lived with HIV for more than five years 17(58.6%). Out of 23 women with thrombocytopenia, 2(6.9%) were HIV positive. However, more than four fifths of them (24[82.8%]) had not experienced any opportunistic infections since HIV diagnosis, although more than a third of those who had a history of opportunistic infections had had tuberculosis 2(40.0%). Almost all the pregnant women living with HIV had never defaulted on taking ART 27(93.1%), and were taking the first line of ART 27(93.1%). More than three quarters of the pregnant women living with HIV had a viral load of <200 copies per ml 23(79.3%) and had a baseline CD4 count of <1000 cells/ml 23(88.5%).

At bivariable level, none of the HIV related characteristics showed statistically significant associations with thrombocytopenia in pregnancy ($p<0.05$), and even the single one that had a p value less than 0.2, still remained statistically insignificant at multivariable level (Table 4.4).

Table 4.4: The association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County

Variable	n (%)	Thrombocytopenia status		cOR 95% CI	P value	aOR 95% CI	P value
		Thrombocytopenia [23]	No Thrombocytopenic [138]				
HIV sero-status							
Positive	29 (18.0)	2(6.9%)	27(93.1%)	0.392(0.086 - 1.773)	0.224		
Negative	132(82.0)	21(15.9%)	111(84.1%)	1.000			
Duration of living with HIV							
Less than five years	12(41.4)	0(0.0%)	12(100.0%)				
More than five years	17(58.6)	2(11.8%)	15(88.2%)				
Experienced any opportunistic infections since HIV diagnosis							
Yes	5(17.2)	1(20.0%)	4(80.0%)	5.750(0.296- 11.879)	0.248		
No	24(82.8)	1(4.2%)	23(95.8%)	1.000			
Opportunistic infections							
T.B	2(40.0)	0(0.0%)	2(100.0%)				
Herpes Zoster and Pneumonia	1(20.0)	0(0.0%)	1(100.0%				
Warts	1(20.0)	0(0.0%)	1(100.0%)				
Pneumonia	1(20.0)	1(100.0%)	0(0.0%)				
Ever defaulted on taking ART							
Yes	2(6.9)	1(50.0%)	1(50.0%)	26.000(0.854 -71.98)	0.062	25.983(0.853-71.69)	0.062
No	27(93.1)	1(3.7%)	26(96.3%)	1.000		1.000	
Line of ART currently							
Line 1	27(93.1)	2(7.4%)	25(92.6%)				
Line 2	2(6.9)	0(0.0%)	2(100.0%)				
Viral load							
<200 copies per ml	23(79.3)	1(4.3%)	22(95.7%)	0.227(0.012 - 4.286)	0.323		
>200 ml per ml	6(20.7)	1(16.7%)	5(83.3%)	1.000			
CD4							
<1000 cells/ml	23(88.5)	1(4.3%)	22(95.7%)	0.091(0.004 - 2.073)	0.133		
>1000 cells/ml	3(11.5)	1(33.3%)	2(66.7%)	1.000			

CHAPTER FIVE

DISCUSSION

5.1 The association between familial characteristics and thrombocytopenia among pregnant women in Homabay County

There have been links suggested to be in existence between heredity (family lineage) and thrombocytopenia, over the past 10 years (Donato, 2021; Chojnowski et al., 2020; Almazni et al., 2019; Noris & Pecci, 2017; Johnson et al., 2016; Nurden & Nurden, 2020; Wang and Zhao, 2020; Tan et al., 2020). In congruence with those studies, the current study also identified a significant association between familial characteristics and thrombocytopenia in pregnancy, although that is inconsistent with what Pujol-Moix et al. (2018) reported, asserting that Immune thrombocytopenia (ITP) was sporadic and not familial. However, the study by Pujol-Moix et al. (2018) was a review of only 8 thrombocytopenia cases, and it did not involve any inferential analysis to prove associations.

Unlike to previous studies (Donato, 2021; Chojnowski et al., 2020; Almazni et al., 2019; Noris & Pecci, 2017; Johnson et al., 2016; Nurden & Nurden, 2020; Wang and Zhao, 2020; Tan et al., 2020) that established positive associations between familial characteristics and thrombocytopenia, the current study established a negative association between the two. The findings obtained show that the odds of having thrombocytopenia in pregnancy were less by 94% among pregnant women whose first or second degree relative had a history of thrombocytopenia (aOR = 0.056 [95% CI = 0.003 - 0.923], P = 0.044). This finding implies that whereas family history was related to thrombocytopenia, such history reduced risk of thrombocytopenia in pregnancy when the family member was a close relative. In essence, the study confirms an association, but, with family history being preventive against thrombocytopenia in pregnancy.

Having had a very close family member with thrombocytopenia, before, and most likely getting to know of the severe sequelae associated with it (Cooper et al., 2021; Chakrabarti et al., 2022; Rovó et al., 2022), along with its substantial treatment costs undoubtedly increased perceived risk of the disease among pregnant women with familial relations to the thrombocytopenic member. Such pregnant women most likely got to appreciate the fact that thrombocytopenia in pregnancy was even more concerning in the context of health complications of maternal and child health importance (Cooper et al., 2021; Chakrabarti et al., 2022; Rovó et al., 2022; Kho et

al., 2018; Mangla et al., 2022). Such knowledge coupled with a high perceived risk of thrombocytopenia, informed by having a close member with it, made the pregnant women to adopt appropriate preventive behavior that could significantly decrease their risk of thrombocytopenia in pregnancy (Venkateshan et al., 2023; Ning et al., 2020; Samadipour et al., 2022). It should be recalled that the majority of the pregnant women whohad family history of thrombocytopenia had aided their family member seek treatment and possibly got to appreciate the causes of thrombocytopenia through their interaction with the healthcare service providers.

When pregnant, therefore, the aforementioned section of pregnant women must have stopped taking medications that reduced platelet count, reduced or stopped alcohol consumption during pregnancy, avoided key nutrient deficiencies, and infection, and also avoided contact with toxic chemicals including pesticides that are known to increase risk for thrombocytopenia (Jinna, S and Khandhar, 2023; Jinna and Khandhar, 2021). Such subsequent behavior certainly reduced the odds of having thrombocytopenia in pregnancy among pregnant women to whom the person with thrombocytopenia history in their family was their first or second degree relative, compared to pregnant women to whom the person with a history of thrombocytopenia was a distant relative. Pregnant women, to whom the member who had thrombocytopenia history was a distant relative, certainly had a comparatively lower perceived risk of thrombocytopenia, which made them adopt preventive behaviors less (Venkateshan et al., 2023; Ning et al., 2020; Samadipour et al., 2022), increasing their risk thrombocytopenia in pregnancy.

5.2 The association between Malaria and thrombocytopenia among pregnant women in Homabay County

The finding of this study indicated that the odds of having thrombocytopenia in the current pregnancy were 8 times higher among pregnant women who had malaria in pregnancy (aPR = 8.199 (95% CI = 2.466 - 27.263], P = 0.001) compared to those who were not currently having malaria in pregnancy. This finding implies that for every single pregnant woman who had thrombocytopenia during their current pregnancies, 8 more had thrombocytopenia concurrent with malaria parasitemia.

It should be noted that the study had two malaria characteristics to test, one of which was current diagnosis of malaria in pregnancy and history of malaria in the same pregnancy (Table 3). Of the two characteristics, the former (current diagnosis of malaria) showed statistical significance,

signifying the fact that active malaria parasitemia as opposed to its history increases thrombocytopenia. This finding was expected, premised on the fact that malaria parasitemia, especially with the parasites involved being plasmodium falciparum (p.falciparum) has been known to significantly perturb the cell-mediated immune system during its acute stage (Mandala et al., 2016; Pradhan and Ghosh, 2013; Hviid et al., 1997). Such perturbations result into lower peripheral platelet production and counts (Gupta et al., 2013; Lacerda et al., 2011; Patel et al., 2004), to levels significantly lower than 150 x 10^9/ml, which is an indication of thrombocytopenia.

Some authors have suggested the effect pathway of p.falciparum on thrombocytopenia, to be related to its causation of increased platelet aggregation (Grau et al., 2003), endothelial activation (Lowenberg et al., 2010; de Mast et al., 2009) and microvascular sequestration (accumulation of red blood cells in blood vessels). Endothelial activation, microvascular sequestration and platelet aggregation are renowned antecedents of low platelet counts (Hanson et al., 2015), especially when incident with malaria (Mahittikorn et al., 2021). On the whole however, there is still no definitive etiological description of how malaria may lead to thrombocytopenia, although some other speculations have it that malaria-induced coagulation disturbances, oxidative stress, splenomegaly, antibody mediated plate destruction, and bone marrow alterations increase thrombocytopenia risk among pregnant women with malaria parasitemia (Lacerda et al., 2011).

The finding that malaria in pregnancy is significantly associated with thrombocytopenia in pregnancy is congruent with numerous studies not limited to Gebreweld et al. (2021), Joshi et al. (2021), Mahittikorn et al. (2021), Santos et al. (2021), Ansah et al. (2021), Kosiyo et al. (2021), Eisa et al (2021), Mboya et al. (2016), Naing and Whittaker (2018) and Punnath et al. (2019), Mahittikorn et al. (2021), Santos et al. (2021) have established significant links between malaria and thrombocytopenia. However, despite that evidence, none had been contextual to pregnant women or Homabay County for that matter. In the context of Homabay County, there hadn't been any establishment of an association between malaria in pregnancy and thrombocytopenia in pregnancy.

5.3 The association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County

When it came to the association between HIV/AIDS characteristics and thrombocytopenia in pregnancy, this study revealed that that association was statistically insignificant. In fact, none of the HIV related characteristics showed statistically significant associations with thrombocytopenia in pregnancy ($p<0.05$). This finding implies that among pregnant women in Homabay County, who currently had thrombocytopenia in pregnancy, HIV/AIDS was inconsequential as a thrombocytopenia risk factor. This finding is incongruent with findings from multiple studies including Liang et al. (2017), Belury et al. (2017), Hileman & Funderburg (2017), Nou et al. (2016), Longenecker et al. (2016), and Liang et al. (2015), Deressa et al. (2018), Gunda et al. (2017), Saha et al. (2015) and Kathuria et al. (2016), Talargia et al. (2021), Bisetegn and Ebrahim (2021), Woldeamanuel et al.(2021), Negesse et al. (2018), Dai et al. (2016).The main difference between the findings of this study and the findings of all the aforementioned studies is the difference in study populations; none of those studies included pregnant women, and as such, their findings were bound to differ.

Current evidence indicates that while the prevalence thrombocytopenia can range from 20 to 25% among people living with HIV/AIDS and not taking antiretroviral therapy, it reduces by up to 80%, when antiretroviral therapy initiated (Getawa et al., 2021; Taylor et al., 2019; Nka et al., 2019; Wankah et al., 2014Henry, 2019). Therefore, the fact that by policy, all pregnant women living with HIV/AIDS receive intensive antiretroviral therapy, with a lot of adherence follow up, implies that all those sampled in this study were on ART (Eke et al., 2023).This assertion is further confirmed by the fact that all the 29 pregnant women living with HIV/AIDS were on a given line of ART (Table 4). As such, it is plausible to assert that most of the pregnant women living with HIV/AIDS, sampled, were virally suppressed, and were as such protected from immunodeficiency-regulated platelet destruction that happens among people living with HIV/AIDS. This explains why mere HIV/AIDS positive sero-status was inconsequential on thrombocytopenia among pregnant women.

It should also be noted that line of ART, opportunistic infections and duration of living with HIV variables could not be analyzed at bivariable level, given that they had null integers (zero counts) in their cross tabulations (Table 4); they may have shown statistical significance otherwise. The

non-computation of p-values for those three HIV/AIDS characteristics due to null integers certainly contributed to the insignificance of HIV/AIDS as a whole, in as regards thrombocytopenia incidence among pregnant women in Homabay.

CHAPTER SIX
ONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

i. Thrombocytopenia is a reality among pregnant women in Homabay and substantially prevalent, going by global and regional prevalence. 14% of pregnant women in Homabay County are thrombocytopenic. The incidence of thrombocytopenia is associated with familial characteristics (first or second degree relative with thrombocytopenia history) and malaria in pregnancy.

ii. The odds of having thrombocytopenia are less by 94% among pregnant women to whom the person with thrombocytopenia history in their family was their first or second degree relative (aOR = 0.056 [95% CI = 0.003 - 0.923], P = 0.044). Therefore, there was a negative association between familial characteristics and thrombocytopenia among pregnant women in Homabay County.

iii. The odds of having thrombocytopenia in the current pregnancy are 8 times higher among pregnant women who had malaria in pregnancy (aOR = 8.199 (95% CI = 2.466 - 27.263], P = 0.001). Therefore, there was a positive association between malaria and thrombocytopenia among pregnant women in Homabay County.

Among pregnant women in Homabay County, HIV/AIDS characteristics are inconsequential on thrombocytopenia pregnancy; none of the HIV/AIDS related characteristics is associated with the incidence of thrombocytopenia in pregnancy. Therefore, there was no association between HIV/AIDS and thrombocytopenia among pregnant women in Homabay County.

6.2 Recommendations

Going by the findings of the study, the following suggestions are made, focused on how thrombocytopenia can be prevented among pregnant women in Homabay County, and perhaps other areas in Kenya the great lakes region.

1. In order to harness the preventive effect of familial characteristics on thrombocytopenia in pregnancy (as observed in this study), there will be need for the health system stakeholders in Homabay county, in conjunction with the administration of Homabay Teaching and Referral Hospital to design a behavior change communication and health education program targeted at creating demand for family-based thrombocytopenia screening, and educating masses

(especially members of families with thrombocytopenia history) about the known causes of the illness. Such a program will increase awareness about thrombocytopenia, increase perceived susceptibility to the disease among pregnant women with familial history, and hence lead to them adopt behaviors that increase risk of thrombocytopenia, that will have been taught to them prior. The same program should be locally adopted at Homabay teaching hospital, to be implemented during antenatal care, targeting all pregnant women seeking ANC from the hospital, particularly during the first trimester.

2. The prevalence of malaria in pregnancy among women who seek antenatal care services at Homabay County is high, implying that malaria in pregnancy has to be prevented if thrombocytopenia in pregnancy has to be prevented as well. To do so, there is great to promote uptake of Intermittent Preventive Therapy (IPTp) in pregnancy to universal levels among all the women who seek ANC at Homabay hospital, given the proven effectiveness of IPTp in preventing malaria in pregnancy. That will be in addition to educating pregnant women about malaria vector control strategies, particularly the use of long lasting insecticide treated, and uptake of indoor residual spraying in their households, throughout pregnancy.
3. While HIV/AIDS characteristics were inconsequential, it was clear that adherence to Antiretrovial therapy and subsequent viral suppression had a lot to do with the suppression of the effect of HIV/AIDS on thrombocytopenia risk. Therefore, maternal healthcare service providers at Homabay are urged to always ensure that all pregnant women enrolled for ANC are tested for HIV/AIDS and if positively, initiated on ART (in a test and treat approach), and constantly followed up to ensure that they adhere to the medication given to them, to achieve viral suppression.

6.3 Recommendations for further studies

This study has only assessed relationships between family, malaria, HIV/AIDS characteristics, and thrombocytopenia in pregnancy. Whereas that was still novel in the Homabay county context, there is still need to assess numerous other potential correlates of thrombocytopenia in pregnancy, among women in the county. This therefore calls for the conduction of more studies on the factors associated with thrombocytopenia among women in Homabay, but with the exposure variables being intrapersonal, dietary, socio-economic and interpersonal characteristics.

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APPENDICES

APPENDIX A: CONSENT FORM

Title of study: Factors associated with thrombocytopenia among pregnant women in Homabay County, Kenya.

Principal investigator: Sebuwufu Pius

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Introduction: Thrombocytopenia has been defined as a bleeding disorder characterized by the circulation of lower than normal amounts of platelets in the blood. Globally, thrombocytopenia is considered to be the most common hematological malignancy among pregnant women. Factors associated with thrombocytopenia among pregnant women include; bone marrow disorder such as leukemia, side effects of taking certain medications, hereditary, gestational related thrombocytopenia, infections such as malaria, HIV/AIDS, and diseases such as leukemia and a plastic anemia. However, thrombocytopenia has also become of maternal health importance, especially during pregnancy given its direct moderation of pregnancy outcomes and indirect effects on severe maternal morbidity. The prevention of thrombocytopenia during pregnancy is thus crucial.

Purpose: The purpose of this study will be to assess the factors associated with thrombocytopenia among pregnant women in Homabay County, Kenya.

Who the study is targeting: The study is targeting 161 pregnant women seeking antenatal care from Homabay hospital

Why you have been sampled: You have been sampled because you happen to be one of the pregnant women seeking antenatal care from Homabay hospital, who is in their third trimester.

What your participation will involve: You will be requested to provide consent as a show of your voluntary will to participate in this study. As a participant, you will be required to provide a sample of your blood for testing, with interest in platelet count, malaria and HIV/AIDS. As the

blood tests are being run, you will give responses to a questionnaire that is expected to last about 30 minutes. Also abstraction of your medical records on malaria and HIV/AIDS will done.

Risks of your participation: Apart from feeling a little pain at the site where blood drawing will be done, we don't expect any risks to accrue during or after your participation in this study. You are not going to be given any drugs.

Benefits of your participation: The administration of Homabay county teaching and referral hospital will also benefit from this study, given that all the study findings will be reflective of the dynamics of pregnant women who seek and received antenatal care from the hospital. The administration of the hospital will appreciate the implications of malaria, and HIV/AIDS in the incidence of thrombocytopenia during pregnancy and perhaps intensify preventive interventions for malaria and HIV/AIDS.

Given that this study will analyse the influence of familial characteristics, malaria, and HIV/AIDS on the incidence of thrombocytopenia among pregnant women, all of which (factors) are within the control of the women, we believe that the study will be of significance to pregnant women at an individual level. It is possible that the women will be in position to appreciate the consequences of malaria and HIV/AIDS, following which they will be endeavor to adopt preventive behavior for malaria and HIV/AIDS. For those that will be found to be already infected, the evidence adduced in this study may trigger behavior change in as regards adherence to medication meant to effective treat the diseases so as to suppress their contributory effects on thrombocytopenia.

Confidentiality and data management: We will not share your responses or health status with anyone else. All questionnaires will be answered in private and if you feel like you do not want to participate, feel free to say so. There will be no repercussions for that decision, in any way.

Inquiries: In case you have any questions pertaining to this study, please contact the principal investigator on Tel: 0748948904

Voluntary participation: Your participation in this study is voluntary, you will not be given any incentives and so, you are free to withdraw from the study at any time, without any repercussions.

PART II: Certificate of Consent

I have been asked to give consent to participate in this research study which will involve my completion of one questionnaire, abstraction of medical records and blood testing for platelet count, malaria and HIV/AIDS. I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this study.

Signature

_____

Date _____

Day/month/year

If illiterate

I have witnessed the accurate reading of the consent form to the pregnant woman, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

*Print name of witness*_____ *AND* *Thumb print of participant*

Signature of witness _____

Date _____

Day/month/year

APPENDIX B: CONSENT FORM (SWAHILI VERSION)
KIAMBATISHO B: FOMU YA RIDHAA

Kichwa cha masomo: Mambo yanayohusiana na thrombocytopeniamiongoni mwa wanawake wajawazito katika Kaunti ya Homabay, Kenya.

Mpelelezi mkuu: Sebuwufu Pius

Simu: +254748948904

Wasifu ya Maseno University Scientific and Ethics Review Committe: muerc-secretariate@maseno.ac.ke

Utangulizi: Thrombocytopenia imefafanuliwa kuwa ugonjwa wa kutokwa na damu unaoonyeshwa na mzunguko wa kiwango cha chini cha kawaida cha sahani katika damu.Ulimwenguni, thrombocytopenia inachukuliwa kuwa ugonjwa mbaya zaidi wa damu kati ya wanawake wajawazito.Mambo yanayohusiana na thrombocytopenia kati ya wanawake wajawazitoni pamoja na;ugonjwa wa uboho kama vile leukemia, athari za kuchukua dawa fulani,thrombocytopenia ya kurithi, inayohusiana na ujauzito, maambukizi kama vile malaria, VVU/UKIMWI, na magonjwa kama vile leukemia na anemia ya plastiki.Hata hivyo, thrombocytopenia pia imekuwa ya umuhimu wa afya ya uzazi, hasa wakati wa ujauzito kutokana na udhibiti wake wa moja kwa moja wa matokeo ya ujauzito na athari zisizo za moja kwa moja kwa magonjwa makubwa ya uzazi. Kwa hivyo, kuzuia thrombocytopenia wakati wa ujauzito ni muhimu.

Kusudi: Madhumuni ya utafiti huu yatakuwa kutathmini mambo yanayohusiana na thrombocytopenia miongoni mwa wanawake wajawazito katika Kaunti ya Homabay, Kenya.

Utafiti unamlenga nani: Utafiti huo unalenga wanawake wajawazito 161 wanaotafuta huduma ya ujauzito kutoka hospitali ya Homabay

Kwa nini umepewa sampuli: Umechukuliwa sampuli kwa sababu wewe ni mmoja wa wanawake wajawazito wanaotafuta utunzaji wa ujauzito kutoka hospitali ya Homabay, ambaye yuko katika miezi mitatu ya tatu ya ujauzito.

Ushiriki wako utahusisha nini: Utaombwa kutoa kibali kama onyesho la utashi wako wa hiari kushiriki katika utafiti huu. Kama mshiriki, utahitajika kutoa sampuli ya damu yako kwa ajili ya

kupima, pamoja na riba katika hesabu ya platelet, malaria na VVU/UKIMWI. Vipimo vya damu vinapoendeshwa, utatoa majibu kwa dodoso ambalo linatarajiwa kudumu kama dakika 30. Pia uondoaji wa rekodi zako za matibabu kuhusu malaria na VVU/UKIMWI utafanywa.

Hatari za ushiriki wako: Kando na kuhisi maumivu kidogo kwenye tovuti ambapo mchoro wa damu utafanywa, hatutarajii hatari zozote kuzuka wakati au baada ya kushiriki kwako katika utafiti huu. Hutapewa dawa yoyote.

Manufaa ya ushiriki wako: Uongozi wa hospitali ya kufundishia na rufaa ya kaunti ya Homabay pia utanufaika na utafiti huu, ikizingatiwa kuwa matokeo yote ya utafiti yataakisi mienendo ya wanawake wajawazito wanaotafuta na kupokea huduma ya ujauzito kutoka kwa hospitali hiyo. Uongozi wa hospitali utathamini athari za malaria, na VVU/UKIMWI katika matukio ya thrombocytopenia wakati wa ujauzito na pengine kuimarisha hatua za kuzuia malaria na VVU/UKIMWI.

Kwa kuzingatia kwamba utafiti huu utachambua athari za sifa za kifamilia, malaria, na VVU/UKIMWI katika matukio ya thrombocytopenia miongoni mwa wanawake wajawazito, ambayo yote (sababu) ziko ndani ya udhibiti wa wanawake, tunaamini kuwa utafiti huo utakuwa wa maana. kwa wanawake wajawazito katika ngazi ya mtu binafsi. Inawezekana kwamba wanawake watakuwa katika nafasi ya kufahamu matokeo ya malaria na VVU/UKIMWI, na baada ya hapo watajitahidi kuwa na tabia ya kuzuia malaria na VVU/UKIMWI. Kwa wale ambao watapatikana kuwa tayari wameambukizwa, ushahidi uliotolewa katika utafiti huu unaweza kusababisha mabadiliko ya tabia kuhusiana na ufuasi wa dawa zinazokusudiwa kutibu magonjwa ili kukandamiza athari zao kwenye thrombocytopenia.

Usiri: Hatutashiriki majibu yako au hali ya afya na mtu mwingine yeyote. Hojaji zote zitajibiwa kwa faragha na ikiwa unahisi kama hutaki kushiriki, jisikie huru kusema hivyo. Hakutakuwa na athari kwa uamuzi huo, kwa njia yoyote.

Maswali: Iwapo una maswali yoyote kuhusu utafiti huu, tafadhali wasiliana na mpelelezi mkuu kwa Simu: 0748948904

Ushiriki wa hiari: Kushiriki kwako katika utafiti huu ni kwa hiari, hutapewa motisha yoyote na hivyo, uko huru kujiondoa kwenye utafiti wakati wowote, bila madhara yoyote.

SEHEMU YA II: Cheti cha Idhini

Nimeombwa kutoa idhini ya kushiriki katika utafiti huu ambao utahusisha ukamilishaji wangu wa dodoso moja, uondoaji wa rekodi za matibabu na upimaji wa damu kwa hesabu ya platelet, malaria na VVU/UKIMWI. Nimesoma habari iliyotangulia, au imesomwa kwangu. Nimepata fursa ya kuuliza maswali kuhusu hilo na maswali yoyote ambayo nimeuliza yamejibiwa kwa kuridhika kwangu. Ninakubali kwa hiari kushiriki kama mshiriki katika utafiti huu.

Sahihi

_____

Tarehe _____

Siku/mwezi/mwaka

Ikiwa hajui kusoma na kuandika

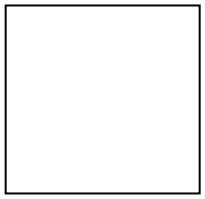
Nimeshuhudia usomaji sahihi wa fomu ya idhini kwa mwanamke mjamzito, na mtu binafsi amepata fursa ya kuuliza maswali. Ninathibitisha kuwa mtu huyo ametoa kibali kwa uhuru.

Chapisha jina la shahidi _____ *NA Alama ya kidole gumba cha mshiriki*

Saini ya shahidi _____

Tarehe _____

Siku/mwezi/mwaka



APPENDIX C: QUESTIONNAIRE

PART A: Socio demographic characteristics

Number	Question	Response	Code of Response given
1	What is your current age in full years?	…… …….	
2	What is your current marital status?	1. Married 2. Single 3. Cohabiting 4. Other…….	
3	To what religious denomination do you subscribe?	1. Catholic 2. Anglican 3. Born again 4. Muslim 5. SDA 6. Other……..	
4	Are you formally educated?	1. Yes 2. No	
5	If yes, to what level have you been educated?	1. Primary 2. Secondary 3. Post-secondary	
6	How many pregnancies have you carried so far?	1. One 2. Two 3. Three 4. More than three	
7	How many antenatal care visits have you so far attended	1. Less than 4 2. More than 4	
8	Have you received and taken iron and folic acid since conception	1. Yes 2. No	

PART B : Family characteristics associated with thrombocytopenia (Objective I)

Number	Question	Response	Code of response given
9	Has anyone in your family ever been diagnosed with too much bleeding, easy bruising or red spots visible under the skin?	1. Yes 2. No	
10	Question 9 above is yes: a) What was your relationship with the person(s)?	1. First degree relative 2. Second degree relative 3. Distant relative	

	b) What was the gender of person(s)?	1. Male 2. Female	
	c) What was the age(s) of the person(s)?	..... ……	
	d) Was the person(s) pregnant?	1. Yes 2. No	
11	If Question 9 is Yes, was the problem handled in the hospital?	1. Yes 2. No	
12	If YES, What did the doctor(s) at the hospital say the name of the disease was?		

PART C: HIV/AIDS Characteristics (Objective III)

Number	Question	Response	Code of response given
13	If positive, for how long have you been living positively?	1. Less than five years 2. More than five years	
14	Have you experienced any opportunistic infections since diagnosis with HIV?	1. Yes 2. No	
15	If yes, which were they?	…….. ……..	
16	Have you ever defaulted on taking your antiretroviral medication?	1. Yes 2. No	

END

APPENDIX C: DATA SHEET

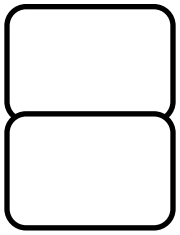
PART I: Platelet Data

Platelet count

……

Diagnosis

Thrombocytopenia

Normal count (No thrombocytopenia) 

PART II: Malaria related clinical data

Number	Question	Response	Code of response given
1	Malaria in pregnancy	1. Positive 2. Negative	
2	Had a diagnosis of malaria made earlier, in current pregnancy (Check records)	1. Yes 2. No	
3	If yes, how many diagnosed with malaria	……..	

PART III: HIV related clinical data

Number	Question	Response	Code of response given
4	HIV status (If negative and has not tested within the last 3 months, test again)	1. Positive 2. Negative	
5	What is your most recent viral load (Check records)	…… ……	
6	What was your baseline CD4 (Check records)	…… ……	
7	Which line of ART are you currently taking?	1. Line 1 2. Line 2 3. Line 3	

APPENDIX E: LETTER (APPROVAL LETTER)

MASENO UNIVERSITY
SCHOOL OF GRADUATE STUDIES

Office of the Dean

Our Ref: EL/ESM/07056/2020

Private Bag, MASENO, KENYA
Tel:(057)351 22/351008/351011
FAX: 254-057-351153/351221
Email: sgs@maseno.ac.ke

Date: 11 March , 2023

"

TO WHOM IT MAY CONCERN

RE: PROPOSAL APPROVAL FOR SEBUWUFU PIUS — EL/ESM/07056/2020

The above named is registered in the programme of Master of Public Health in the School of Public Health and Community Development, Maseno University. This is to confirm that his research proposal titled **"Factors associated with thrombocytopenia among pregnant women in Homabay County, Kenya"** has been approved for conduct of research subject to obtaining all other permissions/clearances that may be required beforehand.

Dr. Patrick Onyango
ASSOCIATE DEAN, SCHOOL OF GRADUATE STUDIES

APPENDIX D: LETTER (MASENO UNIVERSITY ETHICS COMMITTEE)

MASENO UNIVERSITY SCIENTIFIC AND ETHICS REVIEW COMMITTEE

Tel: +254 057 351 622 Ext: 3050
Fax: +254 057 351 221
Private Bag – 40105, Maseno, Kenya
Email: muerc-secretariate@maseno.ac.ke

REF: MSU/DRPI/MUSERC/01222/23 **Date**: 5th June, 2023

TO: Sebuwufu Pius
ESM/O7056/020
Department of Public Health
School of Public Health and Community Development
Maseno University
P. O. Box, Private Bag, Maseno, Kenya

Dear Sir,

RE: Factors Associated with Thrombocytopenia among Pregnant Women in Homabay County, Kenya

This is to inform you that **Maseno University Scientific and Ethics Review Committee (MUSERC)** has reviewed and approved your above research proposal. Your application approval number is MUSERC/01222/23.The approval period is 5th June, 2023 – 4th June, 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by Maseno University Scientific and Ethics Review Committee (MUSERC).
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to Maseno University Scientific and Ethics Review Committee (MUSERC) within 24 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to Maseno University Scientific and Ethics Review Committee (MUSERC) within 24 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
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 to Maseno University Scientific and Ethics Review Committee (MUSERC).

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://oris.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely

MASENO UNIVERSITY ETHICS REVIEW COMMITTEE 05 JUN 2023

Prof. Philip O. Owuor, PhD, FAAS, FKNAS
Chairman, MUSERC

APPENDIX F: LETTER (NACOSTI)

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **237636**

Date of Issue: **30/June/2023**

RESEARCH LICENSE

This is to Certify that Mr.. SEBUWUFU PIUS of Maseno University, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Homabay on the topic: FACTORS ASSOCIATED WITH THROMBOCYTOPENIA AMONG PREGNANT WOMEN IN HOMABAY COUNTY, KENYA for the period ending : 30/June/2024.

License No: **NACOSTI/P/23/26855**

237636

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

See overleaf for conditions

APPENDIX G: COUNTY AUTHORIZATION LETTER

DEPARTMENT OF HEALTH SERVICES

Telegrams: "MOH" Homa Bay
Telephone: 21039
When replying please quote
Homabaychc@gmani.com

OFFICE OF THE DIRECTOR,
HOMA BAY COUNTY,
P.O. BOX 52,
HOMABAY.

REF: MOH/RA/VOL.VI.(25)

5th July 2023

Sebuwufu Pius
ESM/07056/020
Department of Public Health
School of Public Health and Community Development
Maseno University
P. O Box Private Bag
MASENO

RE: AUTHORITY TO COLLECT DATA

Your request to collect data as in your research entitled *"Factors associated with thrombocytopenia among pregnant women in"*, Homa Bay county been granted for the period ending 30th June 2024.

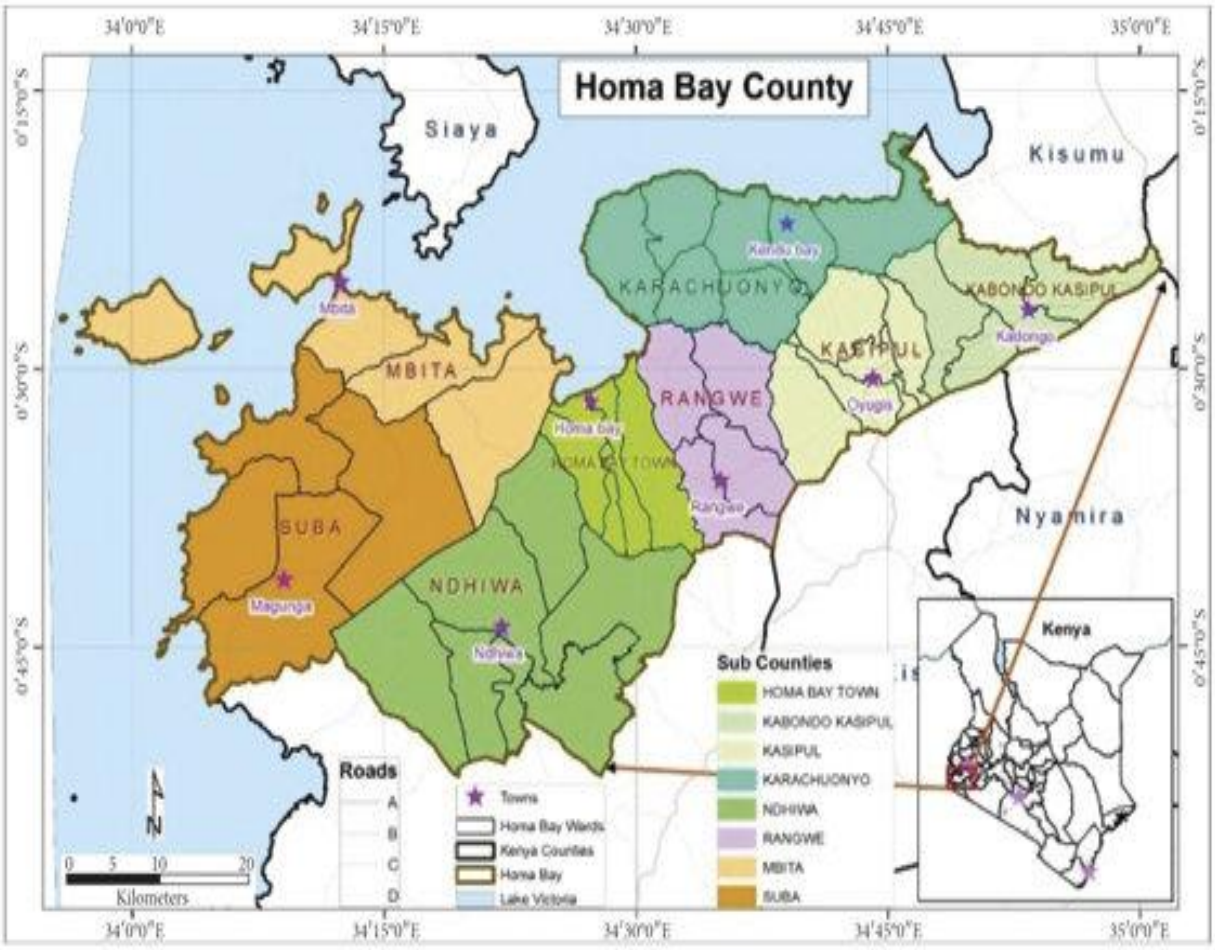
You will be required to adhere to the hospital's norms and regulations, and involve both the County Health Management Team, Sub County Health Management Team, Hospital's staff during the research period. Kindly communicate your findings at the hospital level and the office of the undersigned at the end of the research period.

Wish you all the best in your research.

DEPARTMENT OF HEALTH SERVICES,
COUNTY DIRECTOR OF HEALTH
05 JUL 2023
P.O. BOX 52 - 4300, HOMA BAY - KENYA

Dr. Gordon Okomo
County Director of Health Services
HOMABAY COUNTY.

APPENDIX H: MAP OF STUDY AREA



APPENDIX I: STUDY BUDGET

Activity/Item	Quantity	Unit Cost (Ksh)	Total Cost (Ksh)
Data collection assistant allowance	2	30,000	60,000
Typing, printing and photocopy	-	30,000	30,000
Cost of internet	-	5,000	5,000
Stationery	-	10,000	10,000
Cost of training research assistants	2	2,250	4500
Thesis binding	8	2,000	16,000
MUSERC Fees	-	-	3,000
Hematology Analysis and Tests	161	1,000	161,000
Transport Costs	6	8,000	48,000
Contingency 10% of the total cost	-	-	27750
Total			**371,250**

APPENDIX K: WORK PLAN

Activity	**Time**								
	Feb 2023	**March 2023**	**April 2023**	**May 2023**	**June 2023**	**July 2023**	**Aug 2023**	**Sept 2023**	**Oct 2023**
Proposal development									
Proposal defense									
Ethics approval									
Pilot study									
Data collection									
Data analysis									
Thesis writing									
Thesis submission									