“Molar Pregnancy
in Pietersburg Hospital, Limpopo Province, South Africa”

by

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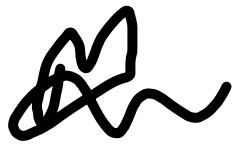
DECLARATION

I declare that the mini-dissertation / thesis hereby submitted to the University of Limpopo, for the degree of Masters in Obstetrics & Gynaecology has not previously been submitted by me for a degree at this or any other university; that it is my work in design and in execution, and that all material contained herein has been duly acknowledged.



30/07/2024

Dr. Khan M

Date

DEDICATION

I dedicate this thesis to all dedicated health workers, the unsung heroes of human development who despite their relentless efforts to save lives of mother and babies have themselves succumbed to health risk.

This is done with the sincere hope that some of the findings and recommendations of this dissertation will contribute to improvement of awareness and services to the women who might be suffering from Molar pregnancy [Hydatidiform mole], a part of Gestational Trophoblastic Disease which is if not diagnosed and treated early can results in death and if managed properly can be cured fully.

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ABSTRACT

Objectives: To investigate Molar pregnancy [Hydatidiform mole] in Pietersburg hospital, a part of tertiary hospital Pietersburg – Mankweng hospital complex in Limpopo Province. South Africa.

Methods: This was a retrospective cross-sectional descriptive study with quantitative data collection methods, conducted among the patients admitted in Gynaecology ward in Pietersburg hospital with early pregnancy complications such as miscarriages including molar pregnancy [Hydatidiform mole] from January 2021 to December 2021. Consecutive sampling was used to select 280 patients who were admitted with above mentioned diagnosis and underwent for uterine evacuation. Data was collected on demography, clinical features, sonographic findings, and laboratory results including histology results of products conception of the patients diagnosed with confirmed Hydatidiform mole [HM] by histology. Data was analysed using STATA software and thematic analysis.

Results: About 280 patients were admitted with early pregnancy complications such as miscarriages, molar pregnancy at gynaecology ward and underwent for uterine evacuation during a year from January 2021 to December 2021. Patient with ectopic pregnancy and Gestational Trophoblastic Neoplasia [GTN] were excluded from this study. Twenty-six patients were diagnosed as confirmed Hydatidiform mole [HM] by histological examination of products of conception, which is the gold standard for diagnosing HM, the mean age of the patient was 31.7 years and mean parity was 2.6. Prevalence of Hydatidiform mole was 9.3%. Approximately 85% patient with HM referred from peripheral hospital around the province and rest came from around Polokwane city where Pietersburg hospital situated as self-referral or referred by general medical practitioners. About 85% patient with HM had complete Hydatidiform mole [CHM] and 15% had partial Hydatidiform mole [PHM] on histological examination of products of conception. One patient was found to have choriocarcinoma [Gestational Trophoblastic Neoplasia] who was excluded from this study. The common presentation of majority of the patients [81%] was vaginal bleeding mostly during 14 to 20 weeks of pregnancy, only 15% did not have vaginal bleeding rather had the

features of HM on routine ultrasound examination. No patient with HM had metastatic disease and approximately 8% had severe anaemia and preoperative/intraoperative blood transfusion.

Conclusion: Geography and ethnicity play a factor in the prevalence of Hydatidiform mole (HM) worldwide. This study was conducted at Pietersburg hospital in South Africa's Limpopo province, even though it had a small sample size, the results showed that the prevalence of HM was 9.3% or 1 in every 11 patients admitted to the Gynaecology ward with miscarriages or molar pregnancies over one year. As women with HM and miscarriages often present with similar symptoms, clinicians should be vigilant about the risks and complications of HM. Early diagnosis, treatment, and follow-up care are critical in managing HM and preventing metastatic disease or Gestational Trophoblastic Neoplasia (GTN), ultimately preventing fatalities from this condition.

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Acronyms and Abbreviations

CDC	:	Centre for Disease Control and Prevention
CHM	:	Complete Hydatidiform Mole
ETT	:	Epithelioid Trophoblastic Tumour
GTN	:	Gestational trophoblastic neoplasia
HCG	:	Human Chorionic Gonadotropin
HM	:	Hydatidiform Mole
PHM	:	Partial Hydatidiform mole
PSTT	:	Placental Site Trophoblastic Tumour
WHO	:	World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

Molar pregnancy or Hydatidiform mole [HM] is a reproductive anomaly which arises from placental trophoblastic tissue after abnormal fertilization. It is the benign form of Gestational Trophoblastic Disease but of clinical and epidemiological significance because of its potential for significant consequences for women's health.

Hydatidiform Mole and Molar pregnancy are synonyms, is a part of diseases classified as Gestational trophoblastic disease[GTD] which comprises a heterogeneous group of related lesions arising from abnormal proliferation of trophoblast of the placenta extending from premalignant conditions of Hydatidiform Mole [HM] which can be further classified into Partial (PHM) and Complete (CHM) Hydatidiform Mole, to malignant conditions called Gestational Trophoblastic Neoplasia [GTN] including Invasive Mole, Choriocarcinoma, and Placental Site Trophoblastic Tumor (PSTT), Epithelioid Trophoblastic Tumor (ETT). GTD spectrum has recently been expanded to include atypical placental site nodule as 10- 15% may coexist with or develop into PSTT/ETT (Seckl. 2010, Ngan. 2021)

The clinical importance of HM is the risk of progression to gestational trophoblastic neoplasia (GTN), the malignant form of GTD, that occurs in about 15–20% of women following CHM and 0.5–5% of women after PHM. It has the potential to easily invade the uterus and the surrounding structures and to metastasize to other organs such as lung, liver, kidney, brain etc. Hence if not identified and treated early it can result in severe morbidity and death. (Ngan. 2021)

The most current evaluations confirm that the majority (80%) of GTDs are Hydatidiform Moles, 15% are Invasive moles, and 5% are Choriocarcinoma (Brown, J. 2017). Approximately 60% of cases of GTN arise from HM, 30% from spontaneous miscarriages and 10% from normal/ectopic pregnancy (Makhathini. 2019).

The prevalence of HM varies by geographical region and ethnicity. The highest prevalence is found in developing countries in patients with low socioeconomic status and in women whose diets are deficient in protein, folic acid, and carotene. It is also found mostly in patients of extreme ages (e.g., younger than 20 years or older than 40 year). It is also highest in Nulliparous women (Igwegbe. 2013). In North America, South America, and in Europe, HM develops in approximately 1 in 500–1000 pregnancies (Berkowitz. 2009*)*. The rate in East Asia is 5- to 15-fold higher, approaching 1 in 120 pregnancies (Mangili, G. 2014*)*. But recent Korean study showed prevalence of HM 1.1 per 1000 pregnancy almost similar to those reported in western population-based study (Jin- Sung Yuk. 2019). Data from South Africa is scarce, one South African study estimates incidence of HM at 1.2/1000 delivery. (Biscaro. 2012).

Early Pregnancy related complications consist of miscarriages, Hydatidiform mole, and ectopic pregnancy. Patients with HM (both complete and partial mole) typically present with vaginal bleeding during early pregnancy and persistent exaggerated pregnancy symptoms, larger uterine size than gestational age and higher serum Beta HCG [Human chorionic gonadotropin] levels than expected, especially in complete Hydatidiform mole [CHM]. Ultrasound scan of uterus may show typical feature of CHM without foetus or partial Hydatidiform mole [PHM] with or without foetus.

The gold standard for diagnosis of HM is by histopathology examination of the products of conception. Treatment of HM involves surgical removal of molar pregnancy either by uterine evacuation by suction and curettage or hysterectomy and send for histopathological examination. Medical induction of labour and hysterotomy are not recommended for molar evacuation since these methods increase maternal morbidity and the development of post molar GTN requiring chemotherapy (Ngan. 2021). Post treatment serial follow up of the patient for certain period is of utmost importance to identify and treat those patients early who may progress to gestational trophoblastic neoplasia [GTN]. Fortunately, cure rate of GTN with current treatment is almost 100% nonmetastatic disease and 80% for metastatic disease (Ramesan. 2021).

1.2 Problem Statement and the Rationale of the Study

HM is associated with remarkable complications such as heavy vaginal bleeding during early pregnancy with hypovolemia, anaemia, risk of uterine perforation and hysterectomy, progression to gestational trophoblastic disease, metastasis to other organs which lead to significant morbidity and mortality of women at reproductive age if not managed properly. Pietersburg hospital is a part of Pietersburg-Mankweng Hospital Complex which is the Provincial Referral Tertiary hospital for whole Limpopo Province. Pietersburg Hospital receives a significant number of patients with HM referred from different districts and regional hospitals around the province for further management.

Though some of the cases of HM are also referred to Mankweng Hospital but majority of the cases are referred to Pietersburg Hospital because Mankweng hospital did not have blood bank facilities afterhours. Availability of blood and blood products all the time is very crucial for managing the patients with HM as patients with this condition are prone to bleed heavily specially during surgical management and likely to need blood transfusion preoperatively or intra operatively or post operatively. As a result, Pietersburg hospital is the largest hospital managing patients with HM in Limpopo province.

Many small studies have been done on the prevalence of HM in Africa but very few studies done in South Africa. There was a study done in Durban, South Africa in 2003, but no study found to be done in Limpopo Province. It was observed that the number of diagnosed HM and its complications are quite significant in our setting, but the exact prevalence of this condition is not known.

The purpose of the study was to determine the prevalence of HM in Pietersburg Hospital among the women with early pregnancy complications. The results of this study may assist in contributing towards the planning and making decisions in improving the quality of health care in this hospital for those patients with Molar Pregnancy as there is no dedicated health centre for managing this condition in the whole Province, whereas a dedicated GTD clinic is an ideal set up for managing this group of patients. This study might also help to identify the characteristics of the patients with HM in our female population.

1.3 Research Question

“What is the Prevalence and associated factors of Molar Pregnancy among the women with early pregnancy complications such as miscarriages including Molar pregnancy in Pietersburg hospital, Polokwane, Limpopo Province, South Africa?”

1.4 Aim and Objectives of the Study

1.4.1 Aim

To investigate Molar Pregnancy at Pietersburg hospital, Limpopo Province, South Africa.

1.4.2 Objectives

- To investigate the Prevalence of Molar pregnancy among the women with early pregnancy complications such as miscarriages including molar pregnancy at Pietersburg hospital.
- To identify the associated factors such as demographic, clinical and laboratory data of the patients diagnosed with Molar Pregnancy at Pietersburg hospital.

1.5 Research setting

This study was conducted in Pietersburg hospital situated in Polokwane CBD at the corner of Dorp and Hospital Street, Polokwane, 0700, part of Pietersburg -Mankweng hospital complex which is a Provincial Tertiary Hospital in Limpopo province. It has got 701 beds [in patient], 33 clinical departments, 24 hours operation theatre facility and specialist outpatient units including Gynaecology and High-risk pregnancy clinic. Gynaecology ward contains 27 beds, an ultrasound room, a diagnostic procedure [colposcopy and hysteroscopy] room and a minor surgical procedure room [biopsy, manual vacuum aspiration]. The patients who present with miscarriages including molar pregnancy get admitted to the gynaecology ward via casualty for evacuation of uterus and the product of conception is sent for histological examination to finalise the diagnosis.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

In this chapter, previous studies related to prevalence of molar pregnancy/Hydatidiform mole are reviewed. This chapter is divided into three sub-sections namely: prevalence of molar pregnancy depending on geographical distribution and ethnicity; patient demographics, risk factors related to molar pregnancy; clinical features for diagnosis of molar pregnancy with histological or cytogenic classification. The articles were searched by using key word Prevalence and Molar pregnancy I used the PubMed, Google Engine search for journal articles, books as my source of literature.

2.2 Prevalence of Molar Pregnancy

Prevalence is a measure of how common a disease process is found in a specified at-risk population at a specific time point or during a specified period (Tenny. 2023). The prevalence of Molar Pregnancy varies depending on geography and ethnicity. In North America, South America, and in Europe, Molar Pregnancy develops in approximately 1 in 500–1000 pregnancies (Berkowitz. 2009*)*. The rate in Southeast Asia is 5- to 15-fold higher, approaching 1 in 120 pregnancies (Mangili. 2014*)*.

Native American women in New Mexico had a higher prevalence than other predominant ethnic groups there (Smith. 2003*)*. While in Kuala Lumpur, Malaysian, Indian, and Chinese ethnic groups all have similar prevalence and Japan has highest prevalence of 2 per 1000 pregnancies (Lurain. 2010*).* Some recent analyses suggest that the prevalence in Southeast Asia now approaches that in Europe (Mangili. 2014*).* A recent Korean study showed prevalence of HM 1.1 per 1000 pregnancy almost like those reported in western population-based study (Jin- Sung Yuk. 2019).

Data from South Africa is scarce, one South African study estimates incidence of HM at 1.2/1000 delivery, two studies from Nigeria reporting a prevalence of HM in Southeast Nigeria are 0.3 per 1000 deliveries (Biscaro. 2012).

A retrospective cohort study on prevalence of gestational trophoblastic diseases (GTD) among pregnant women was conducted in Oman between November 2007 and October 2015 on all women diagnosed with GTD at SQUH [Sultan Qaboos University Hospital], which is one of the largest tertiary centres in Oman. A total 64 women was diagnosed with GTD in that time who were included in this study and total number of deliveries during that time was 23235, the prevalence of GTD was 0.3% equivalent to one in 386 births (Riyami. 2019).

A cross-sectional study was conducted for a one-year duration from April 1, 2020, to April 1, 2021, at department of Maternity Teaching Hospital Erbil city, Kurdistan, Iraq, on prevalence of molar pregnancy among patients with incomplete miscarriage at that hospital, includes 380 patients with incomplete miscarriage included 50 patients had molar pregnancy on histology, prevalence was 13.1% and 70% of the patients were diagnosed with partial HM, the rest were CHM (Ali. 2024).

A retrospective cohort study was done in Stockholm, Sweden which was published in Feb 2018 to examine temporal trends in the prevalence of HM and post-molar gestational trophoblastic neoplasia (GTN) in Stockholm County during 1991–2010. The prevalence of HM was 2.08/1000 deliveries and 1.48/1000 viable conceptions. After stratifying into five-year intervals, the proportion of HM reported to be increased steadily over time, the prevalence increased from 1.66/1000 deliveries and 1.21/1000 viable conceptions in 1991–1995 to 2.31/1000 deliveries and 1.66/1000 viable conceptions in 2006–2010 (Joneborg. 2018).

A cross-sectional study carried out from November 2016 to February 2017 to determine the prevalence and clinical factors associated with Hydatidiform Mole among patients undergoing uterine evacuation at Mbarara Regional Referral Teaching Hospital, Uganda. The sample size was 175. Patients admitted with abortions both spontaneous and therapeutic including those suspicious for Molar pregnancies by ultrasound were included in the study. In this study the prevalence of Hydatidiform Mole was found at 6.1% among patients admitted for uterine evacuation (Mulisya. 2018).

Another cross-sectional study conducted at two hospitals namely, Bugando Medical Centre and Sekou Touré Regional Hospital in Mwanza City, Northwestern Tanzania, was on “Hydatidiform moles among patients with incomplete abortion in Mwanza City”. The study involved patients who were admitted at gynecological wards for incomplete abortion between February 2013 and April 2013.There were180 patients eligible and involved in the study. The products of conception were collected from all participants after evacuation which was analyzed using Hematoxylin and Eosin staining technique. The prevalence of HM was 12.8% which was high (Matovelo. 2015).

A cross-sectional study done in central Tanzania that included 200 women who experienced first trimester pregnancy loss from January to December 2019 at a Regional Referral Hospital aimed at determining the frequency of GTDs among women experiencing first trimester pregnancy loss and the associated patients’ characteristics, the overall frequency of GTDs was 21%, histopathological diagnosis was partial hydatidiform mole 42.9%, followed by complete hydatidiform mole 40.5% and choriocarcinoma 16.5% (Mdoe. 2022).

There was a study done in 2003 by Department of Obstetrics and Gynecology, Nelson R Mandela School of Medicine, University of Natal, Durban, South Africa. It was a retrospective audit-based study which included 112 patients with GTD treated at King Edward VIII Hospital, Durban, South Africa. Clinical records of patients were reviewed with regards to presentation, investigation, management, and outcome. The prevalence of Molar pregnancy and Choriocarcinoma was 1.2 / 1000 and 0.5 / 1000 deliveries, respectively. This is much lower than those quoted from countries such as Japan (Moodley. 2003).

2.3 Patient demographics and risk factors related to Molar Pregnancy

Beside the geography and ethnicity maternal age, previous history of Molar pregnancy are the most important recognized risk factors, and previous history of miscarriage, socioeconomic status are the other risk factors for Hydatidiform mole.

Age:

One of the main risk factors for HM are extremes of maternal age and the history of previous Mole (Altieri. 2003). The highest risk of Molar Pregnancy is in ≤15 and ≥45 years. About 411-fold risk of Hydatidiform Mole for women older than the age of 50 and a 6-fold increased risk for women younger than the age of 15 as compared with the women between ages of 25 and 29 (Sebire. 2003). A case-control study found that the risk for complete Mole was increased twofold for women >35 years and 7.5-fold for women >40 years (Berkowitz.1985).

In the study done in Oman, majority of the GTD cases were diagnosed in women aged 26 to 39 years and multiparous women constituted most of the cases and the most common risk factors were increased maternal age and multiparty (Riyami. 2019). The study in Mbarara Regional Referral Teaching Hospital, Uganda, also showed that a significant increase in risk of molar pregnancy in women above the age of 35 years and even further increase of 10-fold beyond the age of 40 years (Mulisya. 2018).

In the study done in Stockholm, Sweden, the highest prevalence was observed in women above the age of 40 compared to younger women & women of 45 years and above demonstrated prevalence of HM 1 in 17 deliveries and 1 in 43 viable conceptions (Joneborg. 2018).

Previous history of Molar Pregnancy:

Another main risk factor is the history of the previous Mole. The risk for repeat molar pregnancy after the first Mole is approximately 1 to 2 percent and recurrence rate after two molar pregnancies has been reported to range from 15 to 20 percent (Sebire. 2003). Women with a Complete Hydatidiform Mole (CHM) have a 1 in 100 and 1 in 4 risks of further CHM after one and two consecutive CHM, respectively, while women with a Partial Hydatidiform Mole (PM) have only a small increase in risk for further Molar Pregnancy (Seckl. 2015).

History of previous miscarriage:

A history of spontaneous miscarriage is a reported risk factor for molar pregnancies (both complete and partial). The risk of a molar pregnancy in those women who have a history of miscarriage increases by 2-3-fold compared to those who have no history of spontaneous abortion (Lurain. 2010).

The study conducted at department of Maternity Teaching Hospital Erbil city, Kurdistan, Iraq, found more than 50% of the patients who diagnosed with HM among the patients with miscarriages, had previous history of miscarriage (Ali. 2024). On contrast study done in Tanzania, only 18% of patients with GTD among the patients with miscarriages had previous history of miscarriage (Mdoe. 2022).

Socioeconomic condition, dietary factors, alcohol, tobacco smoking:

Low socioeconomic status might be a risk factor for developing molar pregnancy. Lower socioeconomic status in East Asia, the Middle East, the United States and Brazil all have up to a 10-fold greater rate of molar pregnancy than their more affluent counterparts (Soares. 2010).

The relationship between molar pregnancy incidence and geographic region, culture, and socioeconomic status suggests that diet and nutrition may contribute to the etiology but diet and lifestyle factors such as smoking, alcohol consumption and ß-carotene are not proven as risk factors (Altieri. 2003). The use of oral contraceptives, even after evacuation of a molar Pregnancy, does not increase the risk of developing molar pregnancy in subsequent pregnancies (Snyman. 2009).

2.4 Clinical features and diagnosis of Molar pregnancy

Most of the patients with HM are usually diagnosed at late 1st [11 to 13 weeks of gestation] or early 2nd trimester [14 to 20 weeks of gestation] owing to availability of ultrasound examination and quantitative measurement of HCG. Recently the median gestational age at diagnosis of complete mole has decreased from 12 to 9 weeks in high income countries (Makhathini. 2019).

Clinical features of Molar Pregnancy:

Vaginal bleeding during early pregnancy is the most common presentation; in case of complete Mole: uterus large for dates (25%); lower abdominal pain from large benign theca-lutein cysts (20%); vaginal passage of grape-like vesicles (10%); exaggerated pregnancy symptoms including hyperemesis (10%), hyperthyroidism (5%), and early preeclampsia (5%) (Cavaliere. 2009).

Hyperthyroidism may develop in HM mostly in CHM due to thyrotropic action of HCG. The prevalence of hyperthyroidism in GTD varies worldwide, with lower rates associated with early antenatal screening or ultrasound and early detection of GTD. A South African study in 1981 reported higher rates of hyperthyroidism in GTD, about 56% had biochemical and 33% patient had overt hyperthyroidism, most likely explained by later detection of GTD in that study (Norman.1981). A Brazilian study assessed medical records of women diagnosed with complete hydatidiform mole from 1988 to 2012. They analyzed the prevalence of biochemical hyperthyroidism and trends over time, which showed upward trend in the frequency of hyperthyroidism in women with CHM (0.69% in 1988–1992, 0.68% in 1998–2002 and 3.86% in 2008–2012) (Pereira. 2021). A US study analyzed 194 women with CHM and 172 with PHM in a one of the largest gestational trophoblastic cancer registries in the United States and found more patients with CHM develop hyperthyroidism compared to PM [16% vs 4.7%; $p<0.001$] but only 4/194 (2.1%), and 4/172 (2.3%) of patients with CHM and PHM had clinical hyperthyroidism, respectively (Sun.2016). There was an observational study in Brazilian center in 2002 to 2018 to identify possible risk factors associated with development of hyperthyroidism in patient with complete hydatidiform mole (CHM) which includes 137 patients with CHM, 69 patients (50%) had hyperthyroidism (approximately 43% subclinical, 57% overt). This study identified, uterine fundal height more than 16 weeks size or more than gestational age; ovarian theca lutein cyst more than 6 cm and HCG level >400000 IU/L at presentation were significantly associated with development of both subclinical and overt hyperthyroidism. The medium time of normalization of TSH [thyroid stimulating hormone] is 2 to 3 weeks after uterine evacuation when treatment should be discontinued (Ramos. 2022).

Approximately 90% of patients with Partial Moles are thought to have a spontaneous abortion before curettage (*Szulman.1982)*. A retrospective study done by Charles Nicolle University Hospital, Tunis, Tunisia on 90 patients who were diagnosed with molar pregnancy from January 1991 to December 2007 showed median gestational age of diagnosing HM was 13 weeks (Riadh. 2009).

In the study at SQUH in Oman, 93.3% women were diagnosed with HM before 16 weeks and rest diagnosed between 18 to 22 weeks (Riyami.2019).The study in Mbarara Regional Referral Teaching Hospital, Uganda, has shown the patient presented and underwent uterine evacuation at gestational age beyond 1st trimester significantly associated with complete HM and the odd of having HM is 6.2 times higher in patients with gestational age beyond the 1st trimester (Mulisya.2018).

Pelvic ultrasound features of Molar Pregnancy:

In the case of Complete Mole, uterine cavity filled with multiple sonolucent areas of varying size and shape (known as a Snowstorm appearance) without the presence of fetal structures. It may be associated with ovarian theca lutein cysts. Partial Mole presents as an enlarged placenta with multicystic avascular sonolucent spaces ('Swiss cheese' appearance) and a fetus can be demonstrated by ultrasound (Szulman. 1978).

Measurement of Quantitative Serum beta-HCG:

If serum quantitative beta Human Chorionic Gonadotropin [HCG] is more than 5 m IU/L, is regarded as a positive pregnancy test. In Complete Mole, the quantitative serum beta-HCG level is higher than expected as in normal pregnancy, often exceeding 100,000 IU/L. In the case of a Partial Mole, the level of beta-HCG is often within the wide range associated with normal pregnancy and the symptoms are usually less pronounced (Szulman.1982).

Histology and cytogenic classification of Hydatidiform Mole:

The gold standard for the diagnosis of a molar pregnancy is histopathological examination of the products of conception. Cytogenetic techniques, such as chromosomal banding and restriction fragment length polymorphism (RFLP) analysis of DNA, have allowed unique chromosomal patterns of Complete and Partial Molar

Pregnancies to be identified and differentiated (Halperin. 2000*)*. A study showed that ploidy is superior to morphology in discriminating between patients with a high and a low risk of GTN after a molar pregnancy. Diploid Mole has high potential for developing GTN where the triploid Moles have an exceedingly low risk of GTN (Niemann. 2006*)*

Hydatidiform Mole arises from placental trophoblastic tissue after abnormal fertilization. A Complete Hydatidiform Mole develops after either fertilization of an empty ovum [with no chromosomes] by one sperm which duplicate to form diploid [80%] or by two sperm [20%] and contains no fetal tissue and mostly diploid, 90% are 46XX, and 10% are 46XY (Wolf.1995*).* About 98% of complete moles were diploid and 2% were triploid, whereas 98% of Partial moles were triploid and 2% were diploid (Bagshawe.1990).

The Partial Mole contains foetal tissue, results from fertilization of a haploid ovum and duplication of the paternal haploid chromosomes or from di-spermy and the chromosomal complement is mostly triploid such as 69XXX or 69XXY or tetraploid (Watson.1987). Twinning with a Complete Mole and a foetus with a normal placenta has been reported. Cases of healthy infants in these circumstances have also been reported (Fishman.1998).

2.5 Conclusion

Most of the study reviews showed the prevalence of Molar pregnancy widely vary depending on geography and ethnicity, high prevalence in Asia, highest in Japan. This relationship between molar pregnancy incidence and geographic region, culture, and socioeconomic status suggests that diet and nutrition may contribute to the aetiology. Some recent analyses suggest that the prevalence in Southeast Asia now approaches that in Europe owing to improved nutrition may be responsible for a decline in incidence and improvement in outcomes in some populations There is limited evidence between developing molar pregnancy and smoking habits, alcohol consumption, socioeconomic status, and herbicide exposure.

Few small studies in Africa (Uganda and Tunisia) also reported of high prevalence of molar pregnancy among patient underwent uterine evacuation for miscarriages or suspected molar pregnancy. Most of the studies identified important risk factors for

molar pregnancy were extreme of age, risk increases with increasing age more than 35, previous history of molar pregnancy and miscarriages.

CHAPTER 3

METHODOLOGY

3.1 Introduction

This chapter describes the study design, settings, study population, inclusion and exclusion criteria, data collection and data analysis, reliability, validity, bias, and ethical considerations.

3.2 Study Design

This was a retrospective cross-sectional descriptive study. In this study, this design was used to evaluate the prevalence of confirmed molar pregnancy by histology among the patients admitted in gynecology ward with early pregnancy complications such as miscarriages, molar pregnancy in Pietersburg hospital over 12 months from 1st January to 31st December 2021. A cross-sectional study design was chosen because it analyses data collected from a sample at a specific point in time or short period of time.

3.3 Study setting

This study was conducted in Pietersburg hospital situated in Polokwane CBD at the corner of Dorp and Hospital Street, Polokwane, 0700, part of Pietersburg -Mankweng hospital complex which is a Provincial Tertiary Hospital in Limpopo province. It has got 701 beds [in patient], 33 clinical departments, 24 hours operation theatre facility and specialist outpatient units including Gynaecology and High-risk pregnancy clinic. Gynaecology ward contains 27 beds, an ultrasound room, a diagnostic procedure [colposcopy and hysteroscopy] room and a minor surgical procedure room [biopsy, manual vacuum aspiration]. The patients who presented with miscarriages including molar pregnancy got admitted to the gynaecology ward via casualty for evacuation of uterus and the product of conception was sent for histological examination to finalise the diagnosis.

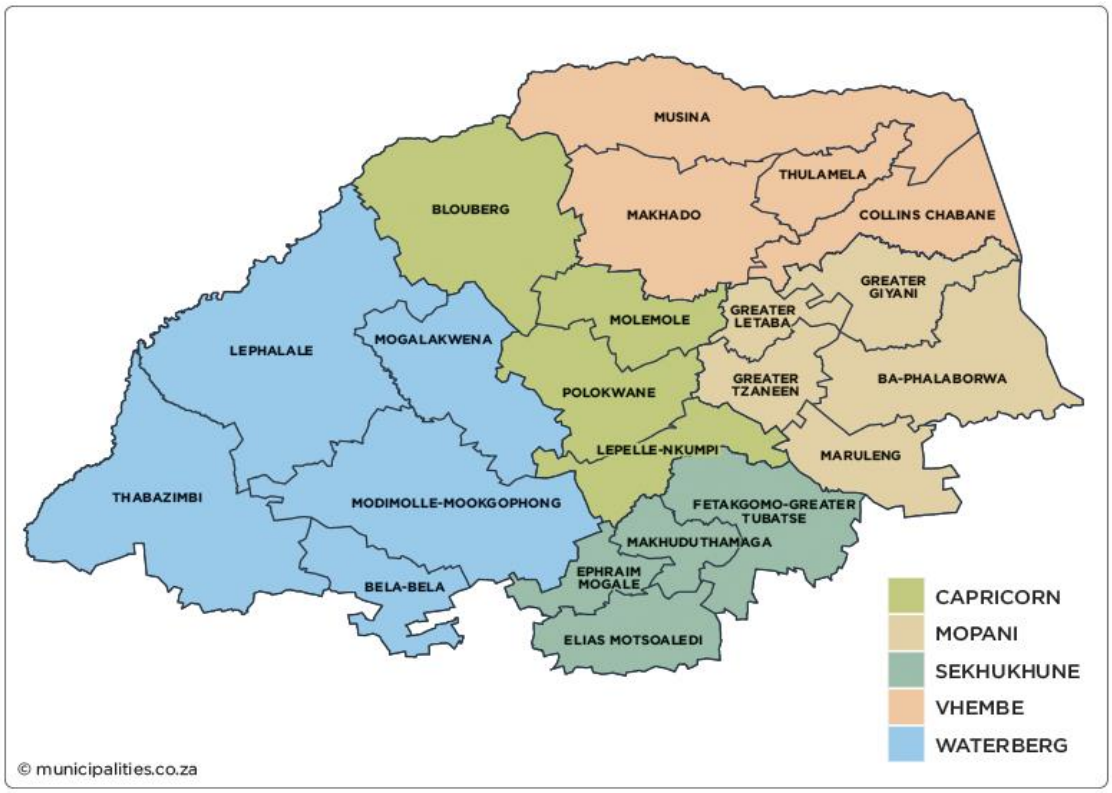

Figure 1: Map of Limpopo Province, South Africa, showing all the districts and Polokwane city, the central city of the province where Pietersburg Hospital [The part of Provincial Tertiary Hospital- Pietersburg Mankweng Hospital complex] situated.

3.4 Study population

The study population included all women who admitted in the gynecology ward with early pregnancy complications such as miscarriages including molar pregnancy during January to December of 2021. The total number of patients admitted with above mentioned diagnosis at the gynecology ward who underwent uterine evacuation during that period was 280.

3.5 Sample size and sampling method

A census sampling method was used in this study, meaning all patients with HM confirmed by histology of products of conception during study period from 01 January to 31 December 2021 was included. The sample size for objective one was 280 which included all the patient admitted in gynaecology ward with early pregnancy complications such as miscarriages or molar pregnancy during study period; and

sample for objective two was 26 that included the patients with confirmed molar pregnancy by histology. The prevalence of molar pregnancy was calculated with total number of patients admitted with early pregnancy complications such as miscarriages excluding ectopic pregnancy during that period.

3.6 Inclusion criteria

- All patients admitted in the gynaecology ward with early pregnancy complications such as miscarriages including molar pregnancy in Pietersburg hospital from 1st January to 31st December 2021 were included.

3.7 Exclusion criteria

The study excluded:

- The patients admitted in gynaecology ward with early pregnancy complication such as ectopic pregnancy during calendar year of 2021.
- The patient diagnosed with gestational trophoblastic disease other than HM such as Gestational Trophoblastic Neoplasia on histology during 2021 calendar year.

3.8 Data collection

Data was collected mainly from two separate register books (gynecology ward admission register book and Molar Pregnancy booklet) and patient's file. The gynecology ward admission register book provided the total number of admissions in the gynecology ward with miscarriage, molar pregnancy during January to December of 2021 which was cross checked by casualty admission register book. The Molar Pregnancy record booklet provided the total number of confirmed Molar pregnancy cases by histology. The patients' file provided the demographic data, history, clinical and laboratory data of the patient.

The Molar Pregnancy booklet provided patient's names, hospital number, cell phone number, date of admission and evacuation of uterus along with histology reference number and follow up date for histology review. This booklet helped to measure the number of patients confirmed molar pregnancy by histological examination.

The patients' files were collected from the patient record section and used to collect patient demographic and clinical data including histology report of products of conception.

The data was collected using structured data collection tools (**Annexure A, B, C, D**) which was prepared by researcher reviewed by peer expert panel. The data collection tools collected information on patient-related factor such as age, race, marital status, alcohol, tobacco use, substance use, urban or rural residences, employment, local or transfer from peripheral hospital, clinical data such as parity, gravidity, gestational age, contraceptive use, history of previous molar pregnancy or miscarriages, presenting features such vaginal bleeding and physical examination findings, laboratory findings such as haemoglobin level, blood group, thyroid function, level of HCG level, ultrasound examination findings, histology findings.

3.9 Data analysis

In this study data collected from patients file and gynecology register books was entered into Microsoft Excel and then exported to Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics were used to summarize the data whereby continuous variables were presented as mean and standard deviation and categorical variables were presented as frequency, percentages, and charts. The prevalence of molar pregnancy was calculated as the proportion of confirmed cases of the patient with Molar pregnancy by histology out of total admitted patients in gynecology ward with early pregnancy complications such as miscarriages including molar pregnancy in Pietersburg hospital from 1st January to 31st December 2021.

3.10 Reliability and Validity

The development of data collection tools used for the study were pretested to test the reliability and validity This study ensured reliability and validity by objectively assessing the number of patients registered in Gynecology admission book, Molar Pregnancy register booklet and compared with the patients' file information including the histopathology report of products of conception to ensure that the same results

are determined. Reliability of data capture onto the software was ensured by a statistician.

3.11 Bias

In this study information bias was avoided by correctly comparing the information from the Gynecology admission register book with casualty admission register book, theatre register book, Molar Pregnancy booklet and the patients' file information. As Pietersburg hospital is a part of Pietersburg Mankweng hospital complex which is the tertiary referral hospital for Limpopo province, some of the patients with molar pregnancy are managed at Mankweng hospital. So, the result of the study was not a true reflection of the prevalence of Molar pregnancy at this tertiary hospital complex which is an unavoidable bias of this study.

3.12 Strength and Limitations

The strength of this study included its comprehensive approach using data from gynaecology register books which was cross checked with patients' file. Since this study was restricted to information retrieved from patient's file, no re-evaluation of pathological slides was done. Thus, it could not be excluded that some women recorded with Molar pregnancy were miss-diagnosed.

Another potential weakness could be that the study was restricted to women reported with miscarriages and Molar pregnancy in the register book. It is possible that a few molar pregnancies were neither reported in the register book nor diagnosed in the pathological report.

3.13 Ethical Considerations

Permission for the study was sought from Department of health Limpopo province [The National Health Research Database]. Department of Obstetrics and Gynaecology and CEO, Pietersburg Hospital. Ethics approval was obtained from the Turfloop Research Ethics Committee (TREC). A consent waiver was requested because this is a low risk, retrospective study and it was difficult to contact all the participants.

Confidentiality, privacy, and anonymity**:**

All efforts were made to keep personal information of the patient confidentiality by using a unique numerical identifier for each patient and a separate participant log linking data collection form to the patient identifiers which was stored securely separate from data forms. The numerical number only to match the data collection questionnaire and no patient's identifiers were used in subsequent data analysis. If the study is to be published, the identity of patients will not be revealed.

CHAPTER 4

PRESENTATION AND INTERPRETATION OF THE RESULTS

4.1 Introduction

In this chapter, the results of the study are presented and interpreted. There were 280 patients admitted in the Gynaecology ward from 1st January to 31st December of year 2021 with early pregnancy complications [excluding ectopic pregnancy] such as miscarriages and molar pregnancy who underwent for uterine evacuation, out of which 26 patients were confirmed cases of molar pregnancy by histological examination of products of conception, 22 patients had complete Hydatidiform mole [CHM] and 4 patients had partial Hydatidiform mole [PHM]. The prevalence of molar pregnancy was calculated as the proportion of confirmed cases of the patients with molar pregnancy by histology out of total admitted patients in gynecology ward with early pregnancy complications such as miscarriages including molar pregnancy in Pietersburg hospital from 1st January to 31st December 2021. The prevalence of molar pregnancy was 9.28 per 100 admissions of patients with miscarriages including molar pregnancy during study period of one calendar year.

Prevalence of Molar pregnancy =

Confirmed cases of Molar pregnancy by Histological examination x100

Total number of patients admitted with early pregnancy complication such as miscarriages including Molar pregnancy in the period of January to December,2021.

$$\text{Prevalence of Molar pregnancy} = \frac{26}{280} \times 100 = 9.28\%$$

This chapter is divided into four sub-sections: (1) demographic profile of the patient (2) clinical history of the patient (3) clinical features of the patients, (4) laboratory results.

4.2 Demographic profile of the patients

The commonest age group with HM, 50% [13] were within 31 to 40 years whereas in the extreme of age bellow 20 years or more than 40 years were 12% [3] and 23% [6] respectively and patients at age of 21 to 30 consisted of 15% [4].

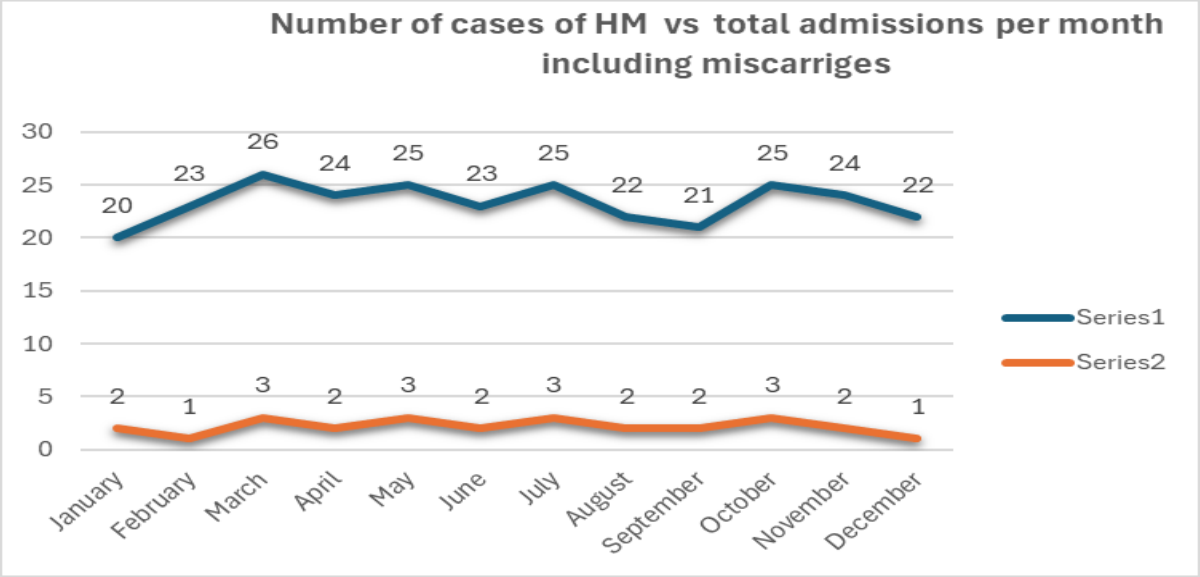

Figure-1: Series 1, showing the number of admissions with early pregnancy complications such as miscarriages including molar pregnancy in each month during calendar year, series 2, showing confirmed cases of molar pregnancy by histology in each month.

Most of the patients seen in Pietersburg hospital are African, so 88% [23] cases of HM were African and the rest, about 8% [2] were white and 4% [1] was coloured. Majority of the patient 96% [25] with HM were unemployed, only 4% [1] were employed.

Table 1: Demographic profile of patients with molar pregnancy.

Demographic profile		Frequency	Percentage
Age	13 to 20 years	3	11,5
in	21 to 30 years	4	15,4
years	31 to 40 years	13	50
	41 to 49 years	6	23,1
Race	African	23	88%
	White	2	8%
	Coloured	1	4%

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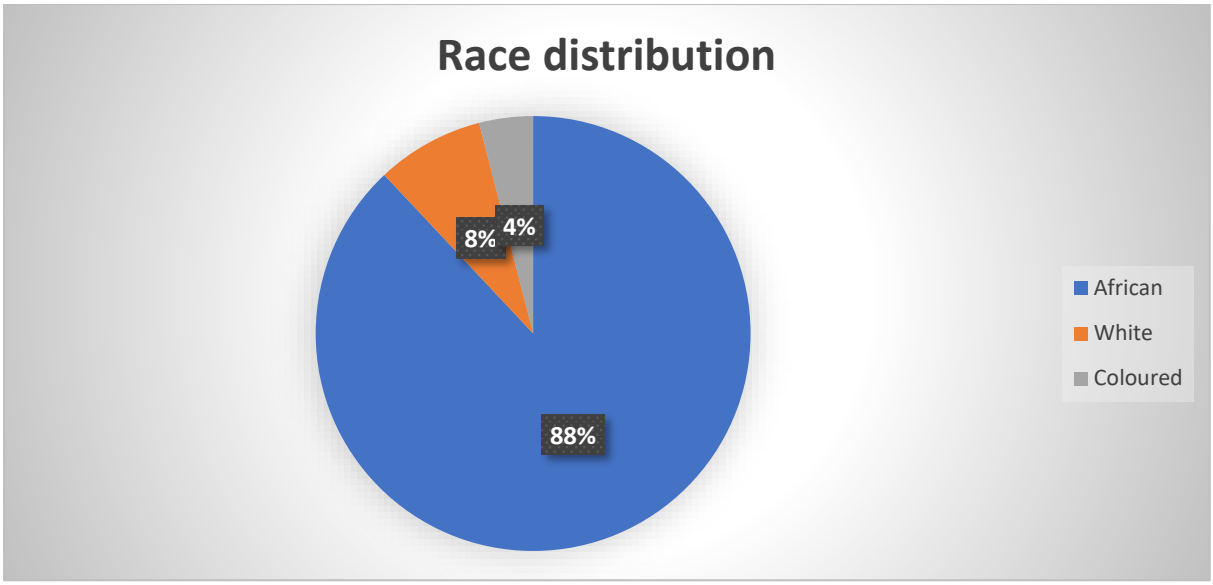

Figure no 2: Race distribution in patients with molar pregnancy.

As Pietersburg Hospital is a part of Provincial Tertiary hospital, majority 85% [22] of the cases of HM came as referral from peripheral hospital [district and regional hospital around Limpopo province] and only 15% [4] cases were local who presented at casualty as self-referral or referred by general medical practitioner around Polokwane town. For 96% [25] of the patient with HM had no history of using alcohol and tobacco where only 4% [1] were using alcohol or tobacco. No patient with HM found to be using recreational substances rather data not available for 54% [14], data for not using recreational substances was 46% [12].

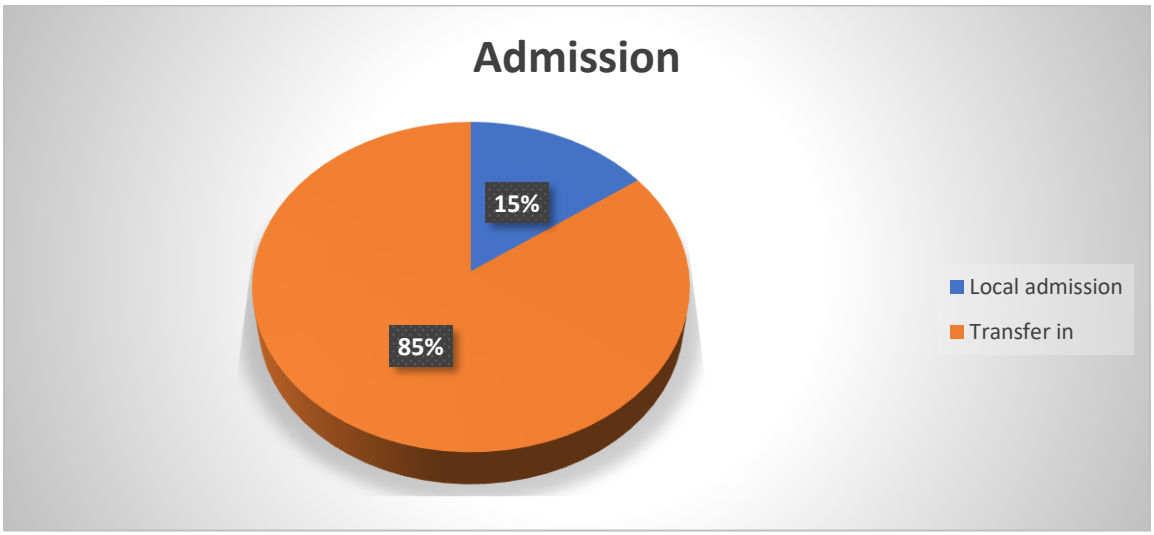

Figure no 3: Admission history of patients with molar pregnancy.

4.3 Clinical history of the patient

Approximately 12% [3] women with HM were nulliparous; 23% [6] were primipara; majority 54% [14] were multipara and another 12% [3] were grand multipara [GMP], where 12% [3] women with HM were primigravida; another 12% [3] were grand multigravida and most of the cases about 76% [20] were multigravida.

Table no 2: Parity of patient with HM.

Parity	Frequency	Percentage
Nulliparous	3	11.5%
Primipara	6	23.2%
Multipara	14	53.8%
Grand multipara	3	11.5%
Total	26	100%

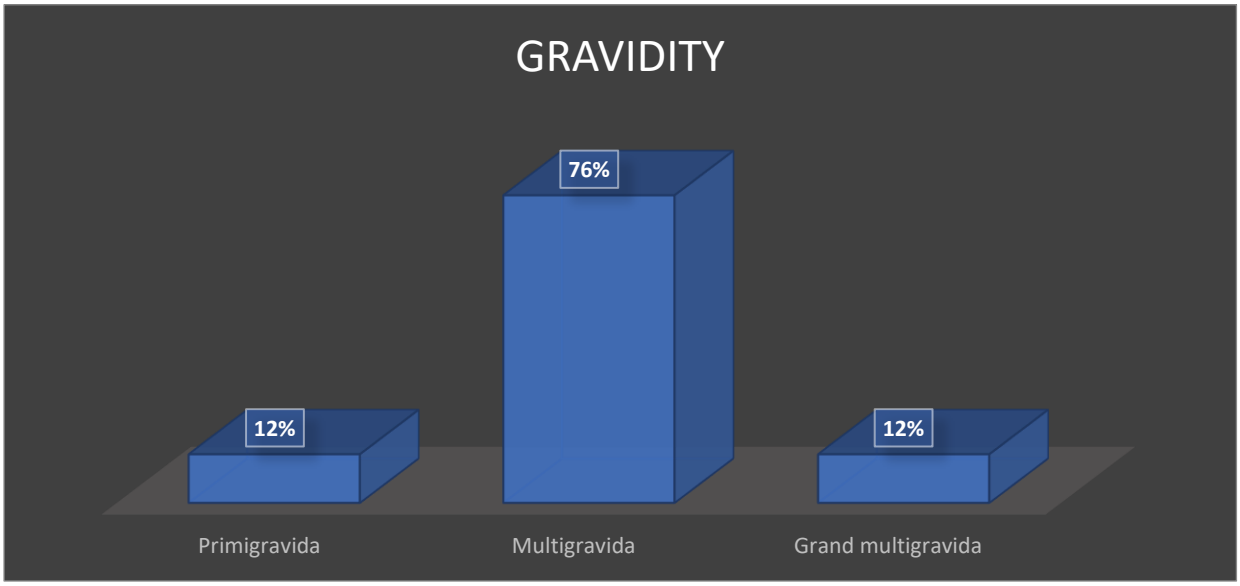

Figure no 4: Gravidity of patients with HM.

Majority of the patient 54% [14] with HM presented at gestational age of 14 to 20 weeks, where 27% [7] patient presented before 14 weeks and 19% [5] patient presented after 20 weeks of gestation.

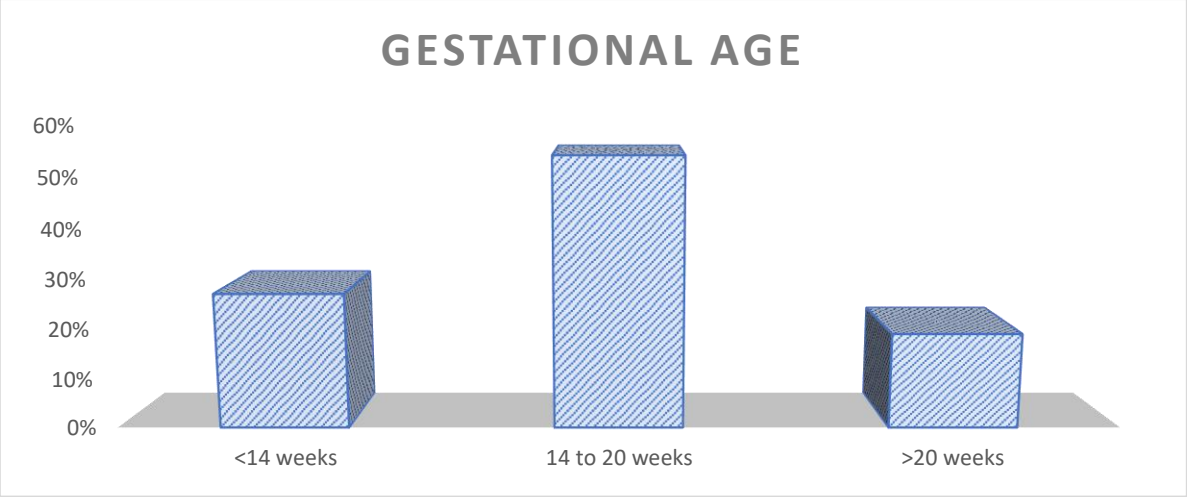

Figure no 5: Gestational age in weeks at presentation of patient with HM.

On contraceptive history, about 23% [6] patients with molar HM had a history of using oral combined contraceptive; about 42% [11] were on injectable contraceptives where around 35% [9] never used any contraceptives. Approximately 69% [18] patient wih HM had no previous history of miscarriage where 31% [8] patient had previous history of miscarriage; no patient with HM were found to have previous history of Molar pregnancy. Fifty percent [13] of patients with HM, there was no family history of molar pregnancy and for 50% [13] patient data was not available in the file.

Approximately 27% [7] patient with molar pregnancy had history of previous caesarean delivery where 73% [19] had no history of caesarean section; about 85% [22] patient with HM did not have any comorbidities where 15% [4] had comorbid conditions such as 2 patients were hypertensive, and another 2 patients had HIV.

4.4 Clinical features of the patient with HM

The most common symptom of HM is vaginal bleeding at early pregnancy. In this study 81% [21] patient presented with vaginal bleeding either heavy for short or prolonged period or spotting like bleeding and, only 4% [1] patient gave the history of passage grape like stuff along with bleeding; 15% [4] patient did not have vaginal bleeding rather diagnosed with routine ultrasound examination.

Figure no 6: Clinical features of patients with HM, series 1: frequency, series 2: percentage.

Molar pregnancy can cause abdominal pain due to rapid growing uterus and during bleeding. About 42% [11] patient complained of abdominal pain and 58% [15] did not complained of abdominal pain at presentation.

Table no 3: Type of vaginal bleeding at presentation of patients with HM.

Vaginal bleeding	Frequency	Percentage
None	4	15,4%
Spotting	7	26,9%
Short heavy	11	42,3%
Prolonged heavy	3	11,5%
Passage of grape like staff	1	3,9%
Total	26	100%

Due to very high level of beta HCG patient with HM may present with excessive nausea and vomiting that leads to dehydration, electrolyte imbalance or more than 5% weight loss. Twenty three percent [6] patient with molar pregnancy presented with hyperemesis graviderum where majority of them, 77% [20] did not have it. Molar pregnancy may cause preeclampsia [PET] such as new development of hypertension/

proteinuria. Only 4% [1] patient with HM had features of preeclampsia and 96% [25] patient did not have any feature of preeclampsia.

In this retrospective study, features of hyperthyroidism in the patient with HM were not fully described or documented in all files. Moreover, pregnancy itself is a hyperdynamic condition so symptoms may overlap with that of hyperthyroidism. However, number of files had some information regarding patients' symptoms and sign which mimic features of hyperthyroidism and same group of patients also had biochemical hyperthyroidism. But there are few patients 12% [3] who had biochemical hyperthyroidism, but no symptoms or sign documented in the files.

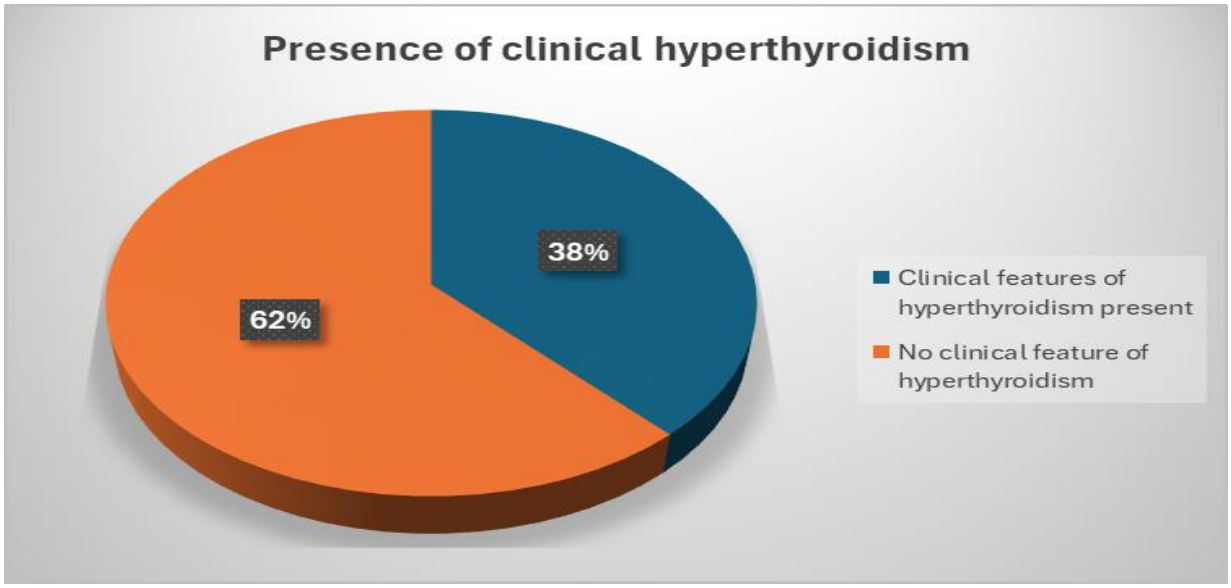

Figure no 7: Presence of clinical hyperthyroidism.

About 38% [10] patient had clinical symptoms or signs of hyperthyroidism such as palpitation 23% [6], excess sweating 12% [3], fatigue 23% [6], weight loss 8% [2], 38% [10] was tachycardic at presentation, 8% [2] patient had tremor, another 8% [2] had exophthalmos, where 62% [16] patient did not have any clinical feature of hyperthyroidism.

No patient with molar pregnancy had any respiratory symptoms like cough or breathing difficulty and no symptoms of CNS abnormality such as headache, confusion, or convulsion. Patients with molar pregnancy or GTD may present with those features only in metastatic disease or GTN.

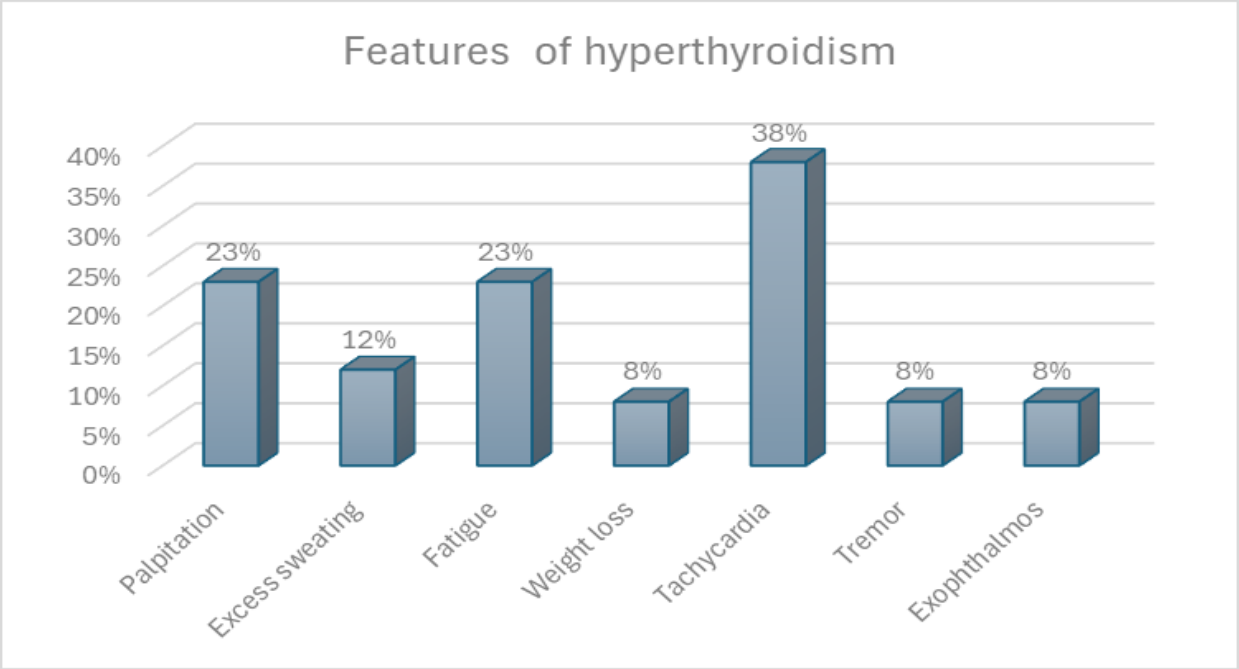

Figure no 8: Clinical features of hyperthyroidism.

Molar pregnancy usually causes growth of uterus more than gestational age specially for complete hydatidiform mole due to high level of beta HCG and excessive trophoblast proliferation. In this study 50% [13] patient with molar pregnancy had the uterine size more than gestational age; uterine size corresponded to gestational age for 38% [10] patient and, only 12% [3] patient had uterine size less than gestational age.

4.5 Laboratory results of the patients

As most the patient with HM presented with vaginal bleeding, 58% [15] of the patient with molar pregnancy had moderate anaemia with haemoglobin level of 7 to 10 gm/dl, 12% [3] of them was severely anaemic with haemoglobin of less than 7 mg/dl; 30% [8] of them had haemoglobin of more than 10gm/dl.

Forty two percent [11] patient with HM had blood group of' “0”, 31% [8] were “B”; 23% [6] were group “A” and 4% [1] was blood group “AB”. About 96% [25] patients were Rhesus positive and only 4% [1] was Rhesus negative.

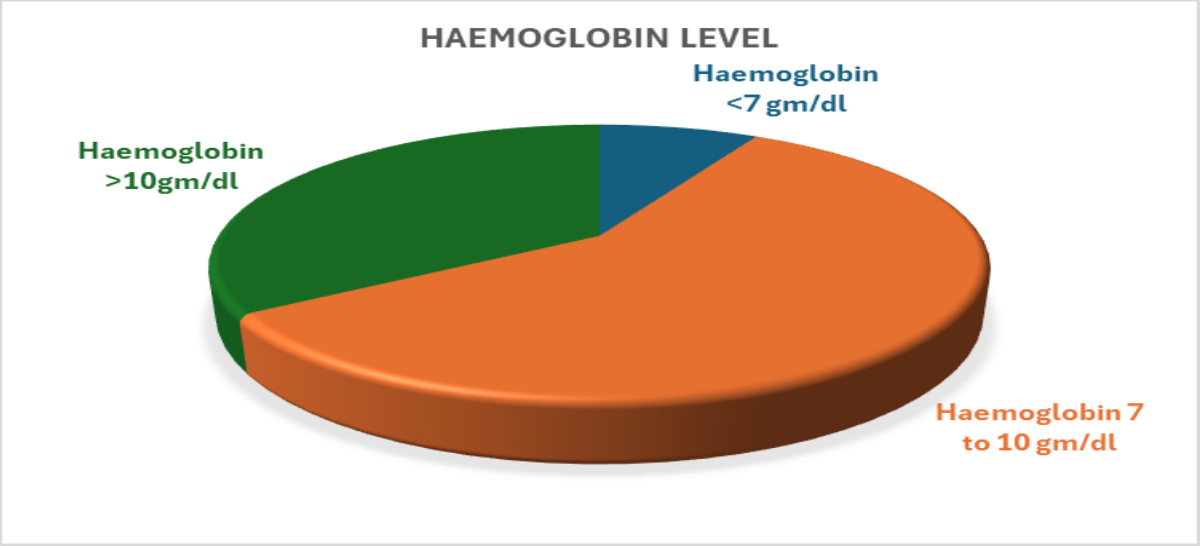

Figure no 9: Haemoglobin level in patients with HM.

In this study, 81% [21] patient with HM had serum level of beta HCG more than 100,000 mili IU/ L and 19% [5] had within 10,000 to less than 100,000 mili IU/L. Fifty percent [13] patients with HM had Biochemical hyperthyroidism with serum TSH level of less than 0.27 miu/L and 50% [13] patient had normal TSH level at 0.27 to 4.20 miu/L.

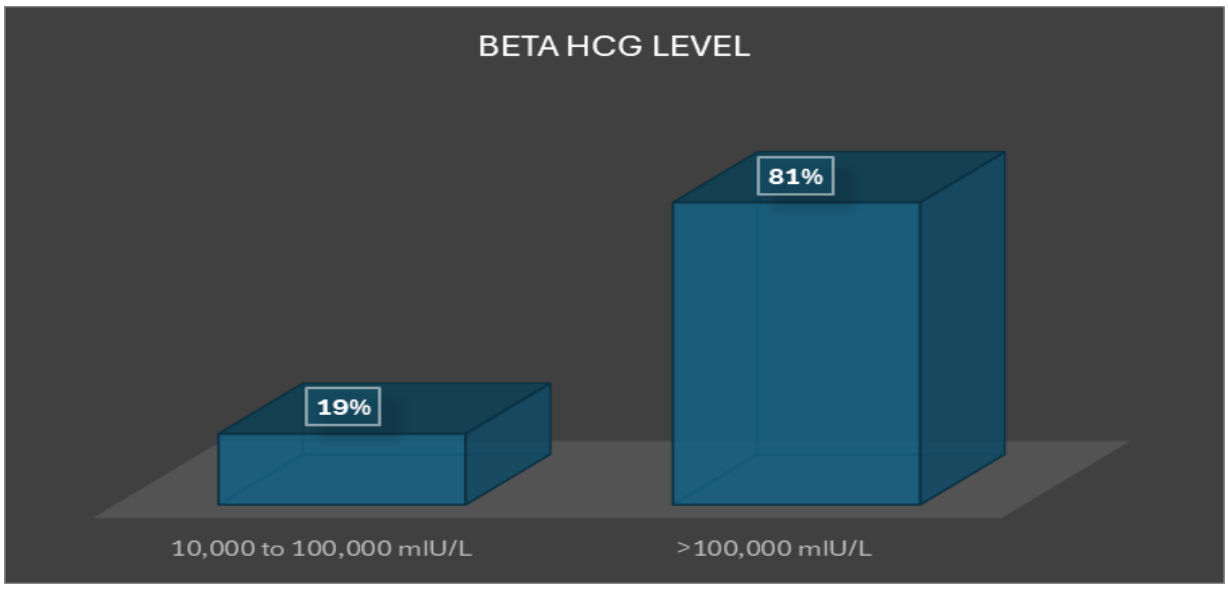

Figure no 10: Serum Beta HCG level in patients with HM.

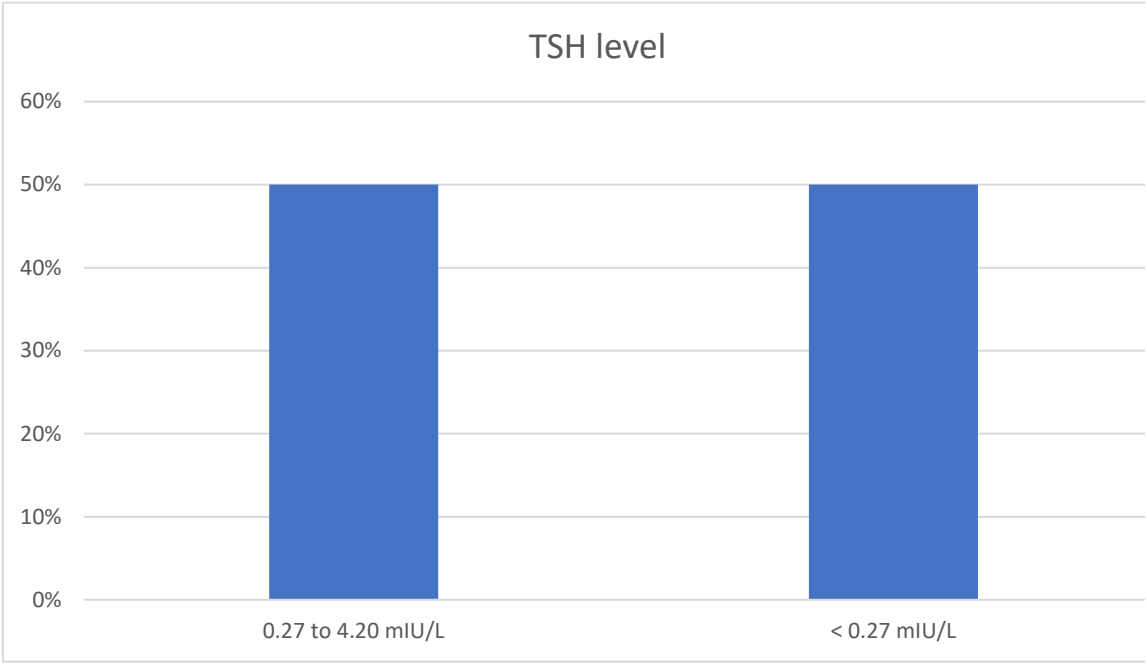

Figure no 11: Serum thyroid stimulating hormone [TSH] in patients with HM.

On ultrasound scan of pelvis, about 65% [17] patient with HM had snowstorm appearances; 31% [8] patient had cystic placental changes without foetus and 4% [1] patient had features of missed miscarriage, and 15% [4] patient also had ovarian theca lutein cyst. On chest Xray of the patients, none had any features of metastesis.

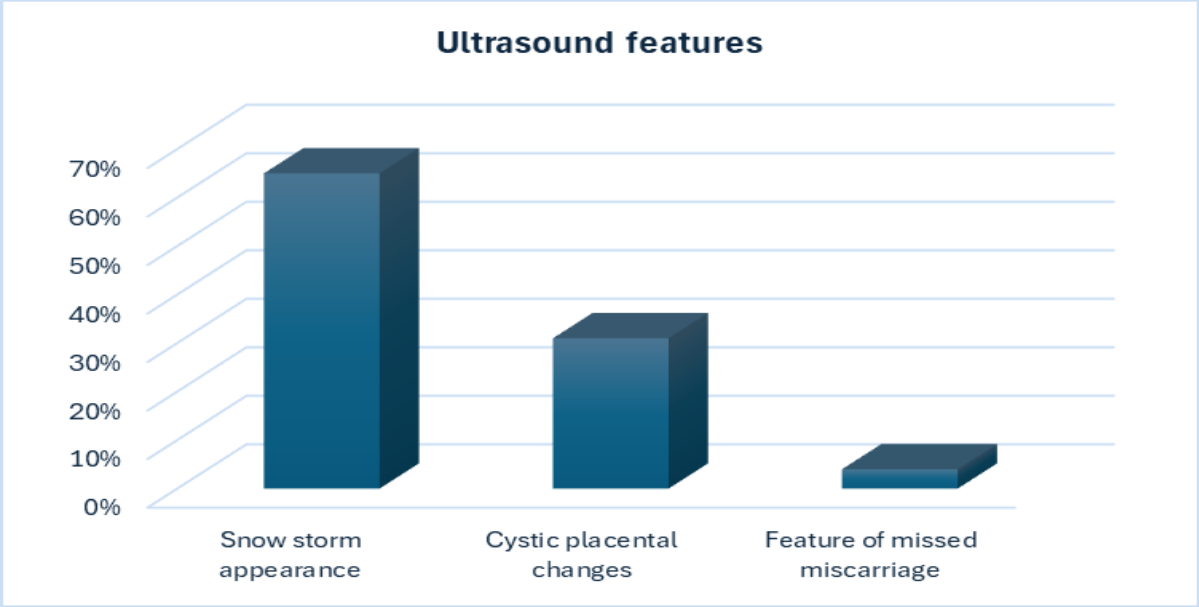

Figure no 12: Ultrasound features in patients with HM.

On histological examination of products of conception about 15% [4] patient had features of partial Hydatidiform mole [PHM] and 85% [22] patient had features of complete Hydatidiform mole [CHM]. One patient was found to have choriocarcinoma on histology who was excluded from this study.

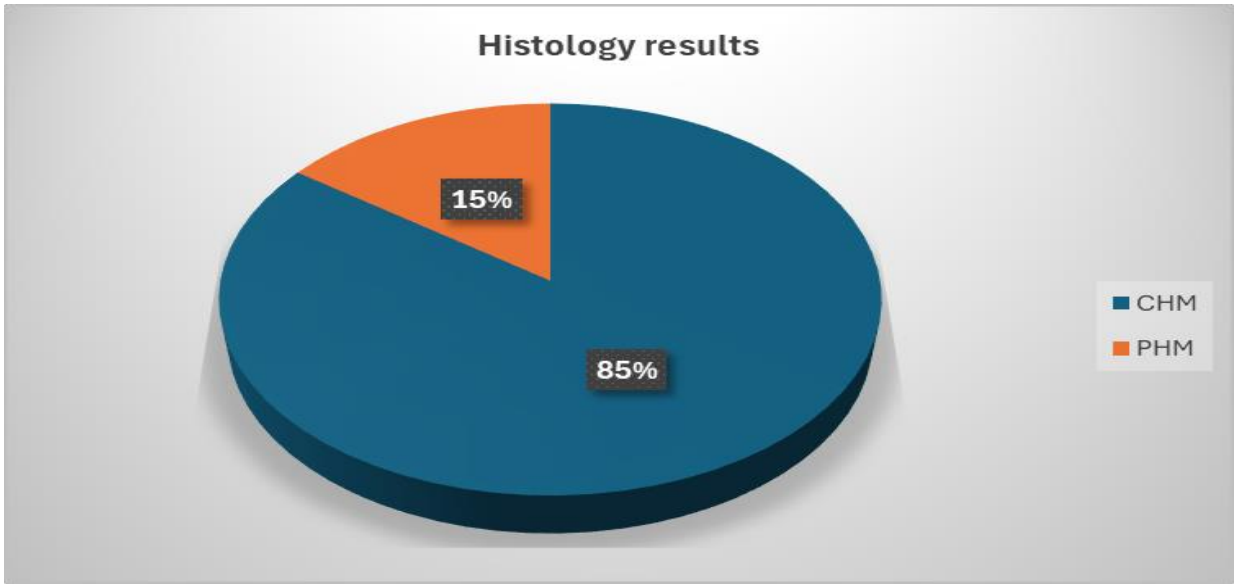

Figure no 13: Histology results of products of conception in patients with HM.

CHAPTER 5

DISCUSSION AND CONCLUSION

5.1 Introduction

In this chapter, the results of the study are discussed and compared with the literature relevant to this study. The chapter is divided into two subsections: prevalence of molar pregnancy, demographic and clinical factors of the patients diagnosed with molar pregnancy.

5.2 Prevalence of Molar pregnancy

Prevalence may be reported as a percentage or as the number of cases per 1000, 10 000 or 100 000 people. It can be “point prevalence” where the proportion of a population that has the condition at specific point in time, or “period prevalence” where the proportion of a population that has the condition at any point during a given period of interest (Tenny.2023). This study measured the period prevalence of molar pregnancy at Pietersburg hospital. It is quite challenging to determine accurate prevalence of molar pregnancy because of the rarity of the disease, lack of centralized databases and variations in control group to compare risk factors. Most countries do not have GTD registry and data are compiled mainly from hospital records and case series, that makes it difficult to determine the prevalence denominators (Makhathini. 2019). In different studies the researchers used different denominators to estimate prevalence of Molar pregnancy. In some studies Molar pregnancy prevalence was calculated per 1000 pregnancies or per 1000 deliveries, where in other studies it was calculated per 100 patients with miscarriages/abortions who underwent uterine evacuation.

This study included 26 women who were diagnosed as HM by histological examination of products of conception among 280 women who admitted in gynaecology ward during study period of one year with preliminary diagnosis of miscarriages or molar pregnancy and underwent uterine evacuation. Among 26 cases 22 were diagnosed complete Hydatidiform mole [CHM] and 4 were partial Hydatidiform mole [PHM]. There were 4 women who were preliminarily admitted as molar pregnancy but not confirmed

on histology. The prevalence of HM in this study 9.28% or 1 in every 11 patients with miscarriages and molar pregnancy admitted in gynaecology ward during the study period of one year had HM.

Comparing the prevalence of molar pregnancy/ Hydatidiform mole [HM] between this study and some studies in different countries or centres, similarity in prevalence of molar pregnancy observed where denominators were the same. The studies on the prevalence of molar pregnancy were done in different centres in Africa continent. In 2017, a cross-sectional study carried out to determine the prevalence of Hydatidiform Mole among patients undergoing uterine evacuation for abortion either spontaneous or induced including suspicious molar pregnancy by ultrasound at Mbarara Regional Referral Teaching Hospital, Uganda with a sample size of 175. The prevalence of Hydatidiform Mole was found at 6.1% among patients admitted for uterine evacuation (Mulisya. 2018). In 2013, another cross-sectional study conducted at Northwestern Tanzania, was on “Hydatidiform moles among patients with incomplete abortion in Mwanza City”. The study involved 180 patients who were admitted at gynaecology wards for incomplete abortion. The prevalence of HM was 12.8% which was high (Matovelo. 2015). The study done in central Tanzania on 2019, the overall frequency of GTD was 21% among the women with miscarriages (Mdoe. 2022). The study conducted in Erbil city in Iraq, found prevalence of HM was 13.1% among the women with incomplete miscarriage (Ali. 2024).
The studies on prevalence of molar pregnancy calculated with different denominators had also comparable results. In the retrospective audit-based study in 2003 at Durban, South Africa, the prevalence of Molar pregnancy and Choriocarcinoma was 1.2/1000 and 0.5/1000 deliveries, respectively (Moodley.2003). Two studies from Nigeria reporting a prevalence of HM in Southeast Nigeria are 0.3 per 1000 deliveries (Biscaro.2012). In a retrospective cohort study on prevalence of gestational trophoblastic diseases (GTD) among pregnant women in Oman between 2007 and 2015, the prevalence of GTD was 0.3% equivalent to one in 386 births (Riyami. 2019).

The prevalence of HM varies depending on geography and ethnicity. In America and Europe prevalence of HM 1 in 500 to 1000 pregnancy (Berkowitz. Goldstein, D P. 2009) where the rate in East Asia is 5- to 15-fold higher, approaching 1 in 120 pregnancies (Mangili. 2014). But recent Korean study showed prevalence of HM 1.1

per 1000 pregnancies which is almost like those reported in western population-based study (Jin-Sung Yuk. 2019). In the study done in Stockholm, Sweden to examine temporal trends in the prevalence of HM, the prevalence of HM was 2.08/1000 deliveries and 1.48/1000 viable conceptions. (Joneborg. 2018). This wide range of variation on prevalence of molar pregnancy in different studies might be due to different denominators and in this study, variation may be also attributed to the smaller sample size.

5.3 Demographic and clinical factors related to cases with molar pregnancy

Most HM cases in this study were diagnosed in women aged 31 to 40 years and second common age group was 41 to 49 years, contrary to the results published in other studies which observed a higher risk of molar pregnancy among women under 20 years or older than 40 years old. (Berkowitz.1985, Mulisya. 2018, Sebire.2003). Multiparous women constituted the majority (> 53%) of the cases in this study as shown multiparity is a risk factor in study done in Oman and some other studies. (Riyami.2019, Altieri.2003).

A history of spontaneous miscarriages is a reported risk factor for molar pregnancies which increases the risk of HM by 2-3-fold compared to those who have no history of spontaneous miscarriages (Lurain. 2010). In this study, out of 26 patients with HM 8 patients (31%) had previous history of miscarriages, where the spontaneous miscarriage rate varies between from 10% to 20% worldwide in general population (Cohain. 2017). The study conducted at department of Maternity Teaching Hospital Erbil city, Kurdistan, Iraq, found more than 50% of the patients who diagnosed with HM among the patients with miscarriages, had previous history of miscarriage (Ali. 2024). On the contrary, the study done in Tanzania, only 18% of patients with GTD among the patients with miscarriages had previous history of miscarriage (Mdoe. 2022). History of previous miscarriage may or may not be a risk factor for molar pregnancy.

Previous personal or family history of molar pregnancy are very important risk factors for HM as shown by different studies, but in this study no patient with HM had any personal history or family history of molar pregnancy. (Sebire. 2003, Seckl.2015). The

study also did not find any association of molar pregnancy with lifestyle factors such as smoking, alcohol consumption and contraceptive use, blood group like other published studies (Altieri. 2003, Snyman. 2009, Ali. 2024). These variations might be attributed to the small sample size, and this is a retrospective study with the probability of missing some of the information.

Most of the cases presented with vaginal bleeding during late 1st trimester or early 2nd trimester of pregnancy as also shown by different studies (Riadh. 2009, Riyami.2019); only few of them did not have any vaginal bleeding rather routine ultrasound examination showed features of molar pregnancy; only one patient had vaginal passage of grape like staff, around 42% had abdominal pain, 23% had hyperemesis graviderum.

In this study, there were 13 [50%] patients with HM had biochemical hyperthyroidism but among them about 10 [38% of total patients with HM] patients had clinical features mimic those of hyperthyroidism such as palpitation, sweating, fatigue, tachycardia, or tremor, and about 3 patients [12%] had no symptoms or sign documented in the files. The result of the study is like those of other studies discussed at literature review. Though this is a retrospective study, features of hyperthyroidism in the patients with HM were not fully described or documented in all files. Moreover, pregnancy itself is a hyperdynamic condition so symptoms might overlap with those of hyperthyroidism. Complete hydatidiform mole is usually associated with development of hyperthyroidism. In a United States study, more patients with CHM developed hyperthyroidism compared to PHM [16% vs 4.7%; $p<0.001$] (Sun.2016). A study done in South Africa, showed 56% patients with GTD had biochemical and 33% had overt or clinical hyperthyroidism [Norman. 1981]. In the study done in Brazilian centre, there were 50% of the patients with CHM had hyperthyroidism [approximately 43% subclinical and 57% overt] (Ramos. 2022).

Molar pregnancy associated subclinical/biochemical or overt/clinical hyperthyroidism is potentially a life-threatening condition if not detected and managed properly. The development of thyroid storm has been reported in CHM and PHM and of diagnostic importance is the fact that patients with short term hyperthyroidism in GTD due to trophoblastic stimulation usually do not exhibit classic features associated with Graves' disease. Some patients develop or present with clinical manifestations of

thyroid storm during admission, there are also cases where thyroid storm developed during or after surgical evacuation of the molar pregnancy likely due to the combination of high hCG levels, stress from the surgical procedure and hypovolemic state from blood loss. This emphasizes the importance of pre-operative evaluation for hyperthyroidism and careful anesthetic considerations. The treatment of HM associated hyperthyroidism with beta blockers and antithyroid drugs before uterine evacuation or surgical treatment is critical to prevent thyroid storm. Thyrotoxicosis resolves rapidly with mole evacuation (Pereira. 2021).

The most of patients [14 patients, 54%] presented with symptoms of HM before 20 weeks of gestation in this study where other published studies also showed similar results. (Cavaliere. 2009, Riyami.2019).Regarding the sonographic findings, 65% of molar pregnancy cases showed the typical snowstorm appearance of CHM picture on ultrasound. Furthermore, the false negative diagnosis of missed miscarriage was reported by ultrasound in 4% cases. The typical appearance of a PHM on ultrasound (cystic placental changes with or without foetus or intrauterine gestational sac) was reported in 31% of cases. These ultrasound results highlight the importance of proper clinical assessment, looking into βhCG levels and the final histological results to reach the correct diagnosis and make the necessary follow-up. Ovarian luteal cysts are usually associated with CHMs due to the high levels βhCG. These cysts were seen in 4 [15%] cases of CHM in this study.

Regarding laboratory findings about >80% HM cases had very high level of βhCG more than 100,000 mIU/ml, compared to 19% had less than 100,000 mIU/ml. In the case of a Partial Mole, the level of beta-HCG is often within the wide range associated with normal pregnancy (Szulman.1982). as most of the patients presented with vaginal bleeding, more than 57% had moderate anemia with hemoglobin of 7 to 10 gm/dl, where 7% had severe form of anemia with hemoglobin level of less than 7mg/dl, and both groups received blood transfusion preoperatively, intraoperative, or postoperatively; 34% cases admitted with hemoglobin level of more than 10mg/dl. No one had any features of metastasis in the lung on chest Xray.

All the patients admitted with either provisional diagnosis of molar pregnancy or miscarriages underwent uterine evacuation in theatre. A total of 26 patients were found

to have Hydatidiform mole on histological examination of products of conception; among them 22 patients [85%] had complete Hydatidiform mole [CHM] and 4 patients [15%] had partial Hydatidiform mole [PHM]. Besides that, one patient was found to have choriocarcinoma, a form of gestational trophoblastic neoplasia, who was excluded from this study. This result differs from those studies discussed in the literature review where most of the patients were diagnosed with PHM among patients with miscarriages. The study conducted at department of Maternity Teaching Hospital Erbil city, Kurdistan, Iraq, found 70% of the patients with HM were partial HM, the rest were CHM (Ali. 2024). The cross-sectional study done in central Tanzania on 2019 found, the histopathological diagnosis of partial hydatidiform mole was 42.9%, followed by complete hydatidiform mole 40.5% and choriocarcinoma 16.5% (Mdoe, 2022).

The Royal College of Obstetricians and Gynecologists recommends that tissue obtained while managing spontaneous miscarriage should be sent for histology to confirm pregnancy and to exclude missed ectopic pregnancy and unsuspected gestational trophoblastic disease which is expensive and not practical for low-income countries. The measurement of the urine or serum human chorionic gonadotropin (hCG) levels between 3 to 4 weeks after miscarriages can be recommended to screen for possible GTD and institute early interventions as necessary which would be more practical and cost-effective (Makhathini.2019).

5.4 Limitation of the Study

My study had several possible limitations:

- Particularly use of a single center
- Small sample size
- The retrospective nature of the study, which may have contributed to missing data.

5.5 Conclusion

The prevalence of Hydatidiform mole (HM) varies significantly based on geography

and ethnicity. The statistics discussed in this study indicate that the prevalence of HM varies widely. The denominator used in different studies may have contributed to this difference. Therefore, obtaining an accurate prevalence of molar pregnancy may be challenging. Despite some limitations, this study found that the prevalence of HM was 9.28% or 1 in every 11 patients admitted to the Gynecology ward with miscarriages and molar pregnancy during the one-year study period. It is possible that we missed some cases where patients presented with spontaneous miscarriages, histological examination of products of conception was not performed, and patients were not followed up. These patients may later present with gestational trophoblastic neoplasia complicated with metastatic disease. Proper and timely treatment of gestational trophoblastic disease leads to a high cure rate, but if left untreated, it can even cause death. Therefore, it is paramount important that all patients who present with spontaneous miscarriages must be followed up at least once after six weeks of treatment at the Gynecology clinic for any persistent clinical symptoms, bedside ultrasound examination of the uterus, and, in suspected cases, measurement of quantitative beta HCG. A dedicated GTD clinic where patients with HM or other types of gestational trophoblastic disease can be properly followed up is essential. If a patient misses an appointment, they can be contacted, counselled, and put under surveillance and treatment, which will aid in preventing the progression of GTD to an advanced stage and death from this condition.

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Data collection tools:

Annexure A: Demographic data

“Molar Pregnancy in Pietersburg hospital, Limpopo Province, South Africa”.

Date: ____/____/____

patient no:

Age: 13 to 20 □ 21 to 30 □ 31 to 40 □ 41 to 49 □ **Race**: Black □ White □ Coloured □ Asian □
Alcohol use: Yes □ No □ Data not available □ **If Yes:** Social Drinker □ Over the weekends only □ > twice a week □ Daily □
Tobacco smoking: Yes □ No □ Data not available □ **Other recreational Substance use**: Yes □ No □ Data not available □
Admission: local □ Transfer from other hospital □

Annexure B: Clinical history data

"Molar Pregnancy in Pietersburg hospital, Limpopo Province, South Africa"

Date: ____/____/____

Patient no:

Parity: Nullipara □ Primipara □ Multipara □ Grand multipara □

Gravidity: 1 □ 2 □ 3 □ 4 or more □

Gestational age: Less than 14 wks □ 14 to 20 wks □ More than 20 wks □

Contraceptive history: OCP □ Injection□ Norplant □ IUD □ Nil □

Previous Miscarriage: Nil □ 1 □ 2 □ 3 or more □

Annexure C: Clinical presentation data

"Molar Pregnancy in Pietersburg hospital, Polokwane, Limpopo Province, South Africa"

Date: ____/____/____

Patient no:

P/V bleeding:

None □ Spotting □ Short-Heavy □ Prolong-heavy □ P/V passage of grape like stuff □

Presence of Hyperemesis graviderum: Yes □ No □

Presence of lower abdominal pain or heaviness: Yes □ No □

Early onset of pre-eclampsia: Yes □ No □

Clinical feature of hyperthyroidism: Yes □ No □

Presence of respiratory sign and symptoms: Yes □ No □

Presence of CNS sign and symptoms: Yes □ No □

Uterine size: Correspond to gestational age □ More than gestational age □

Less than gestational age □

Annexure D: Laboratory data

"Molar Pregnancy in Pietersburg hospital, Limpopo Province, South Africa."

Date: ____/____/____ Patient no:

Haemoglobin: Less than 7mg/dl □ 7 to 10 mg/dl □ more than 10 mg/dl □ **Blood group**: O □ A □ B □ AB □ Not available □ **Rhesus:** Positive □ Negative □ Not available □
Quantitative Beta HCG: <1000 mIU/ml □ 1000 to < 10,000 mIU/ml □ 10,000 to < 100,000 mIU/ml □ > 100,000 mIU/ml □ **TSH**: 0.27 to 4.20 mIU/L □ < 0.27 mIU/L □ > 4.20 mIU/L □ **Ultrasound findings**: Snowstorm appearance: Present □ absent □ Cystic placental changes: with foetus □ without foetus □ Features of missed miscarriage □ Theca lutein cysts: present □ absent □
CXR: Feature of metastasis present □ Feature of metastasis absent □
Histology findings: Complete mole □ Incomplete mole □

Invasive mole □	Choriocarcinoma □
Placental site tumour □	Epithelioid trophoblastic tumour □

ETHICAL CLEARANCE LETTER

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TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: 22 May 2023

PROJECT NUMBER: TREC/137/2023: PG

PROJECT:

Title:	Prevalence of Molar Pregnancy in Pietersburg Hospital, Limpopo Province, South Africa.
Researcher:	M Khan
Supervisor:	Dr. D Muavha
Co-Supervisor/s:	N/A
School:	Medicine
Degree:	Masters in Obstetrics & Gynaecology

PROF D MAPOSA
CHAIRPERSON: TURFLOOP RESEARCH ETHICS COMMITTEE

The Turfloop Research Ethics Committee (TREC) is registered with the National Health Research Ethics Council, Registration Number: **REC-0310111-031**

Note:

i) **This Ethics Clearance Certificate will be valid for one (1) year, as from the abovementioned date. Application for annual renewal (or annual review) need to be received by TREC one month before lapse of this period.**

ii) **Should any departure be contemplated from the research procedure as approved, the researcher(s) must re-submit the protocol to the committee, together with the Application for Amendment form.**

iii) **PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES.**

Finding solutions for Africa

PROVINCIAL RESEARCH CLEARANCE LETTER

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF
HEALTH

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Enquires : Legodi P
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Maliha Khan

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below;

Prevalence of Molar Pregnancy in Pietersburg Hospital, Limpopo Province, South Africa

1. Permission to conduct research study as per your research proposal is hereby Granted.
2. Kindly note the following:
   a. Present this letter of permission to the Office of Clinical Executive Director a week before the study is conducted.
   b. This permission is **ONLY for Pietersburg Hospital**.
   c. In the course of your study, there should be no action that disrupts the routine services or incur any cost on the Department.
   d. After completion of study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   e. The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   f. **The approval is only valid for a 1-year period.**
   g. If the proposal has been amended, a new approval should be sought from the Department of Health
   h. Kindly note that, the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated.

12/9/2023

Head of Department **Date**

pp

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