THE PREVALENCE OF HYDRONEPHROSIS ON ULTRASOUND IMAGING IN WOMEN WITH CERVICAL CANCER IN MANKWENG HOSPITAL, LIMPOPO PROVINCE

by

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DEDICATION

To God, the Father, the Son and the Holy Spirit, without you I am nothing.

I dedicate this mini-dissertation to my husband Nkhensane Hubert Peter Khosa, my blessing from God: Thank you for the love, patience, encouragement and support you afforded me during this milestone in my career.

To my son Tinyiko Khosa, my gift from God: My constant reminder to keep on working harder.

To my uncle Jacob Motau: You saw my dreams before I knew I could dream and made it possible for me to achieve them, for that I will eternally be grateful.

To my mother Rebecca Sesi Motau and grandmother Lenah Motau: thank you for the abundant love you poured into me while bringing me up. It blossoms within me.

To my father Bafana Shadrack Gwebu: thanks for teaching me to know who I am and what I am capable of. Gwebu, Mthembu, Mbulazi omnyama ondlela zimhlophe, wena oluhlata njengencoshane.

To my friend Hlayisani Vinas Mamorobela: thank you for being a true friend and holding my hand through this journey.

DECLARATION

I declare that **THE PREVALENCE OF HYDRONEPHROSIS ON ULTRASOUND IMAGING IN WOMEN WITH CERVICAL CANCER IN MANKWENG HOSPITAL, LIMPOPO PROVINCE** hereby submitted to the University of Limpopo, for the degree of Master of Medicine in Diagnostic Radiology 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 all material contained herein has been duly acknowledged.

Khosa RJ (Dr) Date: 2024

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ABSTRACT

Introduction

Cervical cancer is the leading cause of cancer mortality in females particularly in sub-Saharan Africa and the fourth most frequently diagnosed malignancy globally. In 2020 cervical cancer was responsible for 5870 deaths in South Africa. Hydronephrosis is a frequent urological complication of advanced cancer of the cervix, with a prevalence of between 21.2% and 43.7%. The aim of the study was to evaluate the prevalence of hydronephrosis in women with cervical cancer diagnosed through trans-abdominal ultrasound at Mankweng Tertiary Hospital, Limpopo, South Africa.

Methods

A retrospective record-based analysis was conducted in the Radiology Department of Mankweng Hospital. Patients with histologically diagnosed cervical cancer who underwent trans-abdominal staging ultrasound between 01 July 2019 and 31 December 2019 were included. Data on patient age, parity, source of income, area of residence, size of the cervical lesion and the ultrasound imaging findings were extracted. Data was analysed using STATA v15. Descriptive statistics such as frequency and percentages were used to summarise all variables. Association between hydronephrosis and independent variables was evaluated using the Fisher's exact score. Statistical significance was set at p-value <0.05.

Results

Two hundred patient records were evaluated. The patients' age ranged from 27 to 89 years with the majority (68.4%, n=136) of the women aged between 31 - 60 years, and 28.5% (n=57) being older than 60 years. The majority of the women presented with a large tumour of >4cm (72.5%, n=143). Eighty-five patients had hydronephrosis (prevalence rate =42.5%), which was either bilateral (68.2%), or unilateral (31.8%).

Tumour size was strongly associated with the occurrence of hydronephrosis. Other ultrasound findings were urinary bladder wall infiltration (13%, n=26), liver metastasis (3%, n=6), para-aortic lymph nodes involvement (1%, 2), and vesico-vaginal fistula (0.5%, n=1).

Conclusion

Hydronephrosis was the most frequent urological complication in advanced cancer of the cervix on ultrasound imaging, and was associated with a tumour size of >4cm.

KEYWORDS:

Prevalence, cervical cancer, hydronephrosis, ultrasound

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DEFINITION OF KEY CONCEPTS

Cervical cancer – Cancer of the uterine cervix is a disease in which malignant cells (cancer cells) form in the tissue of the cervix (National Cancer Institute, 2020). In this study, cervical cancer means the disease in which cancer started primarily in the cervix.

Hydronephrosis – Hydronephrosis is defined as blockage of the renal collecting system resulting in the distension of the renal pelvis and renal calyces (Patel, Foster, Kumar, Grudem, Longenbach, Bakkum-Gamez, Haddock, Dowdy, and Jatoi, 2015). In this study, hydronephrosis is the blockage of the renal collecting system by the infiltrating tumour or extrinsic compression by the lymph node resulting in dilatation of the renal pelvis and renal calyces.

Low-middle income countries – Low-middle income countries are countries defined as having gross national income per capita between $1,046 and $4,095 (World Bank, 2021). In this study, South Africa is an upper-middle income country as its national income per capita is $14,340.

Prevalence – Prevalence is the total number of people in a particular population at a given time who have a particular disease (Bruni, Alberto, Serrano, Mena, Gómez, Muñoz, Bosch, and de Sanjosé, 2019)**.** In this study, it is the number of hydronephrosis cases in women with cervical cancer seen in Mankweng Hospital from 01 July 2019 to 31 December 2019.

Ultrasound – Ultrasound is an imaging modality that uses high-frequency sound waves to visualise and differentiate tissues. (Morgan, Weerakkay, Tatco, Sharma, Bell, Kobbani, and Rasuli, 2020). In this study, ultrasound is the imaging modality used to image the kidneys to assess hydronephrosis.

LIST OF ABBREVIATIONS

CT	Computed Tomography
eGFR	Estimated Glomerular Filtration Rate
FDG PET/CT	Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography/ Computed Tomography
FIGO	International Federation of Gynecology and Obstetrics
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
IVP	Intravenous Pyelogram
LMIC	Low- and Middle-Income Countries
MRI	Magnetic Resonance Imaging
OS	Overall Survival
PFS	Progression-Free Survival
TAH	Total Abdominal Hysterectomy
TREC	Turfloop Research and Ethics Committee
USA	United States of America

CHAPTER ONE: INTRODUCTION AND BACKGROUND

1.1 Introduction

Cancer of the uterine cervix is the leading cause of cancer deaths in Southern African women (Sung, Ferlay, Siegel, Laversanne, Soerjomataram, Jemal, Bray 2021). An estimated 604 000 cases and 342 000 deaths worldwide were reported in 2020, with the highest incidence and mortality occurring in sub-Saharan Africa (Sung et al 2021). Southern Africa in particular, had an age-standardised incidence rate of 36.4/100 000 with an age-standardised mortality rate of 20.6/100 000 (Sung et al 2021). In 2020, there were 10 702 new cases of cervical cancer diagnosed in South Africa, which represented 18.7% of all cancer cases in women diagnosed in that year (Sung et al 2021). Cervical cancer was responsible for 5 870 deaths in 2020, and it is the leading cause of female cancer deaths in South Africa (Sung et al 2021). In Mankweng Hospital, patients diagnosed with cancer of the cervix are managed by the gynaecology clinic. The clinic offered services to 1 249 women with cancer of the cervix in 2019. Of these women, 37% were new cases of cervical cancer.

Cervical cancer is a malignancy associated with poor socio-economic status. The majority of women in Low Middle-Income Countries (LMIC) who are diagnosed with cervical cancer present in advanced stages. There are multiple reasons stated in literature associated with late presentation. According to Mlange, Matovelo, Rambau and Kidenya (2016), poverty, poor access to healthcare facilities, attending alternative health practitioners, lack of knowledge of cervical cancer by women, and lack of personal initiative to attend healthcare facilities, are some of the reasons why women only present with advanced cervical cancer. Advanced stage disease presentation is associated with complications of cervical cancer, poor prognosis and high mortality.

Globally, the staging of cervical cancer is guided by latest research and new technologies, and is based on knowledge, skills and resources available (Bhatla and Denny 2019).

Cervical cancer is staged through the use of clinical assessment, imaging modalities and pathology assessment (Bhatla, Berek, Fredes, Denny, Grenman, Karunarashe, Kehoe, Konishi, Olawaiye and Sankaranarayanan 2019). Due to scarce resources in LMIC, there is limited use of imaging modalities and pathological assessment for staging of cervical cancer (Bhatla et al 2019). The 2018 International Federation of Gynecology and Obstetrics **(**FIGO) (Annexure 1) revised guidelines recommend the use of clinical staging irrespective of its limitations when assessing the parametrial involvement and lymph node assessment, as 85% of cervical cancers occur in LMIC where there are limited modern imaging resources (Bhatla and Denny 2019). The fundamental role of imaging is guidance and planning of the treatment of cervical cancer and for predicting the prognosis. Imaging also addresses the inaccuracies of clinical staging (Bhatla et al 2019).

According to the 2018 revised FIGO staging of cervical cancer, stage IIIB is defined as a tumour that extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidneys (Bhatla et al 2019). Hydronephrosis in cervical cancer can be caused by malignant tumor infiltration of the ureters or extrinsic compression of the ureters by enlarged lymph nodes or pelvic brim scarring (Patel et al 2015). It can be unilateral or bilateral and can result in renal insufficiency. Renal insufficiency in hydronephrosis occurs as a result of renal parenchymal damage due to an increase in pressure in the urinary system. Raised serum urea and creatinine levels are approximately 4 times more likely to occur in women with hydronephrosis (Atuhairwe et al 2011). In a study by Mlange et al (2016), 21.2% of women with cervical cancer had complications from hydronephrosis. The incidence of hydronephrosis in women with cervical cancer in Lagos, Nigeria increased annually between 2010 and 2012 (Sowunmi, Ajekigbe, Alabi, Popoola, Fatiregun and Akinyanju 2015). Hydronephrosis is associated with reduced survival rate, regardless of its laterality, and is not always associated with pelvic wall involvement (Goklu, Seckin, Togrul, Goklu, Tahaoglu, Oz and Ertas 2015). In a Ugandan study, Mcardle and Kigula-Mugambe (2007) established that hydronephrosis was one of the most common exclusion criteria for Cisplatin chemotherapy. Trans-abdominal ultrasound has high sensitivity in the detection of hydronephrosis and tumour volume in cervical cancer patients (Atuhairwe, Busingye, Sekikubo, Nakimuli and Mutyaba 2011).

1.2 Research problem

1.2.1 Source and background of the problem

Despite cervical cancer being a preventable malignancy, a significant number of women in LMIC are diagnosed at an advanced stage of the disease with hydronephrosis as a common complication. The incidence of hydronephrosis in cervical cancer ranges between 14%-44.2% (Pradhan, Duan, Katsoulakis, Salame, Lee and Abulafia 2011). Hydronephrosis occurs in advanced cancer of the cervix, disease recurrence, or in progression of the malignant tumour after treatment. Rose, Ali, Whitney, Lanciano and Stehma (2010) concluded that hydronephrosis is associated with poor progression free survival (PFS) and overall survival (OS) in women with stage IIIB disease. Women with cervical cancer complicated by hydronephrosis also had a markedly shortened median time to death in comparison to those without hydronephrosis (Pradhan et al 2011).

The aim of the current study is to determine the prevalence of hydronephrosis and to describe ultrasound findings in women with cervical cancer at Mankweng Hospital. The knowledge of hydronephrosis in women presenting with advanced cervical cancer will assist in identifying women who are at greater risk of a poor outcome and enable fast tracking referral of these women to hospitals with oncology services. The knowledge will also assist in the needs analysis for appropriate allocation of resources for better management of women with cervical cancer and those complicated by hydronephrosis. This is aligned with the goal of the South African National Department of Health Cervical Cancer Treatment and Control Policy which aims to decrease the age-standardised mortality rate of cervical cancer from 18/100 000 women in 2017 to 15/100 000 by 2022 (National Department of Health South Africa 2017).

According to the researcher's knowledge, hydronephrosis among women with cervical cancer in Limpopo province has not been well documented or studied. There is therefore

a need for this problem to be defined in our setting. Not only will the study give information regarding the prevalence of the problem, but it will also assist in defining the characteristics of women who present with hydronephrosis. This will in turn add to the information available to the attending doctors to better manage and care for the affected women. They will also be better enabled to stratify and fast-track women with hydronephrosis who are at risk of developing complications due to advanced cervical cancer.

It is for the above-mentioned reasons that the researcher conducted this study, to evaluate and alleviate the problem of hydronephrosis in women with cervical cancer in Mankweng Hospital.

1.2.2 Problem statement

Hydronephrosis is indicative of advanced disease in women with cervical cancer, and may present with varying stages of renal impairment. Hydronephrosis as a complication has a poor prognostic outcome with high morbidity and mortality (Rose et al 2010). Understanding the prevalence of hydronephrosis in women with cervical cancer at first presentation in our setting will give insight into the extent of the problem in patients only coming to the hospital and being diagnosed at a late stage. This information is critical in formulating guidelines for provision of services to cater for patients with advanced disease and also to develop measures to sensitise and educate communities on the importance of early diagnosis and treatment of cervical cancer.

1.2.3 Hypothesis

Hydronephrosis in women with cervical cancer at Mankweng Hospital is not a common finding on ultrasound imaging.

1.2.4 Rational and motivation for research

Research has shown that there is a high incidence of cervical cancer in sub-Saharan Africa (Sung et al 2021). Many women with cervical cancer present with advanced disease and related complications (Mlange et al 2016). Hydronephrosis as a complication of cervical cancer has a negative effect on the 5-year overall survival rates of women with cervical cancer (Pergialiotis, Bellos, Thomakos, Haidopoulos, Perrea, Kontzoglou, Daskalakis and Rodolakis, 2019). As a doctor working in a hospital and noting the prevalence of complicated, advanced stage cervical cancer, I was motivated to research the prevalence of the complicating hydronephrosis in order to improve the healthcare services we provide to our community and to help reduce the number of unnecessary deaths. While established in a South African context, the research results can then be used to improve treatment in LMIC countries particularly badly affected across the rest of the African continent.

1.3 Study purpose

1.3.1 Aim

To evaluate the extent of hydronephrosis and its associated factors in women with cervical cancer at Mankweng Hospital, using ultrasound imaging.

1.3.2 Objectives

- To evaluate the prevalence of hydronephrosis in women with cervical cancer in Mankweng Hospital.
- To describe the findings of ultrasound imaging in women with cervical cancer at Mankweng Hospital.

1.4 Research questions

- What proportion of women with cervical cancer present with hydronephrosis on ultrasound imaging in Mankweng Hospital?
- What are the findings on ultrasound imaging in women with cervical cancer at Mankweng Hospital?

1.5 Research methods

1.5.1 Research design

A quantitative, retrospective descriptive review of clinical records of women with cervical cancer was conducted in Mankweng Hospital.

1.5.2 Sampling

All clinical records of women who fulfilled the inclusion criteria during the study period were enumerated.

1.5.3 Data collection

Data was collected in Mankweng Hospital in September 2022. An ultrasound record book in the Radiology Department was used to identify women who fulfilled the inclusion criteria of the study. A data collection tool was used to collect data from the ultrasound report and the patient's file.

1.5.4 Data analysis

Data was entered into Microsoft Excel® and analysed using STATA version 15. Microsoft Excel® was used to plot the graphs. Descriptive statistics of frequency and percentages were used to summarise all the variables. Association between hydronephrosis and independent variables was done using the Fischer's exact test. The level of significance was set at a p-value less than 0.05.

1.5.5 Reliability and validity

The reliability of the study was accounted for by using the same data collection tool, imaging ultrasound machine, procedure and reporting protocols for all patients thus consistent results were attained.

Validity of the study was ensured by using an ultrasound machine with high resolution to stage the women diagnosed with cervical cancer. The ultrasound reports were written following the departmental protocols. Registrars and medical officers who performed the ultrasound studies were working under the supervision of a radiologist consultant and sonographer.

1.5.6 Bias and objectivity

Data of study was collected without any amendment and analysed by an independent statistician to improve the objectivity of the study.

Bias was avoided in the study by using the whole population. Collaboration of clinical notes and radiology reports was used to minimise information bias.

1.6 Ethical considerations

Ethical approval and waiver of consent application to conduct the study were obtained from Turfloop Research and Ethics Committee (TREC) with the project number TREC/324/2021: PG (Annexure 4) before the study commenced. Permission to conduct

research was obtained from the Limpopo Department of Health research office with reference number: LP-2022-01-002 (Annexure 5). Medical records (Annexure 6) access was given by the Chief Executive Officer of Mankweng Hospital and the acting head of the radiology department.

1.7 Significance of the study

This study's results assist in formulating guidance to educate women at primary health care services about cervical cancer complications and its impact in their health. This will in turn reduce the morbidity and mortality of cervical cancer. Health care provider awareness and implementation of tertiary prevention of cervical cancer focusing on early diagnosis, staging of cancer and early referral are key to reducing the mortality of cervical cancer.

The findings of this study will enable the Limpopo Department of Health to allocate adequate resources to facilitate radiological diagnosis and staging of cervical cancer. Due to high prevalence of advanced disease in this research, palliative care service is an important sector that needs to be strengthened by the Department of Health to manage the symptoms associated with advanced cancer of the cervix with hydronephrosis. These symptoms of pain and kidney failure are often associated with poor quality of life, depression and anxiety.

1.8 Outline of the dissertation

Chapter 1: Describes the background and structure of this research study.
Chapter 2: Explores studies regarding hydronephrosis in cervical cancer.
Chapter 3: Discusses the research method.
Chapter 4: Presents the study results.
Chapter 5: Study results are discussed and compared with literature reviewed in Chapter 2. Limitations and recommendations of the study are also outlined in this chapter.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

A literature review is when a researcher embarks on a journey to investigate what is known about the topic of interest before the study commences (Mouton 2013). The literature review is done at the onset of the study to assist in the planning and implementation of the study of interest (Brink, Van der Walt, C and Van Rensburg 2018). In this chapter, the researcher examined existing literature on hydronephrosis in cervical cancer. Science Direct, Elsevier, Clinical Key, and internet search engines were used as data resources to review literature for the study topic.

This chapter is presented under the following headings:

- 2.2 Cervical cancer as a disease
- 2.3 Staging of cervical cancer and imaging of hydronephrosis
- 2.4 Incidence of hydronephrosis in cervical cancer
- 2.5 Complications of hydronephrosis in cervical cancer
- 2.6 Conclusion

2.2 Cervical cancer as a disease

Cervical cancer is a health challenge in the world, particularly in the LMIC. The 5-year estimated average relative cervical cancer survival in sub-Saharan Africa is 33.1% (Sengayi-Muchengeti, Joko-Fru, Miranda-Filho, Egue, Akele-Akpo, N'da, Mathewos, Buziba, Korir, Manraj, Lorenzoni, Carrilho, Hansen, Finesse, Somdyala, Wabinga, Chingonzoh, Borok, Chokunonga, Liu, Singh, Kantelhardt, and Parkin 2020). An estimated 604 000 cases and 342 000 deaths worldwide were reported in 2020, with the highest incidence and mortality occurring in sub-Saharan Africa (Sung et al 2021). In 2020, there were 10 702 new cases of cervical cancer diagnosed in South Africa, which represented 18.7% of all cancer cases in women diagnosed in that year (Sung et al 2021).

Cervical cancer was responsible for 5 870 deaths in 2020, and it is the leading cause of female cancer deaths in South Africa (Sung et al 2021). Most women diagnosed with cervical cancer are in the reproductive age group. This is at a period in their life when they are crucial to the economic and social development of their families, and thus removing them from society after being diagnosed with cervical cancer has knock-on negative effects on their communities and families (Anorlu 2008; National Department of Health South Africa 2017). Cervical cancer is a gynaecological malignancy that is preventable through primary prevention. The preventative measures entail Human Papilloma Virus (HPV) vaccination of pre-teenage girls and secondary prevention achieved by Papanicola screening of cervical mucosa to detect cancer risk and precursor lesions of cervical cancer (National Department of Health South Africa 2017). The number of sexual partners, polygamy, early age of first sexual debut, parity, age, cigarette smoking, diet, sexually transmitted infections, and Human Immunodeficiency Virus (HIV) are some of the notable risk factors associated with high cervical cancer prevalence globally (Anorlu 2008). The prevalence of advanced cervical cancer in the LMIC is high due to multiple factors such as limited health services for early screening and diagnosis, lack of formal education, residing in a rural area, and having no medical insurance (Mlange et al 2016). HPV infection alone remains the major risk factor for the development of cervical cancer (National Department of Health South Africa 2017). In contrast, cervical cancer incidence in developed countries has markedly decreased due to effective implementation of screening program and HPV DNA testing (Jedy-Agba, Joko, Liu, Buziba, Borok, Korir, Masamba, Manraj, Finesse, Wabinga, Somdyala and Parkin 2020). Other factors that decreased cervical cancer rates in developed countries were an increase in average socio-economic levels, reduced parity and decrease in the sexually transmitted disease prevalence (Sung et al 2021).

The majority of women in LMIC present with advanced-stage cervical cancer, with some complicated by hydronephrosis (Mlange et al 2016). Sowunmi et al (2015) showed that cervical cancer is still a significant cause of morbidity in the LMIC worsened by late advanced stage presentation. Some LMIC examples of this include Nepal where four out of five women with cervical cancer presented with advanced disease (Gyenwali, Pariyar,

and Onta 2013), and the prevalence of advanced cervical cancer presentation in northwestern Tanzania being 63.9% (Mlange et al 2016). There is an increased likelihood of death in women with stage III-IV cervical cancer compared to the ones with stage I-II (Sengayi-Muchengeti et al 2020).

2.3 Staging of cervical cancer and imaging of hydronephrosis

Staging of malignancy is a constantly changing process, revised periodically and guided by emerging new technology and research to improve diagnosis and management (Bhatla et al 2019). Accurate staging of malignancies assists oncologists to design a personalised patient management plan and to predict outcomes. Staging guidelines are applied globally based on the skills and availability of resources in each setting (Bhatla and Denny 2019).

Cervical cancer is staged by assessing the size of the primary lesion and pelvic wall extension of the tumour. The 2018 Revised FIGO guidelines use the combination of findings from clinical assessment, together with imaging modalities and pathological assessment (Bhatla and Denny 2019). Patient examination by palpation and inspection using colposcopy, cystoscopy and proctoscopy are methods used for clinical assessment of cervical cancer (Olpin, Chaung, Berek and Gaffney 2018). On the other hand, pathologic staging is dependent on the availability of a surgical specimen to assess the primary tumour and lymph nodes (Bhatla et al 2018). It is not a requirement to use all modalities for staging (Bhatla et al 2019), so the method used for assigning a stage should be recorded (Cohen, Jhingran, Oakin and Denny, 2019). Although radiological imaging is regarded as more superior to clinical staging, the preferred method of staging remains clinical as it is more commonly available in the LMIC compared to surgical and radiological imaging (Bhatla and Denny 2019; Hricak and Yu, 1996). However, imaging and pathological findings (if available) can be used to change the initial clinical stage (Bhatla and Denny 2019). Clinical staging is a subjective method as it varies from one examiner to the other. In Canada, Kupets, Giede, Power and Agrawal (2016) distributed a questionaire to gynaecology oncologists with scenarios representing women with

gynaecology malignancies including cervical cancer. The results of the Canadian study showed that 56% of gynaecology oncologists preffered not to wait for other investigations in cervical cancer patients before referral (Kupets et al 2016). However, the majority of the gynaecolgy oncologists relied on MRI imaging to plan oncology treatment (Kupets et al 2016).

The challenges of clinical staging are in the assessment of the pelvic sidewall invasion, bladder wall invasion, rectal wall invasion and distant metastasis of the malignancy. In a study conducted by Amendola, Hricak, Mitchell, Snyder, Chi, Long III, Fiorica and Gatsonis (2005), FIGO clinical staging resulted in the under staging of cervical cancer stage IB by almost 20% - 30%, stage IIB by up to 23%, stage IIIB by about 40%, with stage IIIB also being upstaged by approximately 64% in comparison to surgical staging. Certainly, clinical staging alone without the aid of other staging modalities fails to give accurate prognostic information and affects oncology management planning (Olpin et al 2018).

Radiological imaging modalities are important objective tools that are used to measure tumour size and detect hydronephrosis (Pradhan et al 2011). In developed countries, modern state-of-the-art cross-sectional imaging modalities (i.e. Computed Tomography, Magnetic Resonance Imaging) and functional imaging modalities (i.e. Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography / Computed Tomography) are currently used for cervical cancer staging to assist in oncology treatment planning and prediction of cancer prognosis (Lee and Atri 2019). Magnetic Resonance Imaging (MRI) is the preferred imaging modality to assess tumour size and local spread with trans-vaginal ultrasound as the next preferred modality when MRI is not available (Lee and Atri 2019). In the same way, Otero-garcía, Mesa-Álvarez, Nikolic, Blanco-Lobato, Basta-Nikolic, Menéndez de Llano-Ortega, Paredes-Velázquez, Nikolic and Szewczyk-Bieda (2019) and Olpin et al (2018) concur with Lee and Atri (2019) that MRI is superior in local staging of cervical cancer. Ultrasound is more available in LMIC and less expensive than MRI and CT and thus should be considered when imaging cervical cancer. Lymphadenopathy can be assessed using Fluorine 18 Fluorodeoxyglucose Positron

Emission Tomography / Computed Tomography (FDG PET/CT), with MRI and CT with FDG PET/CT having a higher sensitivity in detection when comparing the two modalities (Lee and Atri 2019). LMIC have a limitation when it comes to imaging due to reduced access to radiological imaging services, more so cross-sectional imaging. The choice of imaging modality to be used is dependent on availability and expertise.

Ultrasound plays a major role as an effective and relatively low cost imaging modality with no requirement for patient preparation in diagnosing hydronephrosis specifically in LMIC, thus making trans-abdominal ultrasound a first choice imaging modality in the diagnosis of hydronephrosis (Olpin et al 2018; Ong, Rivera and Pauig 2022). Historically, there has been a decline in the use of Intravenous Pyelogram (IVP) in the assessment of hydronephrosis (Montana, Hanlon, Brickner, Owen, Hanks, Ling, Komaki, Marcial, Thomas and Lanciano 1995). Montana et al (1995) reviewed care study surveys of cancer of the cervix and observed a decline in the use of IVP in pretreatment evaluation of cervical cancer from 91% in the second survey in 1983 to 42% in the third survey in 1988-1989. Russel, Shingleton, Jones, Fregmen, Winchester, Clive and Chmiel (1996) concurs with Montana et al (1995) where IVP use in the assessment of patients with invasive cancer of the cervix decreased from 63.7% in 1984 to 31.5% in 1990.

Trans-abdominal ultrasound has an advantage of assessing bladder wall invasion, tumour size and in ureteral obstruction relieving procedures (i.e. percutaneous nephrostomy) (Vanderpuye 2002). According to Vanderpuye (2002), renal ultrasound has a sensitivity, specificity, and positive and negative predictive value of 76.5%, 100%, 100% and 85% respectively in diagnosing hydronephrosis. Additionally, a comparative study between a non-contrast CT scan and renal ultrasound to evaluate hydronephrosis in patients with cervical cancer demonstrated that ultrasound has sensitivity, specificity, positive and negative predictive values of 91.3%, 95.1%, 91.3% and 95.1% respectively (Ong et al 2022). Results of an old study comparing radionuclide scanning and trans-abdominal ultrasound to diagnose hydronephrosis found that ultrasound had a sensitivity, specificity and accuracy of 90%, 98% and 97% respectively (Malave, Neiman, Spies, Cisternino and Adamo 1980).

Trans-abdominal ultrasound diagnoses and grades hydronephrosis without using ionizing radiation. The advantage of radionuclide scanning is assessing renal function as well; however, when there is severe renal failure, renal obstruction cannot be assessed (Malave et al 1980). Vanderpuye (2002), postulated that radiological staging is more accurate than clinical staging in women with cervical cancer and highlighted the importance of excluding other causes of hydronephrosis, for example renal calculi, when staging cervical cancer to avoid upstaging the patient. Trans-abdominal ultrasound is the recommended imaging modality to evaluate hydronephrosis in cervical cancer when CT and MRI cannot be performed (Lee and Atri 2019). Ultrasound is a reliable imaging modality evidenced by the high negative predictive values indicated by Vanderpuye (2002) and Ong et al (2022).

2.4 Incidence of hydronephrosis in cervical cancer

Hydronephrosis is a sign of advanced stage cervical cancer, and it is associated with high mortality and poor prognosis. In two studies conducted in the United States of America (USA), the incidence rate of hydronephrosis ranged from 44.2% to 48.9% (Pradhan et al 2011; Rose et al 2010). Comparatively, the incidence of hydronephrosis in three African studies conducted in Uganda, Tanzania and Nigeria ranged from 21.2% to 43.7% (Atuhairwe et al 2011; Mlange et al 2016; Sowunmi et al 2015). In Tanzania and Nigeria, the study populations were of women with cervical cancer who presented to the health facilities in any clinical stage (Mlange et al 2016; Sowunmi et al 2015).

Similar to South Africa; Brazil and Turkey are upper middle-income countries. A Brazilian study by Nóbrega, Zanon, da Cunha Andrade, Schmidt, dos Santos and Dos Reis (2022) investigated the prognostic role of hydronephrosis on the outcome of patients with locally advanced cervical cancer, where patients with hydronephrosis contributed 58.9%. In another Brazilian study, 37.9% of patients had hydronephrosis (Damian, de Almeida, Fernandes and Jimenez 2022). The Damian et al (2022) population included women who were diagnosed before and during treatment of cervical cancer. The incidence of

hydronephrosis was 44.8% in Turkey, where Goklu et al (2015) evaluated the effect of hydronephrosis on survival in advanced stage cervical cancer. More than 50% of patients having hydronephrosis in the Brazilian study by Nóbrega et al (2022) is justifiable as they evaluated patients who had advanced cervical cancer disease. Similarly, the Turkish (Goklu et al (2015)) and two USA (Pradhan et al (2011)) and (Rose et al (2010)), study populations were of women with stage IIIB cervical cancer and above, hence the resulting incidence of 44.8%, 48.9% and 44.2% of hydronephrosis respectively were valid findings in keeping with revised FIGO 2018 staging (Bhatla et al 2019) (Annexure 1).

Incidence of hydronephrosis in women with cervical cancer showed a gradual annual increase from 2010 to 2012 in a tertiary hospital in Lagos, Nigeria (Sowunmi et al 2015). In this study, the incidence of hydronephrosis increased by 5.4% from 2010 to 2011 and by 13.3% in 2012. Advanced cervical cancer presentation to the health facility was linked to the increasing incidence of hydronephrosis (Sowunmi et al 2015). In a Ugandan study, the results revealed an incidence of hydronephrosis to be 39.6% (Atuhairwe et al 2011). Furthermore, Atuhairwe et al (2011) study results showed that urologic complications are associated with increased tumour volume. Cervical cancer treatment is determined by the stage of the disease. Its treatment ranges from surgery, radiotherapy and chemoradiotherapy. Total abdominal hysterectomy (TAH) is a management practice of early cervical cancer, and the urological complications of TAH include ureteric injury that may result in hydronephrosis. Pelvic scarring can occur as a complication of radiotherapy and can result in hydronephrosis. The limitation of the Brazilian study was the inclusion of patients who were undergoing radiotherapy (Damian et al 2022). This could have increased the number of hydronephrosis cases as the causes of hydronephrosis was not outlined. Similarly, Patel et al (2015) in the USA included patients who had surgery and radiotherapy with cause of hydronephrosis not specified.

Hydronephrosis can be unilateral or bilateral in women with cervical cancer. According to Mlange et al (2016) women with hydronephrosis were 21.2% of the study population and, of these, 65.1% had unilateral hydronephrosis and 34.9% had bilateral hydronephrosis.

Comparatively, Damian et al (2022) results showed 37.9% of women had hydronephrosis, with unilateral and bilateral involvement contributing 52.8% and 47.2% respectively.

Revised FIGO 2018 guidelines classify the presence of hydronephrosis as stage IIIB in cervical cancer (Annexure 1). Sowunmi et al (2015) demonstrated that 95.6% of women with FIGO stage IIIB cervical cancer in their study had hydronephrosis. These results in Sowunmi et al (2015) are congruent with a study in Uganda by Atuhairwe et al. (2011) where advanced stage cervical cancer was associated with urological complications. Furthermore Mlange et al (2016) reaffirms both studies as hydronephrosis was one of the most common complications of advanced cervical cancer in northwestern Tanzania.

2.5 Complications of hydronephrosis in cervical cancer

Renal insufficiency of varying degrees occurs as a result of hydronephrosis in cervical cancer, more so if it is bilateral, and hydronephrosis might have an impact on the oncology treatment (Rose et al 2010). Estimated Glomerular Filtration Rate (eGFR) is a mathematical formula used to assess renal function using patient's creatinine levels as a metric. Serum urea and creatinine are waste products that are produced by the body and are excreted by the kidneys (Gowda, Desai, Kulkarni, Hull, Math and Vernekar 2010). Elevated serum urea and creatine, and low eGFR are suggestive of renal insufficiency (Gowda et al 2010). Raised serum urea and creatinine levels are approximately 4 times more likely to occur in women with hydronephrosis (Atuhairwe et al 2011). In this study by Atuhairwe et al (2011) 71.4% of the women with hydronephrosis had elevated serum urea and creatinine with an odds ratio of 3.88. The Damian et al (2022) study showed a decline of eGFR in patients with hydronephrosis, where women with bilateral hydronephrosis, unilateral hydronephrosis and those with no hydronephrosis had eGFR of 37.6, 84.6 and 107.2ml/min/1.73m^2 respectively. Mcardle and Kigula-Mugambe (2007) in a study in Uganda established that hydronephrosis was one of the most common exclusion criteria for Cisplatin chemotherapy. A systematic review by Pergialiotis et al (2019) could not conclude if the poor survival in women with hydronephrosis was due to hydronephrosis or its complications, namely uremia and sepsis.

Hydronephrosis is relieved with either percutaneous nephrostomy, ureteral stenting, or both to improve the renal function (Wilson, Urwin, and Stower 2005). Some authors believe that there is an associated ethical dilemma with relieving hydronephrosis as there are complications associated with percutaneous nephrostomy which is an invasive procedure (De Souza, Souza, Kirsztajn and Kirsztajn 2015). The complications associated with the percutaneous nephrostomy procedure are sepsis, severe bleeding and injury to the organs adjacent to the kidney, for example the colon, liver, spleen and lung (Dagli and Ramchandani 2011). According to Wilson et al (2005) the renal function of patients with malignant ureteric obstruction improved after the insertion of a percutaneous nephrostomy. In comparison, a South African study by Van Aardt, Van Aardt and Mouton (2017) demonstrated 50% improvement of renal function post insertion of the percutaneous nephrostomy in women with cervical cancer. Additionally, the results of Damian et al (2022) showed an increase in eGFR from 10.6 to 59.7ml/min/1.73m^2 in women who had a hydronephrosis-relieving procedure. Post insertion of percutaneous nephrostomy in women with cervical cancer in the Van Aardt et al (2017) study demonstrated a higher number of women who were initiated into or completed oncology treatment in the nephrostomy group compared to the group that did not receive percutaneous nephrostomy.

Hydronephrosis whether unilateral or bilateral is a significant predictor of poor survival in women with cervical cancer (Goklu et al 2015). Further, the 5-year progression-free survival was worse in women with hydronephrosis without tumour extension to the pelvic sidewall compared to those with hydronephrosis in the presence of tumour extension to the pelvic sidewall; thus highlighting the importance of lymph nodes assessment through radiological imaging or pathological assessment in cervical cancer staging (Chao, Leung, Mutch, Herzog and Perez 1998). As highlighted by Pradhan et al (2011) “hydronephrosis in women with cervical cancer is an independent poor prognostic indicator of survival; where bilateral involvement has a worse overall prognosis compared to unilateral involvement”. Pradhan et al (2011) had a population of women with stage IIIB and above with cervical cancer. In this study by Pradhan et al (2011) the results demonstrated a high

mortality rate associated with hydronephrosis in women with cervical cancer who underwent oncology treatment compared to those without hydronephrosis who underwent oncology treatment. The median time to death in women with unilateral or bilateral hydronephrosis was significantly shorter compared to the ones who did not have hydronephrosis (Pradhan et al 2011).

2.6 Conclusion

In conclusion, cervical cancer is a growing health concern, globally. Despite widely available screening modalities, women are still presenting with advanced disease. Through research, we now understand the impact of the condition not only on the health of the women themselves, but also on the health system and economy at large. Hydronephrosis is one of the more serious complications in women with advanced cervical cancer resulting in renal dysfunction and poor survival outcome. In LMIC, there are constraints when it comes to accessing sophisticated imaging modalities. However, ultrasound is the most accessible and cost-effective imaging modality for the staging of cervical cancer as it also detects hydronephrosis. Therefore, it is important for the clinicians who are involved with management of patients with cervical cancer to understand the significance of hydronephrosis, including the implications for treatment outcomes and resource allocation for both patients already diagnosed and those still undergoing diagnostic and staging processes.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Introduction

Chapter 3 outlines the research method for this study. This chapter describes the study design, setting and population, inclusion and exclusion criteria, sampling procedure and sample size, data collection, reliability, validity, bias, and ethical considerations of the study.

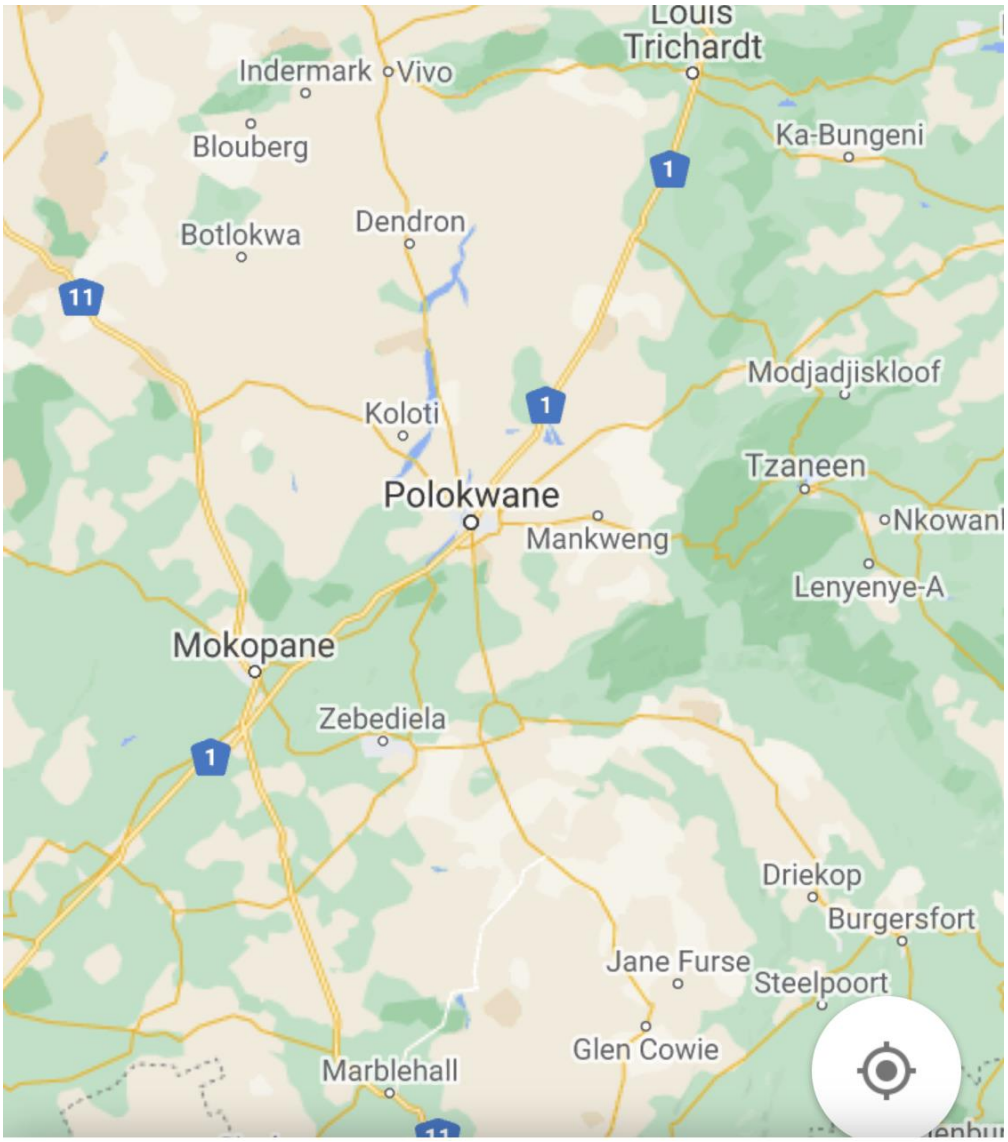
3.2 Study design

This study was a retrospective descriptive review of clinical records of women with cervical cancer treated at Mankweng Tertiary Hospital, Limpopo province, South Africa between 01 July 2019 and 31 December 2019.

3.3 Study setting

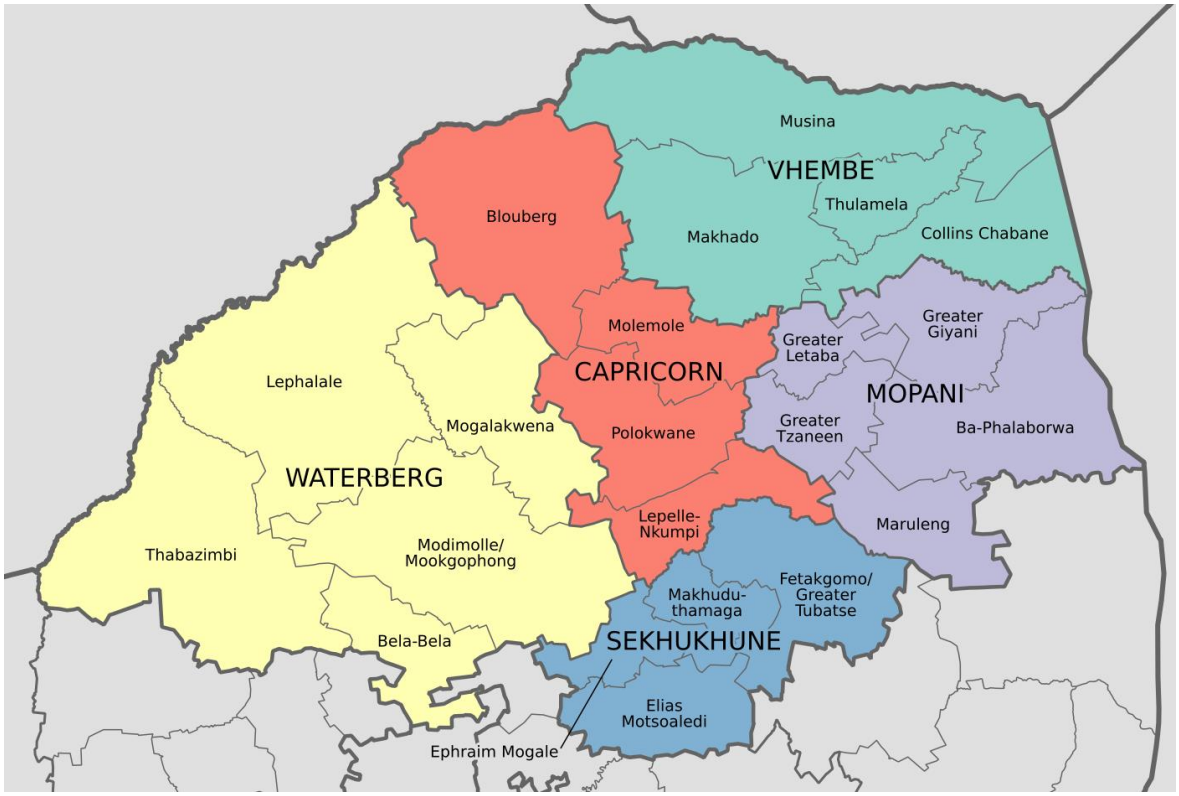
The study was carried out in Mankweng Hospital (Figure 3.1) in the Capricorn district (Figure 3.2) of Limpopo province. Mankweng Hospital is a tertiary academic hospital that runs a gynaecology oncology clinic, managing patients referred from all the hospitals in the five districts of province.

This hospital was selected as it is one of the two teaching hospitals in the province with staff including radiologists, gynaecologists and gynaecology oncologists; all women diagnosed with cervical cancer in the province seeking management of gynaecological malignancies are referred to this hospital. The Department of Radiology in Mankweng Hospital performs staging trans-abdominal ultrasounds imaging or investigation for all women diagnosed with cervical cancer. The Department of Radiology has a procedure and reporting protocol that is followed for each patient investigated.



https://www.google.co.za/maps/maps/search/mankweng

Figure 3.1 Area map of the research study site



https://upload.wikimedia.org/wikipedia/commons/thumb/8/81/Map_of_Limpopo_with_municipalities_named_and_districts_shaded_%282016%29.svg/1400px

Figure 3.2 District map of Limpopo province

3.4 Sampling

3.4.1 Study population

In this study, all clinical records of women diagnosed with cervical cancer who presented to Mankweng Hospital's Department of Radiology for staging trans-abdominal ultrasound from 01July 2019 to 31 December 2019 were evaluated.

3.4.2 Eligibility criteria

- Inclusion criteria

The following were the inclusion criteria:

- Female patients older than 18 years
- Cervical cancer diagnosis confirmed by histology
- Trans-abdominal staging ultrasounds performed within the study period
- No previous diagnosis of hydronephrosis

- Exclusion criteria

The exclusion criteria were:

- Cervical cancer recurrence or progression. Definition of Cervical cancer recurrence is the regrowth of primary lesion or development of metastasis that occurs 6-months after lesion regression post treatment (Antunes and Cunha 2013). Cervical cancer progression is defined as the increase in size of the primary lesion by 25% or distant metastasis while patient is on treatment (Oxnard, Morris, Hodi, Baker, Kris, Venook and Schwartz 2012).
- Prior treatment of cancer by radiotherapy
- Previous pelvic surgery for any reason other than cervical cancer
- Hydronephrosis caused by any other medical or surgical condition
- Patients with missing critical information

3.4.3 Sampling method and sample size

A census method, where the entire population was included, was adopted in this study. The clinical records of women diagnosed with cervical cancer who presented to Mankweng Hospital for staging trans-abdominal ultrasound within the specified period of the study were included.

Patients who present to Mankweng Hospital Department of Radiology are given a number for the radiological study performed (e.g., ultrasound 15/2019) for easy filling and tracing of study reports, thus each radiological study has an allocated number. The ultrasound numbers were used to retrieve clinical records of patients. The data collection tool (Annexure 2) was used to extract information from the clinical records.

3.5 Data collection

A list of patients' file numbers that fulfilled the inclusion criteria was compiled using the ultrasound record book in the Department of Radiology. This list was submitted to the hospital record department to request the patients' records. An ultrasound number was also used to retrieve the ultrasound reports filed in the Department of Radiology. Two register logs were used to collect data from the patient's file and ultrasound report. One register log had the patient's file number and the study code in case verification of information is needed later. The second register log contained data that was collected and a study code without the patient's file number and name to de-identify participants. In this second log, the clinical records were only identified by a study code. The second log was used as a data collection tool in this study, and is composed of three sections: socio-demographic-, clinical- and radiologic data (Annexure 2). The socio-demographic data is composed of age, marital status, parity, source of income, area and district where the women reside. Clinical and radiological data included clinical staging, largest tumour dimension, the presence or absence of hydronephrosis, and other ultrasound findings.

Trans-abdominal ultrasound using an Aloka Prosound α6 (Figure 3.3) machine was used to image women with cervical cancer for staging purposes during the specified period of the study. Senior radiology registrars and medical officers in the radiology department performed the trans-abdominal ultrasound under the supervision of a radiologist and sonographer.

The Department of Radiology in Mankweng Hospital has an ultrasound procedure and reporting protocol that is followed by every doctor who performs the procedure. When a trans-abdominal ultrasound is performed these steps are followed:

Preparation:

- Patient comes to the Department of Radiology with a filled form with patient's details and indication of the study from the referring doctor, in addition to a hospital file. An ultrasound number is allocated to the study and documented on the request form, study report and hospital file.
- Before performing a trans-abdominal ultrasound, the doctor introduces himself or herself to the patient and confirms the patient's name and procedure to be performed. This is done to confirm if a relevant procedure is performed on the correct patient.
- To reduce bowel gas, the patient fasts from 22:00 the night before the procedure until the procedure is performed. The procedure is performed with the patient having a full bladder to optimise visualisation of the pelvic organs.
- The patient lies supine on the bed with the skirt or pants lowered to expose the abdomen and pelvis. A drape is tucked in over their clothes to protect the clothes. The top is lifted to the breast level again to expose the abdomen. Privacy of the patient is assured at all times.
- Ultrasound machine is prepared by choosing an allotted mode for abdomen and pelvis on the ultrasound machine and the correct probe (curvilinear probe bandwidth 2-6 MHz).
- Lights are dimmed for better visualisation of the ultrasound screen.

Procedure:

- Ultrasound gel is applied to the patient's abdomen to disperse air between the ultrasound probe and patient's skin. With gentle motion, an ultrasound probe is used to scan the abdomen and pelvis in transverse and longitudinal planes covering the whole abdomen and pelvis.

Assessed organs:

- When staging cancer of the cervix, the following organs are assessed: cervix, uterus, ovaries and adnexa, urinary bladder, vesico-vaginal pouch, recto-vaginal pouch, kidneys, liver, para-aortic region, and bowel loops.
- The full urinary bladder is used as an acoustic window to visualise the uterus, cervix, vesico-vaginal pouch, and recto-vaginal pouch.

Measurements:

- The sizes of the organs are measured in two dimensions, namely length and width. If a mass is visualised it is measured in three dimensions namely length, width and antero-posterior.

Documentation

- Ultrasound findings are documented according to the Mankweng Hospital Department of Radiology protocol. One copy of the report remains in the department for filling and another remains in the patient's file to be viewed by the clinician.
- Documented ultrasound findings include the organs and abnormalities visualised with their measurements and assessment.

Figure 3.3 An Aloka Prosound α6 ultrasound machine

3.6 Data analysis

Data was captured and managed using Microsoft Excel®. Data analysis was done using STATA version 15, and Microsoft Excel® was used to plot the graphs. Descriptive statistics of frequency and percentages were used to summarise all the variables. Association between hydronephrosis and independent variables was done using the

Fischer's exact test. Fischer's exact test is recommended where there are <5 cases per cell (McDonald 2014). The level of significance was set at a p-value of less than 0.05.

3.7 Reliability and validity

3.7.1 Reliability

Reliability is the term used to describe a study that produces similar results under same conditions at different times (consistent results) (Brink et al 2018). The data collection tool was constructed using the reviewed literature. The collected data was documented accurately using the same data collection tool for all the clinical records thus consistent results were attained. In the Mankweng Hospital Department of Radiology, every doctor and radiographer follow departmental procedure and reporting protocols when they perform an imaging study. Therefore, the same protocol to image and report ultrasound studies was followed for all women with cervical cancer on whom a trans-abdominal ultrasound was performed.

3.7.2 Validity

'Validity' refers to how effective an instrument is at measuring what it claims to measure (Khalid, Hilman and Kumar 2012). The ultrasound machine used in the Mankweng Hospital Department of Radiology to stage the women diagnosed with cervical cancer is the Aloka Prosound α6-ultrasound machine. It is an easy-to-use machine with high quality images and high resolution, making it easier to differentiate between two different organs (Healthcare-in-europe.com 2009). Registrars and medical officers employed in the Department of Radiology work under the supervision of a radiologist consultant and sonographer. The registrars and medical officers who perform ultrasounds have two or more years of experience in the department, and departmental procedure and reporting protocols are followed for every patient seen. Therefore, the radiological imaging reports and conclusions drawn from these studies are considered valid.

3.8 Bias and objectivity

'Bias' is when an error is introduced in a study and impacts the quality of that study (Brink et al, 2018). Bias should be minimised to increase the accuracy of the study results. Selection bias occurs when a wrong sampling method is used. In this study, the human factor was removed from the selection of participants, as the whole population was included.

In a retrospective study, information bias might not be avoided due to missing clinical information. To minimise information bias in this study, clinical notes and radiology reports were corroborated. Where information is not available on both the clinical notes and radiology report, this was reported as a limitation to the study.

Objective research is one that is free from bias. Results of the study were therefore interpreted by an independent statistician in order to improve the objectivity of the study.

3.9 Ethical considerations

3.9.1 Ethical clearance

The research proposal was presented in a meeting of the Department of Radiology, chaired by the acting Head of Department. The proposal was then submitted to the School of Medicine Research Ethics Committee and Faculty Higher Degrees Committee for approval. Ethical clearance application to conduct research was made to Turfloop Research and Ethics Committee (TREC). Waiver of consent was requested, and ethical clearance was approved by TREC with project number TREC/324/2021: PG (Annexure 4). Upon ethics approval, the research proposal was loaded on the National Health research database to obtain gatekeeper permission from the Limpopo Department of Health, with the reference number LP-2022-01-002 (Annexure 5). Permission to access

patient medical records (Annexure 6) was obtained from the Chief Executive Officer of Mankweng Hospital and the acting head of the radiology department.

3.9.2 Confidentiality and anonymity

The Hippocratic Oath is a promise undertaken by every medical doctor to guide him or her to uphold medical ethics while practicing the art of medicine. Amongst other principles, medical ethics guide medical doctors in protecting patient's confidentiality and doing no harm to patients (Nicolaides 2014). The clinical records collected by the researcher while collecting data for this research were stored in the Department of Radiology office which is always locked. The Head of Department, his secretary, and the researcher were the only people who had access to the office. The researcher made use of two register logs to record data. These register logs were only accessed by the researcher and were also kept in the Department of Radiology office. One register log has the patient's file number and a study code. The second register log, which is the data collection tool, contains a study code to de-identify participants. The patient's name or any identifying information does not appear on the data collection tool or on any report or publication that arises from this research. This confidential information will remain anonymous. The data collection tools were too kept safe in the locked Department of Radiology office. A password-protected computer was used to keep electronic data.

Informed consent is one of the important principles of ethics in research. Informed consent gives information to a participant pertaining to the risks and benefits of the research so that the participant can make a well-informed decision to participate in the research or not (Samedical 2012). A waiver of consent is important in this proposed study, as clinical records were evaluated retrospectively. In a retrospective review of clinical records, it is difficult for the researcher to access all the participants for the study. Waiver of consent is important as it ensures that there is reduced risk with no negative effects to the subjects involved in the research. Waiver of consent application was addressed to the TREC. The permission to access patient medical records was obtained from the Chief Executive Officer of Mankweng Hospital (Annexure 6).

3.9.3 Non-maleficence

The researcher did not have any physical contact with the participants, as the researcher used only the clinical records to obtain relevant data. The clinical records are of women who are already diagnosed with cervical cancer, and the staging abdominal ultrasound forms part of their oncology treatment management.

3.9.4 Distributive justice

Distributive justice is ensured by fairly selecting the participants for the research (Brink et al 2018)**.** In this study, all clinical records of women who were diagnosed with cervical cancer and staged with an ultrasound within the study period, and met the inclusion criteria, were included. Only the women who did not meet the inclusion criteria were excluded. Distributive justice, anonymity and confidentiality are interlinked (Brink et al 2018**).** Confidentiality of clinical records is assured, as no information that may potentially identify any of the participants is included in the results of this study, or any publications that may result from this study.

CHAPTER FOUR: RESULTS

4.1 Introduction

Results of the study are presented in Chapter 4. The aim of the study was to evaluate the prevalence of hydronephrosis on ultrasound imaging in women with cervical cancer at Mankweng Hospital over a period of 6 months.

A total of 218 staging trans-abdominal ultrasounds were performed over the 6-months study period (Table 4.1). From the 218 studies, 5 were of women with pre-cancerous lesions and 13 were of tumour recurrence. These 18 clinical records were excluded from the study. The total number of clinical records that fulfilled the inclusion criteria were 200 and their ultrasound findings were analysed. From this study sample size of 200, 3 clinical records were of women staged post TAH for a pre-cancerous lesion of cervical cancer, as part of the management of those lesions. The histology results of these lesions were found to be an invasive squamous cell carcinoma, thus staging ultrasound was performed and the women could be included in the study.

Table 4.1: Number of abdomino-pelvic ultrasounds preformed at Mankweng Hospital radiology department in Q3 and Q4, 2019

	Number	Percentage
July 2019	49	22%
August 2019	30	14%
September 2019	40	18%
October 2019	41	19%
November 2019	41	19%
December 2019	17	8%
Total (6 months)	218	100%

Chapter 4 is subdivided into:

- Socio-demographic characteristics of the patients
- Clinical and radiological data
- Prevalence of hydronephrosis
- Other ultrasound findings

- Association of hydronephrosis with other variables

4.2 Socio-demographic characteristics

200 Clinical records from the radiology department and the hospital records of the women diagnosed with cervical cancer who had ultrasound staging in Mankweng Hospital over a period of 6-months from 01/07/2019 to 31/12/2019 were evaluated.

The patients ages ranged from 27 years to 89 years with 68.4% (n=136) of the women aged between 31-60 years and 28.5% (n=57) older than 60 years (Figure 4.1).

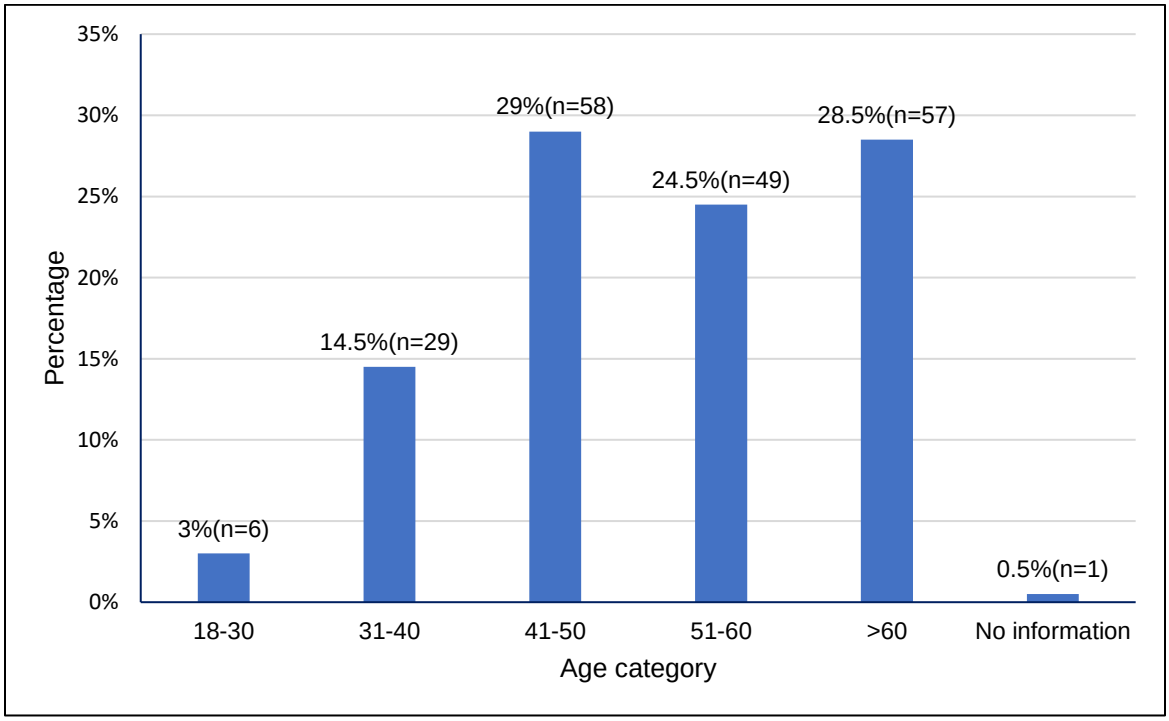


Figure 4.1 Age range of the patients

Figure 4.2 demonstrates the marital status of women in this study. The majority of women were single (45.5%, n=91) while a small minority were either divorced or separated (1.5%, n=3). Married women contributed 23.5% (n=47) of the sample, and marital status was not known for the rest of the patients (29.5%, n=59).

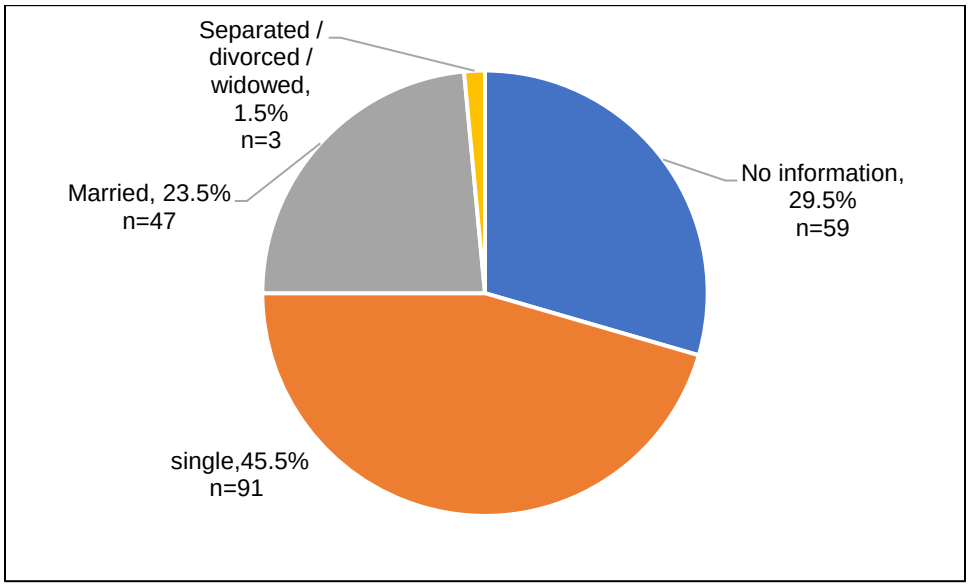


Figure 4.2 Marital status of patients

Women in the study came from all the 5 districts in Limpopo province. Regarding place of residence, 90.5% (n=181) of women were from a rural area (Figure 4.3), and only 3.5% (n=7) from urban areas. Place of residence was unknown in 6% (n=12). For district of residence, the majority were from Mopani district (26.5%, n=53), followed by Vhembe (21.5%, n=43), Sekhukhune (18.5%, n=37), Waterberg (16.5%, n=33) and Capricorn (15.5%, n=31) districts, respectively (Figure 4.4).

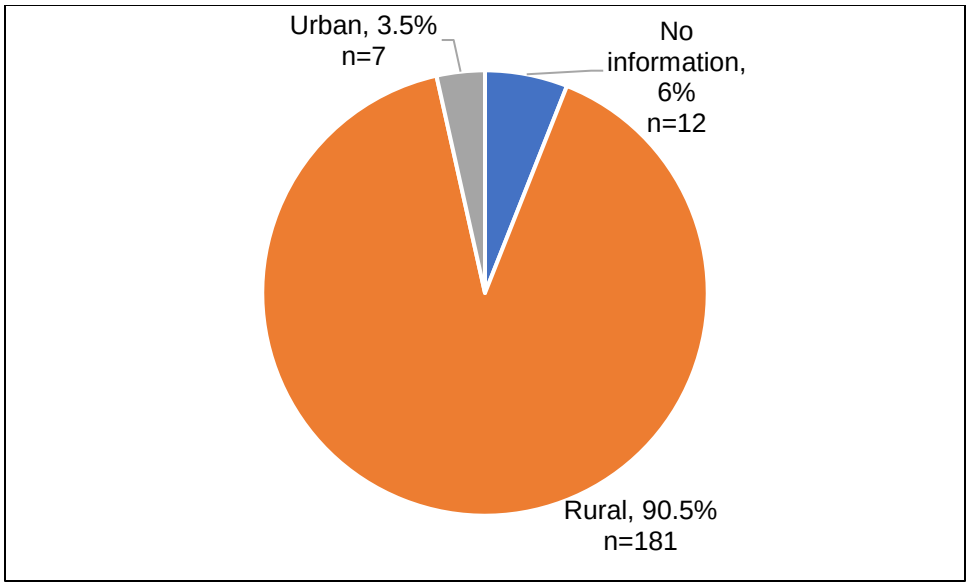


Figure 4.3 Distribution by place of residence

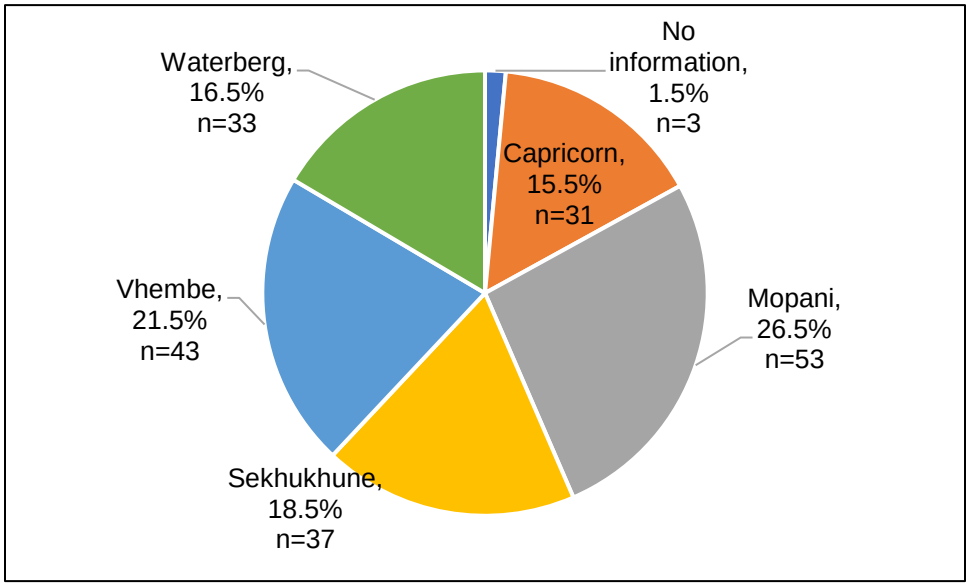


Figure 4.4 Distribution by district of residence

Employment status (Figure 4.5) was mostly not recorded in the hospital file. More than 50% (n=109) of the clinical records did not have information about the employment status of the women. Of the clinical records that contained this information, 21.5% (n=43) were

pensioners, followed by 20.5% (n=41) who were unemployed. Only 1.5% (n=3) were formally employed with 2.0% (n=4) receiving social grants.

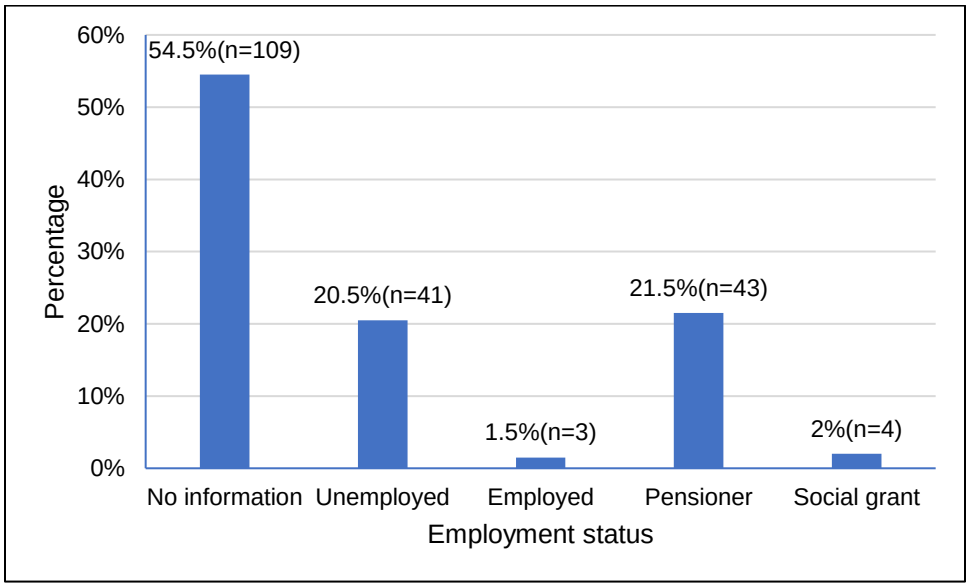


Figure 4.5 Employment status of participants

Figure 4.6 displays the parity of the women. Mostly the information on parity was not captured in the clinical records (44.5%, n=89). Of those where parity was recorded, 34% (n=68) were para 1-4 (meaning had 1 – 4 births), 18.5% (n=37) were para 5 or higher (meaning had 5 or more births), and 3% (n=6) were nulliparous (never given birth).

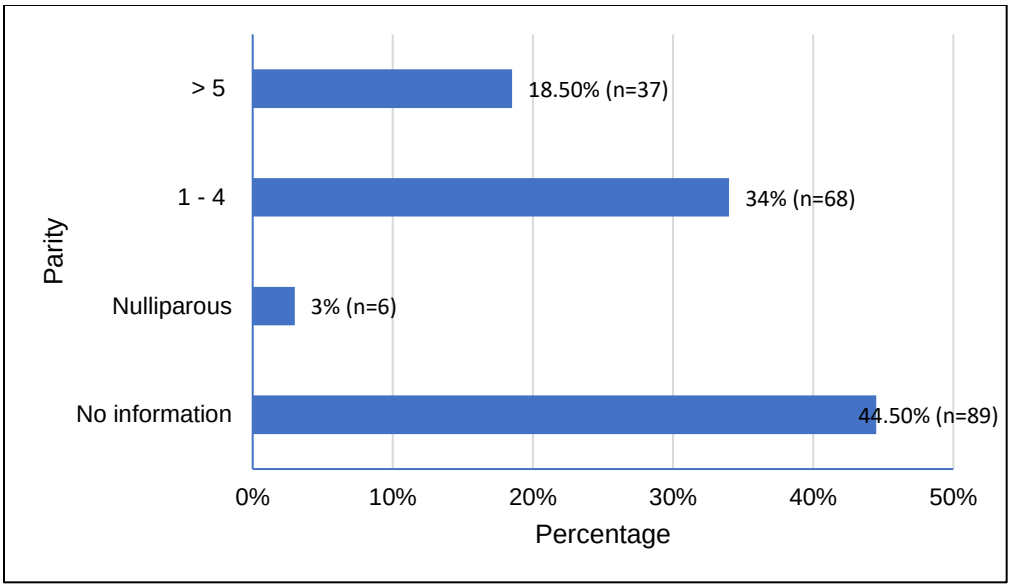


Figure 4.6 Parity of participants

4.3 Clinical and radiological data

Women who were not clinically staged before radiological staging in Mankweng Hospital contributed more than 50% (n=111) of the total sample (Figure 4.7). Of the 45% who were clinically staged prior to radiological staging, 17% (n=34) were stage IIIB, making up the majority of those clinically staged. Women with clinical stage IIa and below contributed only 15.5% (n=31).

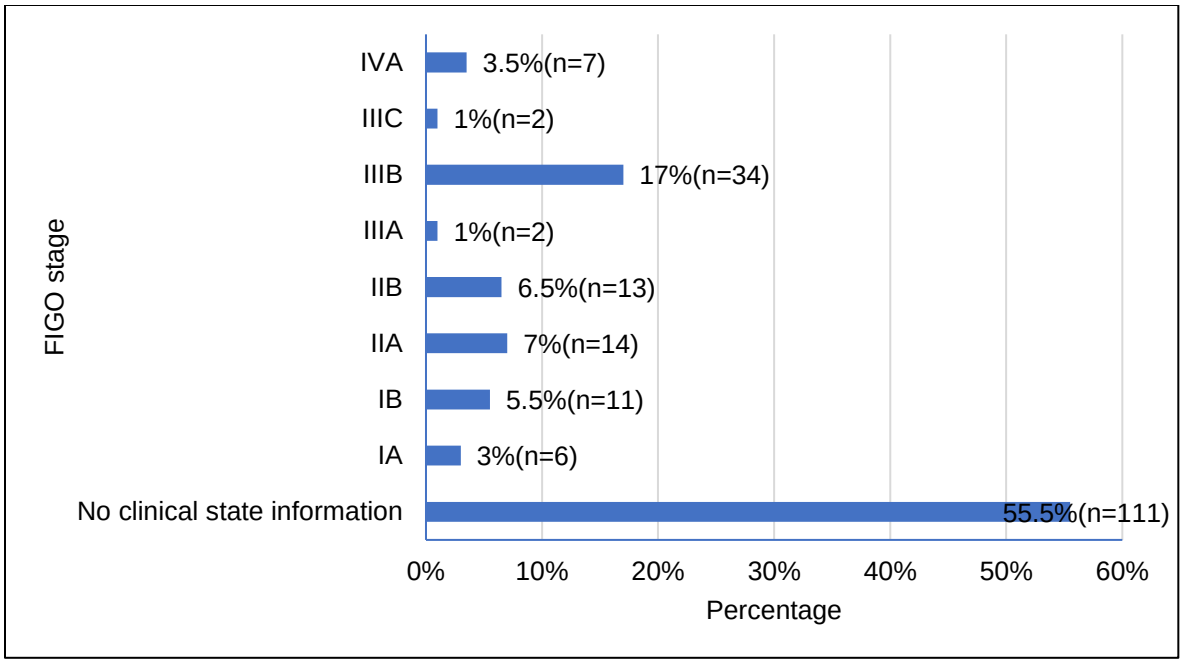


Figure 4.7 Clinical staging of patients

Table 4.2 demonstrates the cervical tumour size of women in the sample. 71.5% (n=143) had a tumour size of >4cm, while 10.5% (n=21) had no pelvic or abdominal mass detected on the ultrasound imaging. Cervical tumour sizes of <2cm and 2-4cm contributed 2.5% (n=5) and 15% (n=30) respectively. Of the three women who were imaged with ultrasound post TAH, two had no mass detected on ultrasound imaging and one had a tumour infiltrating the urinary bladder wall detected.

Table 4.2: Cervical tumour size of participants (N=200)

Tumour	n	%
No information	1	0.5
No mass	19	9.5
< 2 cm	5	2.5
>2-4 cm	30	15
>4cm	143	71.5
Post TAH (no mass measurement)	2	1

4.4 Prevalence of hydronephrosis

Out of the 200 women, 85 had hydronephrosis, a prevalence of 42.5% (Figure 4.8). One woman from the three women who had ultrasound staging post TAH had hydronephrosis

on ultrasound imaging. Of the 85 women with hydronephrosis, 68.2% (n=58) were bilateral, while 31.8% (n=27) were unilateral (Figure 4.9).

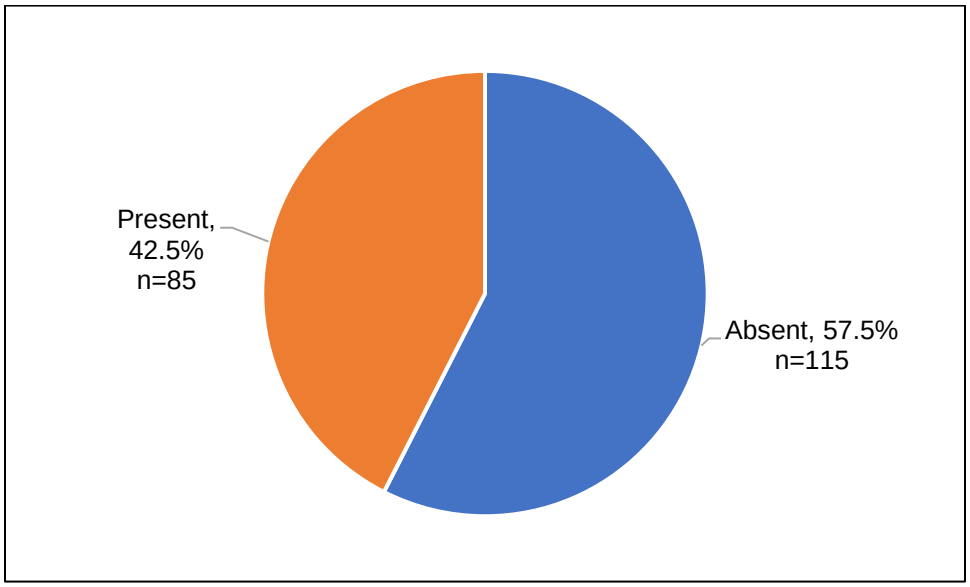


Figure 4.8 Prevalence of hydronephrosis (N=200)

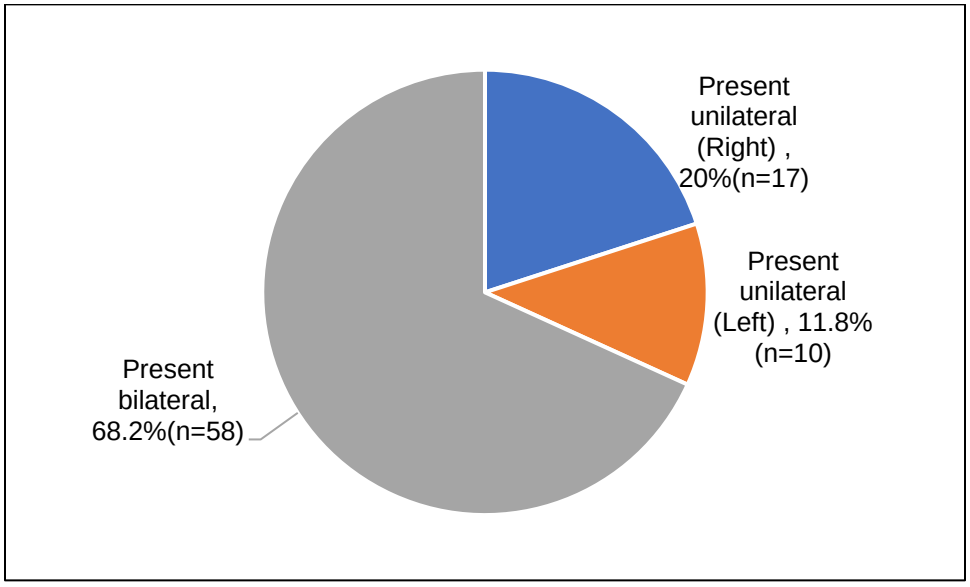


Figure 4.9 Laterality of hydronephrosis (n=85)

4.5 Other ultrasound findings

Other ultrasound findings were urinary bladder wall infiltration by the cervical tumour in 13% (n=26) (Figure 4.10) and vesico-vaginal fistula in 0.5% (n=1) of cases (Figure 4.11). Liver metastasis was found in 3% (n=6) (Figure 4.12) and para-aortic lymph nodes in 1% of cases (n=2) (Figure 4.13).

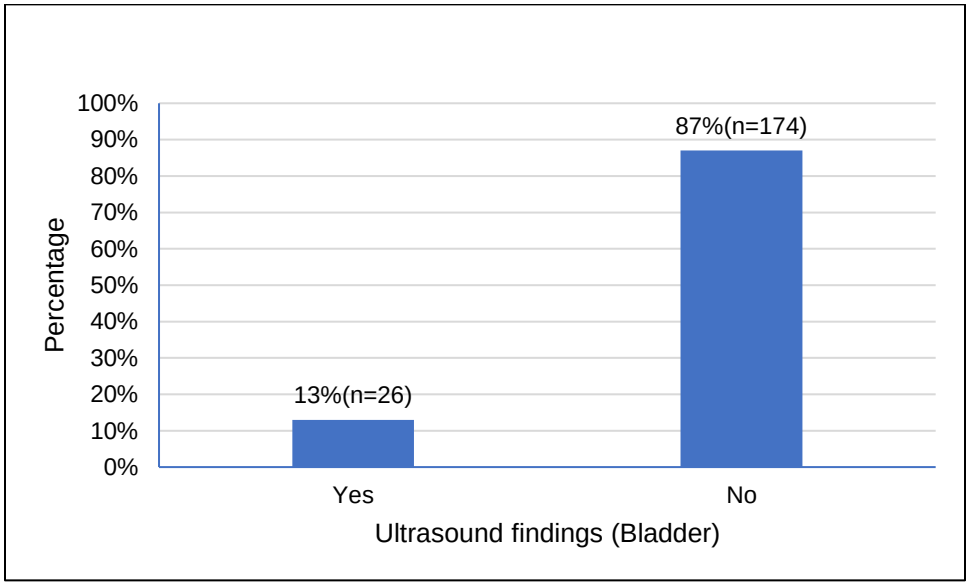


Figure 4.10 Urinary bladder wall infiltration

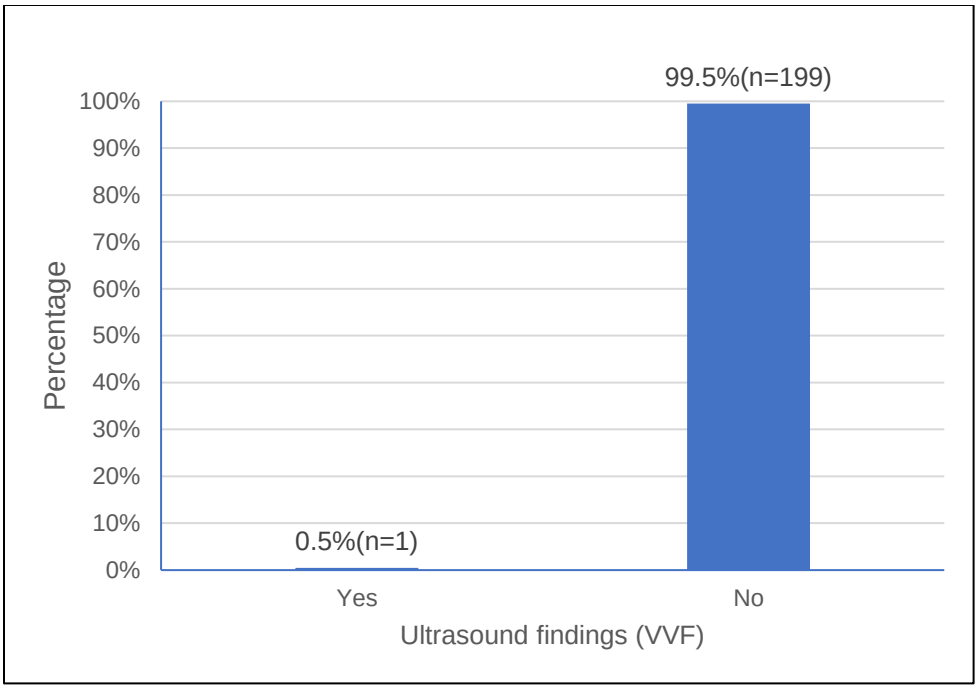


Figure 4.11 Vesico-vaginal fistula findings

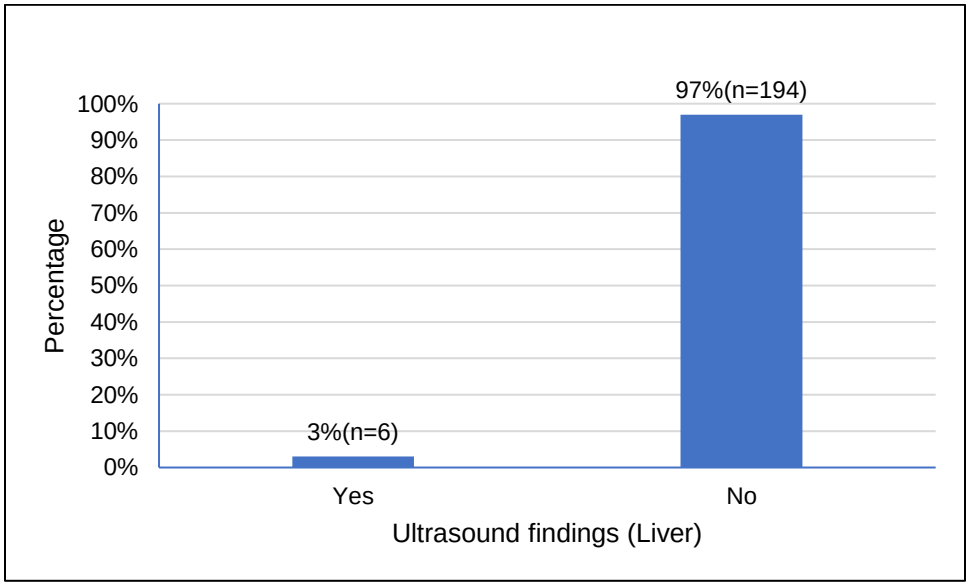


Figure 4.12 Liver metastasis

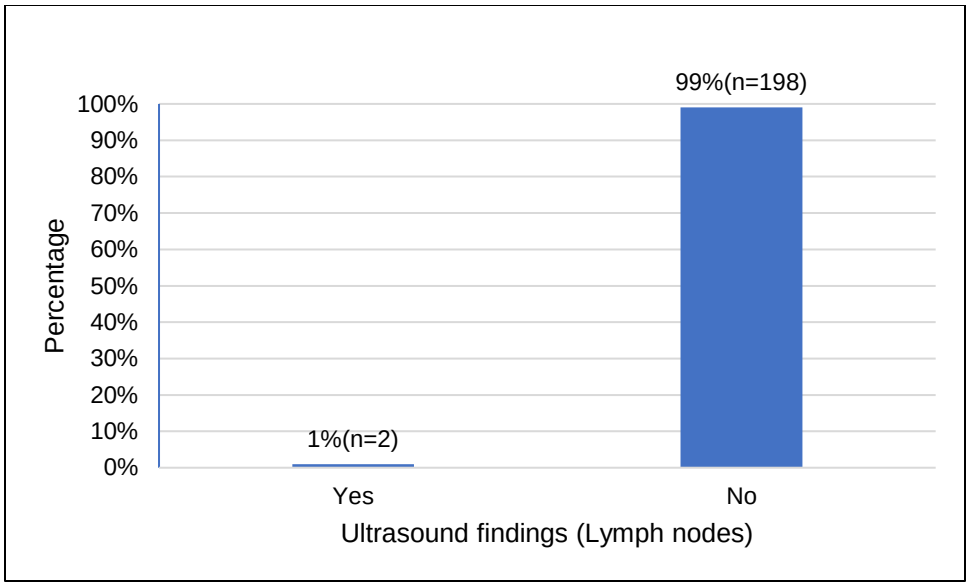


Figure 4.13 Para-aortic lymph nodes

4.6 Association of hydronephrosis with other variables

Association of hydronephrosis was evaluated with age, parity, area, district and cervical tumour size.

There was an association between hydronephrosis and tumour size (p=0.001) [Table 4.7]. No significant association was found between hydronephrosis and age (p=0.57), parity (0.58), area (p=0.93), or district of residence (0.36) [Table 4.3, 4.4, 4.5 and 4.6 respectively].

Table 4.3: Association between hydronephrosis and age of participants

	Hydronephrosis				Fischer's exact test
	Present		Absent		
Age	**N**	**%**	**N**	**%**	**p-value**
18 – 30 years	3	50	3	50	3.92 (0.57)
31 – 40 years	15	51.7	14	48.3	
41 – 50 years	22	37.9	36	62.1	
51 – 60 years	18	36.7	31	63.3	
>60 years	26	45.6	31	54.4	
No information	1	100	0	0	

Table 4.4: Association between hydronephrosis and parity					
	Hydronephrosis				Fischer's exact test
Parity	Present		Absent		p-value
	N	%	N	%	
No information	39	43.8	50	56.2	2.01 (0.58)
Nulliparous	4	66.7	2	33.3	
1 – 4	26	38.2	42	61.8	
≥ 5	16	43.2	21	56.8	

Table 4.5: Association between hydronephrosis and residential area					
	Hydronephrosis				Fischer's exact test
	Present		Absent		
Area	N	%	N	%	Fischer's exact test (p-value) (p-value)
No information	6	50	6	50	0.43 (0.93)
Urban	3	42.9	4	57.1	
Rural	105	58	76	42	

Table 4.6: Association between hydronephrosis and residential district					
	Hydronephrosis				Fischer's exact test
	Present		Absent		
District	N	%	N	%	p-value
No information	2	66.7	1	33.3	5.42 (0.36)
Capricorn	16	51.6	15	48.4	
Mopani	25	47.2	28	52.8	
Sekhukhune	11	29.7	26	70.3	
Vhembe	16	37.2	27	62.8	
Waterberg	15	45.5	18	54.5	

Table 4.7: Association betweeen hydronephrosis and cervical tumour size					
	Hydronephrosis				
Tumor size	Present		Absent		Fisher's exact test (p-value)
	N	%	N	%	
No information	1	1.2	0	0.0	24.70 (<0.001)
No mass	0	0.0	19	16.5	
Less than 2cm	1	1.2	4	3.5	
Between 2 and 4 cm	10	11.8	20	17.4	
More than 4 cm	72	84.7	71	61.7	
Post TAH (no mass measurement)	1	1.2	1	0.9	

CHAPTER 5: DISCUSSION

5.1 Introduction

Chapter 5 discusses the study results and compares these findings to previous studies related to the research topic. The chapter is subdivided into:

1. Background
2. Prevalence of hydronephrosis and other complications
3. Socio-demographic factors and association with hydronephrosis
4. Clinical and radiological findings and association with hydronephrosis
5. Conclusion
6. Limitations
7. Recommendations for further research

5.2 Background

Hydronephrosis is a complication of cervical cancer resulting from either a direct infiltration of the tumour to the urinary collecting system or due to external pressure from cancer affected lymph nodes. Hydronephrosis may obstruct the flow of urine from the kidneys to the bladder resulting in back pressure and damage to the kidneys. Damage to the kidneys may result in renal failure with increased morbidity and mortality in women with advanced cervical cancer. Hydronephrosis in cervical cancer has a negative impact on the oncology management.

5.3 Prevalence of hydronephrosis and other complications

Urological complications in cervical cancer are associated with advanced disease (Atuhairwe et al 2011). In the current study, hydronephrosis, bladder wall infiltration and vesico-vaginal fistula were the urological complications found on ultrasound imaging, with

hydronephrosis being the most frequent. In this study, the frequency of vesico-vaginal fistula (0.5%) findings was lower than that found by Mlange et al (2016) in Tanzania (6.4%) and by Atuhairwe et al (2011) in Uganda (7.4%). Vesico-vaginal fistula formation may be due to tumour extension into the urinary bladder or as a complication of radiotherapy (Kinjyo, Kudaka, Toita, Nakamoto,Nagai, Maemoto, Hashimoto, Ariga, Heianna and Aoki 2017). The current study as well as those by Mlange et al (2016) and Atuhairwe et al (2011) are similar in that one of the exclusion criteria was all women who had had radiotherapy. Admittedly this is corroborated by the 2018 Revised FIGO guidelines, where urological complications are evidence of advanced cervical cancer.

The prevalence of hydronephrosis of 42.5% in the current study demonstrates comparable findings with two African studies in Uganda and Nigeria, in which the prevalence was 39.6% and 43.7% respectively (Atuhairwe et al 2011; Sowunmi et al 2015). Interestingly, the current study and that of Sowunmi et al (2015) are similar in that both populations included women with early- and late-stage cervical cancer at presentation. Furthermore, the current study as well as the Ugandan and the Nigerian studies used a similar radiology imaging modality (trans-abdominal ultrasound) to diagnose hydronephrosis (Atuhairwe et al 2011; Sowunmi et al 2015). However, the study populations of research conducted by Goklu et al (2015) in Turkey, Pradhan et al (2011) in the USA, Rose et al (2010) in the USA, and Nóbrega et al 2022 in Brazil were composed of women with advanced disease, which may have explained the high incidence of hydronephrosis ranging from 44.2% to 58.9%. Women with hydronephrosis had a statistically significant shorter mean survival in comparison to those without hydronephrosis (Goklu et al 2015). Goklu et al 2015 results further demonstrated that bilateral hydronephrosis had a shorter mean survival of 29.93 months in comparison to 42.21 months in unilateral hydronephrosis.

Hydronephrosis, particularly if bilateral, may result in renal insufficiency which has a negative impact on oncology management (McArdle and Kigula-Mugambe 2007). In the current study unilateral hydroneprhosis was 31.8% and bilateral hydronephrosis was 68.2%. In a Gynecologic Oncology Group (GOG) study, stage IIIB women who had

hydronephrosis had a poor PFS and OS, regardless of them receiving similar doses of radiation and cisplastin-based chemotherapy compared with those without hydronephrosis (Rose et al 2010). A sub-Saharan study by McArdle and Kigula-Mugambe (2007) found that 29 out of 99 (29.3%) patients with hydronephrosis secondary to cervical cancer had abnormal creatinine. Patients with eGFR of <60ml/min/1.73m² before cervical cancer management had a statistically significant worse OS (Damian et al 2022). In a Brazilian study by Damian et al (2022), women with bilateral hydronephrosis had a significantly (p=0001) low eGFR in comparison to those without hydronephrosis. Hydronephrosis in McArdle and Kigula-Mugambe (2007)'s study in sub-Saharan Africa was diagnosed in 99 patients. Of the 99 patients 56% had unilateral hydronephrosis and 44% had bilateral (McArdle and Kigula-Mugambe 2007). Comparatively, a lower percentage (31.8%) of women in the current study had unilateral hydronephrosis from a total of 85 while Damian et al (2022), Atuhairwe et al (2011) and Mlange et al (2016) found a higher percentage of unilateral hydronephrosis at 52.8%, 60.3% and 65.1% respectively. Interestingly, the findings in the study by Atuhairwe et al (2011) is similar to the current study, where right unilateral kidney hydronephrosis is the most common site of involvement. In the Atuhairwe et al (2011) study, the frequency of right kidney hydronephrosis was 41.4% and left kidney hydronephrosis was 18.9%. In the current study, right and left kidney hydronephrosis were found to be 20% and 11.8% respectively.

Distant metastasis from cervical cancer can involve the liver, lungs and bones. In the current study, trans-abdominal ultrasound was used for staging, thus the presence of liver and lymph nodes metastasis was also assessed as this influences the cancer staging. Liver or lymph node metastasis was detected in 3% and 1% of our study population, respectively. Comparitively, Mlange et al (2016) demonstrated that only 0.9% of women in the Tanzanian study study sample had liver metastasis as a complication of cervical cancer.

5.4 Socio-demographic factors and association with hydronephrosis

5.4.1 Age

The majority (68.4%) of women with cancer of the cervix in the current study were between the ages of 31 and 60 years. Anorlu (2008) and the National Department of Health South Africa (2017) concurs with these findings, determining that most women are diagnosed with cervical cancer at an age when they are economically and socially active. As a result, these women are excluded from participating in the economic and social activities that uplift their families from poverty. These women are excluded from contributing positively to the country's economy, either in the formal or informal sector, by the disease.

In Uganda, Atuhairwe et al (2011) found that advanced age (≥60 years) is associated with an increase in urolological complications at 59.4% but this was not statistically significant. Findings from the current study seem to suggest that younger women presented with hydronephrosis: (>50% of the women with hydronephrosis were between the ages of 31 and 40 while <50% of women with hydronephrosis were older than 60 years) although this was not statistically significant p= 0.57.

5.4.2 Parity and marital status

Mlange et al (2016:3) in Tanzania demostrated that parity of more than 5 is associated with increased cervical cancer cases. In the current study, no association was found between hydronephrosis and parity (p=0.58). This finding may have been influenced by the insufficient capturing of data on parity where almost 50% of the clinical records had no record of parity.

5.4.3 Area and district of residence

In sub-Saharan Africa, the majority (60-75%) of women diagnosed with cervical cancer come from rural areas (Anorlu 2008). According to Statistics South Africa, Limpopo province is a predominantly rural area divided into 25 municipalities, of which 23 are classified as rural municipalities (Stats SA Provinces at a glance 2016:19). The majority (90.5%, n=181) of women were from a rural area according to the current study. However, the association between hydronephrosis and area of residence identified as rural or urban was not found to be statistically significant (p-value of 0.43) in this study.

According to district of residence, Mopani had high representation of women with cervical cancer. This is regardless of the Greater Sekhukhune district being classified more rural than the other districts. On the contrary, women from the more urban Capricorn district had a high prevalence of hydronephrosis, followed by the Mopani district. The association of hydronephrosis and district of residence was not found to be statistically significant (p-value of 0.36).

5.5 Clinical and radiological findings and association with hydronephrosis

According to Bhatla and Denny (2019) and Hricak and Yu (1996), clinical staging is the preferred method of staging cervical cancer due to limited radiological imaging and surgical skills in the LMIC, despite its limitation in the assessment of pelvic sidewall invasion, and local or distant metastasis (Amendola et al 2005). The results of the current study demonstrated that more than 50% of the patients had no clinical staging prior to radiological staging. Similarly, Senganyi-Muchengeti et al (2020) revealed from a population-based cancer registry study that staging information was available in only 45% of records from the African cancer registry network. Among 89 (45.5%) patients who were clinically staged before radiological staging in the current study, the majority (58 patients) had advanced disease with stages ranging from stage IIB to stage IVA. Advanced cervical cancer leads to increased demand for a multidisciplinary management involving radiology, pathology, oncology and psychiatry in these women as it is associated with a higher rate of complications (Finocchario-Kessler et al 2016). 71.5% Of the participants had a tumour of >4cm in largest diameter. According to the 2018 Revised FIGO Staging

of cervical cancer, a tumour of ≥4cm implies an advanced stage carcinoma (Annexure 1). In the current study, there is a significant association between tumour size and hydronephrosis (p-value of <0.001). This is corroborated by Atuhairwe et al (2011) who demonstrated an increase in the number of urological complications with a larger tumour size, although not statistically significant in their study with a p-value of 0.059.

5.6 Conclusion

In conclusion, this study found that urological complications (hydronephrosis, bladder infiltration and vesico-vaginal fistula) were the most common ultrasound findings in cervical cancer patients attending Mankweng Tertiary Hospital, with hydronephrosis being the most prevalent. Other ultrasound findings were liver metastasis and intra-abdominal lymph nodes that might not have been evident through clinical assessment only. Hydronephrosis had a prevalence of more than one third of the studied population, consistent with the results of other African studies. Compared to unilateral hydronephrosis, bilateral hydronephrosis affected two thirds of all women in this study. Consequently, there is an increased probability of having renal insufficiency which will ultimately affect oncology management.

Radiological imaging plays an important role in the staging of cervical cancer. This is demonstrated by other ultrasound findings i.e. liver metastasis and intra-abdominal lymph nodes in this study that might not be observed through clinical assessment. Resource allocation for healthcare in LMIC should be improved to reduce cervical cancer mortality. Increasing resourses to healthcare organisations in these LMIC will enable the purchase of imaging systems which will improve the accuracy of diagnosis compared to only clinical assessment. More accurate diagnoses will potentially enable diagnosis of cervical cancer at earlier stages, leading to better oncology management and increased rates of survival.

5.7 Limitations

The current study included three women who were post TAH. Of these three women, one had hydronephrosis. Hydronephrosis can be due to post TAH complications like ureteric injury and not necessary to cervical cancer complications. Thus inclusion of these patients in the study has contributed to the number of hydronephrosis cases in this study that may be from other causes.

The study is retrospective, thus relies on pre-collected data that is available in the hospital records. Missing clinical information was the main limitation due to the very nature of retrospective studies on pre-existing data.
Lost clinical records and paucity of documentation in the hospital records department may limit the extent to which the findings of this study can be generalised to the rest of the population.

5.8 Recommendations of future research arising from this study

Future research of cervical cancer in Limpopo province arising from the findings of this study could include:

(i) Investigate the cost-effectiveness of clinical staging and basic radiological staging with trans-abdominal ultrasound versus the use of advanced imaging studies such as CT, MRI, and PET/CT in the diagnosis and staging of cervical cancer in Limpopo province.
(ii) Role of intervention radiology in management of hydronephrosis
(iii) How to care for women with cervical cancer and hydronephrosis to prevent complications and improve the quality of life
(iv) To conduct population studies that will investigate risk factors responsible for late diagnosis of cervical cancer at presentation in Limpopo province

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ANNEXURES

Annexure 1: FIGO Staging of the Cervical Cancer (2018)

Box 1 FIGO staging of carcinoma of the cervix uteri (2018).

Stage I:

The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded)

- **IA** Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm[a]
  - **IA1** Measured stromal invasion <3 mm in depth
  - **IA2** Measured stromal invasion ≥3 mm and <5 mm in depth
- **IB** Invasive carcinoma with measured deepest invasion ≥5 mm (greater than stage IA), lesion limited to the cervix uteri[b]
  - **IB1** Invasive carcinoma ≥5 mm depth of stromal invasion and <2 cm in greatest dimension
  - **IB2** Invasive carcinoma ≥2 cm and <4 cm in greatest dimension
  - **IB3** Invasive carcinoma ≥4 cm in greatest dimension

Stage II:

The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall

- **IIA** Involvement limited to the upper two-thirds of the vagina without parametrial involvement
  - **IIA1** Invasive carcinoma <4 cm in greatest dimension
  - **IIA2** Invasive carcinoma ≥4 cm in greatest dimension
- **IIB** With parametrial involvement but not up to the pelvic wall

Stage III:

The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes[c]

- **IIIA** Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
- **IIIB** Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- **IIIC** Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
  - **IIIC1** Pelvic lymph node metastasis only
  - **IIIC2** Paraaortic lymph node metastasis

Stage IV:

The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV

- **IVA** Spread of the growth to adjacent organs
- **IVB** Spread to distant organs

[a]Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all stages.

[b]The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.

[c]Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to stage IIIC. For example, if imaging indicates pelvic lymph node metastasis, the stage allocation would be stage IIIC1r and, if confirmed by pathological findings, it would be Stage IIIc1p. The type of imaging modality or pathology technique used should always be documented. When in doubt, the lower staging should be assigned.

Source: Bhatla *et al.*, 2019:131

Annexure 2: Data collection tool

Study no					
Socio-demographic data					
Age group					
No information	18- 30years	31- 40 years	41- 50 years	51- 60 years	>60 years
Marital status					
No information	Single	Married	Divorced /separated	Widowed	
Parity (number of children)					
No information	Nulliparous (0)	1-2	3-4	≥5	
Source of income					
No information	Unemployed	Employed (formal sector)	Employed (informal sector)	Self employed	
District					
No information	Capricorn	Mopani	Sekhukhune	Vhembe	Waterberg
Area					
No information	Rural	Urban			

Study no				
Clinical and radiological data				
Clinical staging				
No information	IA	IB	IIA	IIB
IIIA	IIIB	IIIC	IVA	IVB
Largest tumour dimension				
No information	<2cm	≥2- 4cm	≥4cm	Post hysterectomy
Hydronephrosis				
Absent	Unilateral (right)	Unilateral (left)	Bilateral	
Other abnormal ultrasound findings				
Absent	Present	Specify if present		

Annexure 3: FHS approval letter

University of Limpopo
Faculty of Health Sciences
Executive Dean
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 2149, Fax: (015) 268 2685, Email:tebogo.mothiba@ul.ac.za

DATE: 15 September 2021

NAME OF STUDENT: **KHOSA RJ**
STUDENT NUMBER: **19900373**
DEPARTMENT: **DIAGNOSTIC RADIOLOGY**
SCHOOL: **MEDICINE**
QUALIFICATION: **MMED**

Dear Student

FACULTY APPROVAL OF PROPOSAL (PROPOSAL NO. FHDC2021/7)

I have pleasure in informing you that your MMED proposal served at the Faculty Higher Degrees Meeting on the 01 September 2021 and your title was approved as follows:

Approved Title: "The prevalence of Hydronephrosis on ultrasound imaging in Women with cervical cancer in Mankweng Hospital, Limpopo Province"

Note the following:

Ethical Clearance	**Tick ne**
Requires no ethical clearance Proceed with the study	
Requires ethical clearance (TREC) (apply online) Proceed with the study only after receipt of ethical clearance certificate	√

Yours faithfully

Prof T.M Mothiba
Chairperson

CC: **Supervisor:** Dr N Muambadzi
Co- Supervisor: Dr F Ooko

Finding solutions for Africa

Annexure 4: TREC Ethics clearance certificate

University of Limpopo
Department of Research Administration and Development
Private Bag X1106, Sovenga, 0727, South Africa
Tel: (015) 268 3935, Fax: (015) 268 2306, Email: anastasia.ngobe@ul.ac.za

TURFLOOP RESEARCH ETHICS COMMITTEE

ETHICS CLEARANCE CERTIFICATE

MEETING: **08 December 2021**

PROJECT NUMBER: **TREC/324/2021: PG**

PROJECT:

Title:	The Prevalence of Hydronephrosis on Ultrasound Imaging in Women with Cervical Cancer in Mankweng Hospital, Limpopo Province
Researcher:	RJ Khosa
Supervisor:	Dr N Muambadzi
Co-Supervisor/s:	Dr F Ooko
School:	Medicine
Degree:	Masters of Medicine in Diagnostic Radiology

PROF P MASOKO
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

Annexure 5: Limpopo Department of Health permission letter

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

Department of Health

Ref : LP-2022-01-002
Enquires : Ms PF Mahlokwane
Tel : 015-293 6028
Email : Phoebe.Mahlokwane@dhsd.limpopo.gov.za

Khosa Refiloe Johana

PERMISSION TO CONDUCT RESEARCH IN DEPARTMENTAL FACILITIES

Your Study Topic as indicated below**;**

The prevalence of hydronephrosis on ultrasound imaging in women with cervical cancer in Mankweng hospital, Limpopo province

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 institution supervisor/s a week before the study is conducted.
    b. The approval is **ONLY** for Mankweng 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

pp **Head of Department** **Date** 07/02/2022

Private Bag X9302 Polokwane
Fidel Castro Ruz House, 18 College Street. Polokwane 0700. Tel: 015 293 6000/12. Fax: 015 293 6211.
Website: http/www.limpopo.gov.za

Annexure 6: Mankweng Hospital permission letter to collect data

Restricted

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH
MANKWENG HOSPITAL

Ref: S5/3/1/2
Enq: Modula MC
From: HR Training and Capacity Development
Date: 10/02/2022
TO : KHOSA RJ

REQUEST FOR PERMISSION TO CONDUCT RESEARCH AT MANKWENG HOSPITAL: "THE PREVALENCE OF HYDRONEPHROSIS ON ULTRASOUND IMAGING IN WOMEN WITH CERVICAL CANCER IN MANKWENG HOSPITAL, CAPRICORN DISTRICT, LIMPOPO PROINCE".

1. The above matter has reference.
2. This is to confirm that the CEO has granted permission to conduct research on **"THE PREVALENCE OF HYDRONEPHROSIS ON ULTRASOUND IMAGING IN WOMEN WITH CERVICAL CANCER IN MANKWENG HOSPITAL, CAPRICORN DISTRICT, LIMPOPO PROVINCE".**
3. Attached please find their application letter, approval from Provincial Office, Research Proposal, and Ethic Committee Clearance Certificate.

Yours in service delivery

Acting Chief Executive Officer
Dr. Muila SL

11/02/2022
Date

DEPARTMENT OF HEALTH
CHIEF EXECUTIVE OFFICER
2022 -02- 10
PRIVATE BAG X 1117 SOVENGA 0727
LIMPOPO PROVINCE

NT.

Private Bag X1117, SOVENGA, 0727 Tel: 015 286 1000 Fax: 015 267 0206
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Restricted
The heartland of Southern Africa – development is about people!