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CLINICOPATHOLOGICAL CHARACTERISTICS OF PANCREATIC CANCER AND THEIR ASSOCIATION WITH MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE: A FIVE-YEAR RETROSPECTIVE CROSS-SECTIONAL STUDY.

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DECLARATION

I, **Wamala Pius**, do hereby declare that this dissertation is my original work and has not been submitted in part or in whole, for publication or for the award of any degree at Makerere University or any other institution. Unless otherwise stated, the views expressed herein are my own, with appropriate references cited

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APPROVAL

This report, titled " **CLINICOPATHOLOGICAL CHARACTERISTICS OF PANCREATIC CANCER AND THEIR ASSOCIATION WITH MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE** ", has been approved for submission by the following supervisors:

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LIST OF ABBREVIATIONS

AE1/AE3	Broad spectrum anti- pan cytokeratin antibody
AJCC	American Joint Committee on Cancer
APC	Adenomatous Polyposis Coli
BRCA2	Breast Cancer Gene 2
CA125	Carbohydrate antigen 125
CAM 5.2	Cytokeratin CAM5.2
CD10	Cluster of Differentiation 10
CD56	Cluster of Differentiation 56
CDKN2A	Cyclin-Dependent Kinase Inhibitor 2A
CEA	Carcinoembryonic antigen
CK 13	Cytokeratin 13
CK 18	Cytokeratin 18
CK 19	Cytokeratin 19
CK 7	Cytokeratin 7
CK8	Cytokeratin 8
CKs	Cytokeratins
CONKO	Charite Onkologie 001 trial
DPC4	Deleted in Pancreatic Carcinoma Locus 4
DUPAN 2	Duke pancreatic monoclonal antigen type 2
HIC	High-income countries
HIV	Human Immunodeficiency Virus
HPF	High power field
IPMNs	Intraductal papillary mucinous neoplasms
KRAS	Ki-ras2 Kirsten rat sarcoma viral oncogene homolog
LKB1	Liver Kinase B1
LMIC:	Low and middle-income countries

MCNs:	Mucinous cystic neoplasms
MUC2	Mucin 2
MUC5AC	Mucin 5 AC
NECs	Neuroendocrine Carcinomas
NETs	Neuroendocrine tumors
NSE	Neuron Specific Enolase
P16	Tumor suppressor gene p16
PALB2	Partner and Localizer of BRCA2
PAS	Period Acid Schiff
PDAC	Pancreatic ductal adenocarcinoma
PENs	Pancreatic endocrine neoplasms
PIK3CA	**Phosphatidy**linositol 4,5-bisphosphate 3-kinase catalytic subunit alpha
SMAD4	Mothers against decapentaplegic homolog 4
SOMREC	School of Medicine Research and Ethics Committee
STK11	Serine threonine kinase 11
TNM	Tumor/Node/Metastasis
TP53	Tumor Suppressor Gene 53
UCI	Uganda Cancer Institute

OPERATIONAL DEFINITIONS

A complete file	A medical record containing patient demographics (age and sex), clinical history, examination findings, and a confirmed pathological and/or radiological diagnosis of pancreatic cancer.
Clinicopathological characteristics**:**	Clinical features (signs and symptoms from history and examination findings), radiological findings, and pathological features (location, tumour size, histological type) of pancreatic cancer.
Cohort**:**	Patients diagnosed with pancreatic cancer from 1st July 2018 to 30th June 2023
Pancreatic cancer:	A histologically confirmed and/or radiologically highly suggestive of malignancy primary to the pancreas.
Mortality rate**:**	The number of deaths per 100,000 individuals per year.
Loss to follow-up**:**	Patients with pancreatic cancer who lacked documentation of follow-up within a year of diagnosis and were unreachable by phone call during the study period.

ABSTRACT

Introduction: Pancreatic cancer is increasingly prevalent in low- and middle-income countries with a poor prognosis. However, its clinico pathological characteristics and outcomes are not well documented in Uganda.

Objective: To describe the clinicopathological characteristics of pancreatic cancer and their association with one-year mortality at Uganda Cancer Institute.

Methods: A five-year retrospective chart review (July 2018-june 2023) was conducted at UCI, analysing medical records of patients with histologically confirmed and/or radiologically highly suggestive of pancreatic cancer. Data on Socio-demographics, clinical characteristics, histopathological features, radiological features, and one-year mortality were collected using a pre-tested pre-coded tool. Outcomes about whether alive or dead were verified via medical records and telephone follow-ups. Statistical analysis was performed using STATA 16.0 with logistic regression to assess associations between clinicopathological characteristics and one-year mortality (odds ratios-OR and 95%confidence intervals). A p-value <0.05 was considered statistically significant.

Results: Of 138 patients (46.4% male and 53.6% female, mean age 54.2 years), epigastric pain was the most common symptom (84.9%) with a median symptom duration of 3.5 months. Tumours were predominantly located in the pancreatic head (68%), followed by the body (21.5%), tail (6.2%), and mixed locations at 4.6%. Adenocarcinoma was the most common histological type (93.8%), followed by intraductal papillary mucinous neoplasm (2.3%), pancreatic neuroendocrine neoplasm (0.8%), acinar cell carcinoma (1.6%), and solid pseudopapillary neoplasm 1.6%. Most tumours were moderately differentiated tumours (58.5%), 31.7% poorly differentiated tumours, and 9.8% well differentiated tumours. The one-year mortality rate was 69.5% with 60%of deaths occurring within 3 months of diagnosis. Weight loss (p value 0.025), low albumin levels (p value 0.023), and elevated levels of CA 19-9(p value 0.029) were significantly associated with mortality.

Conclusion: Pancreatic cancer in Uganda primarily affects middle-aged individuals with a slight female predominance and is associated with a high one-year mortality rate (69.5%), driven by late presentation (stage III and IV). Weight loss, low albumin, and elevated CA 19-9 are significant predictors of mortality.

CHAPTER ONE: INTRODUCTION

1.1 Background

Pancreatic cancer is the sixth leading cause of cancer-related mortality worldwide, with an age-standardized incidence rate rising from 5.0 per 100,000 person-years in 1990 to 5.7 per 100,000 person-years in 2017 (Sung et al., 2021). Although more prevalent in high-income countries, its incidence is increasing in low and middle-income countries, including Uganda, due to lifestyle changes and industrialization(Pourshams et al., 2019). In Uganda, pancreatic cancer ranks as the sixth most common gastrointestinal malignancy(Obayo et al., 2017).

The disease predominantly affects older adults with peak incidence at 65-69 years for males and 75-79 years for females(Pourshams et al., 2019). However, its epidemiology in Uganda remains poorly characterized. With a global five-year survival rate of less than 10%, pancreatic cancer has a dismal prognosis due to late presentation and aggressive tumor biology(Ayres Pereira & Chio, 2019; Deplanque & Demartines, 2017; Siegel et al., 2018; Sung et al., 2021). A study done in Kenya found a one-year survival of only 32%(Muchiri et al., 2024). About 70% of pancreatic cancers originate from the head of the pancreas, presenting with biliary obstruction, manifesting as dark urine, jaundice, anorexia, fatigue, weight loss, and pancreatic insufficiency. Patients with pancreatic cancer in the body and tail of the pancreas present with abdominal pain, back pain, anorexia, weight loss, and fatigue (Park et al., 2021; Walter et al., 2016). Features of biliary obstruction are red-flag signs of an advanced disease among these patients. Most patients present with metastatic disease or locally advanced disease, and only 10-15% have resectable tumors at diagnosis(Kolbeinsson et al., 2023)

The prognosis of pancreatic cancer depends on several factors such as age, sex, tumor size and location, histological type, histologic differentiation, and treatment modalities (Kang et al., 2021; Ren et al., 2022; Zhang et al., 2021). Despite advanced diagnostic and therapeutic capabilities at Uganda Cancer Institute, a regional center of excellence, local data on clinic pathological characteristics and mortality rate are scarce. This study aims to address this gap by examining these factors and their association with one-year mortality at UCI

1.2 Problem Statement

Pancreatic cancer has a high mortality rate. The five-year survival rate of pancreatic cancer globally is less than 10%. Despite the advancements in diagnostic and management strategies for pancreatic cancer over the last four decades, the prognosis has barely improved (Hall et al., 2018). A recent Kenya study reported a one-year survival rate of only 32% reflecting late presentation, with 60% of patients having metastatic disease and 25-30% having locally advanced disease at diagnosis (Kolbeinsson et al., 2023; Muchiri et al., 2024). Nonspecific signs and symptoms often lead to delayed diagnosis and management.

Although the Uganda Cancer Institute is equipped to diagnose and treat pancreatic cancer, there is limited local data on its clinicopathological characteristics and their association with mortality, particularly within the first year of diagnosis. This gap in the literature limits the ability to evaluate patient outcomes and optimize treatment strategies in a Ugandan context. Given the increasing burden of pancreatic cancer in LMIC and MIC, generating such data is critical for improving early diagnosis, guiding clinical decision making and and enhancing survival outcomes..

1.3 Justification

Pancreatic cancer's high mortality rate and late presentation necessitate a deeper understanding of its clinicopathological characteristics in Uganda. The global five-year survival rate is less than 10% and a Kenyan study reported a one-year survival rate of 32%(Muchiri et al., 2024). Non-specific symptoms contribute to delayed diagnosis, with most patients presenting with advanced disease. This study will provide critical data on the clinical presentation, tumour characteristics, and one-year mortality at UCI, informing clinical practice and guiding treatment decisions. The findings will also contribute to the limited literature on pancreatic cancer in sub-Saharan Africa, facilitating regional comparisons with HICs, supporting evidence-based interventions, and guiding future research directions.

1.4 Significance for the study

This study will provide foundational insights into the clinicopathological characteristics of pancreatic cancer and their association with 1-year mortality rates at UCI. These findings will enhance clinical management in the country by informing treatment protocols and highlighting prognostic factors. Additionally, the study will contribute to the sparse literature on pancreatic

cancer in sub-Saharan Africa, enabling comparisons with HICs and addressing regional disparities in disease presentation and outcomes. The results may guide future research and policy to improve early diagnosis and survival rates.

1.5 Research Questions

1. What are the clinicopathological characteristics of pancreatic cancer patients at the Uganda Cancer Institute?
2. What is the one-year mortality rate among pancreatic cancer patients at the Uganda Cancer Institute?
3. How are the clinicopathological characteristics associated with the year mortality rate at Uganda Cancer Institute?

1.6 Study Objectives

1.6.1 General Objective

To describe the clinicopathological characteristics and the associated mortality rate within a year of diagnosis among patients with pancreatic cancer at Uganda Cancer Institute.

1.6.2 Specific Objectives

1. To characterize the clinicopathological characteristics of patients with pancreatic cancer at the time of diagnosis at the Uganda Cancer Institute.
2. To determine the mortality rate among patients with pancreatic cancer within a year after diagnosis at Uganda Cancer Institute.
3. To evaluate the association between the clinicopathological characteristics of pancreatic cancer and the mortality rate within a year of diagnosis

1.7 Conceptual framework

Fig.1: A conceptual framework

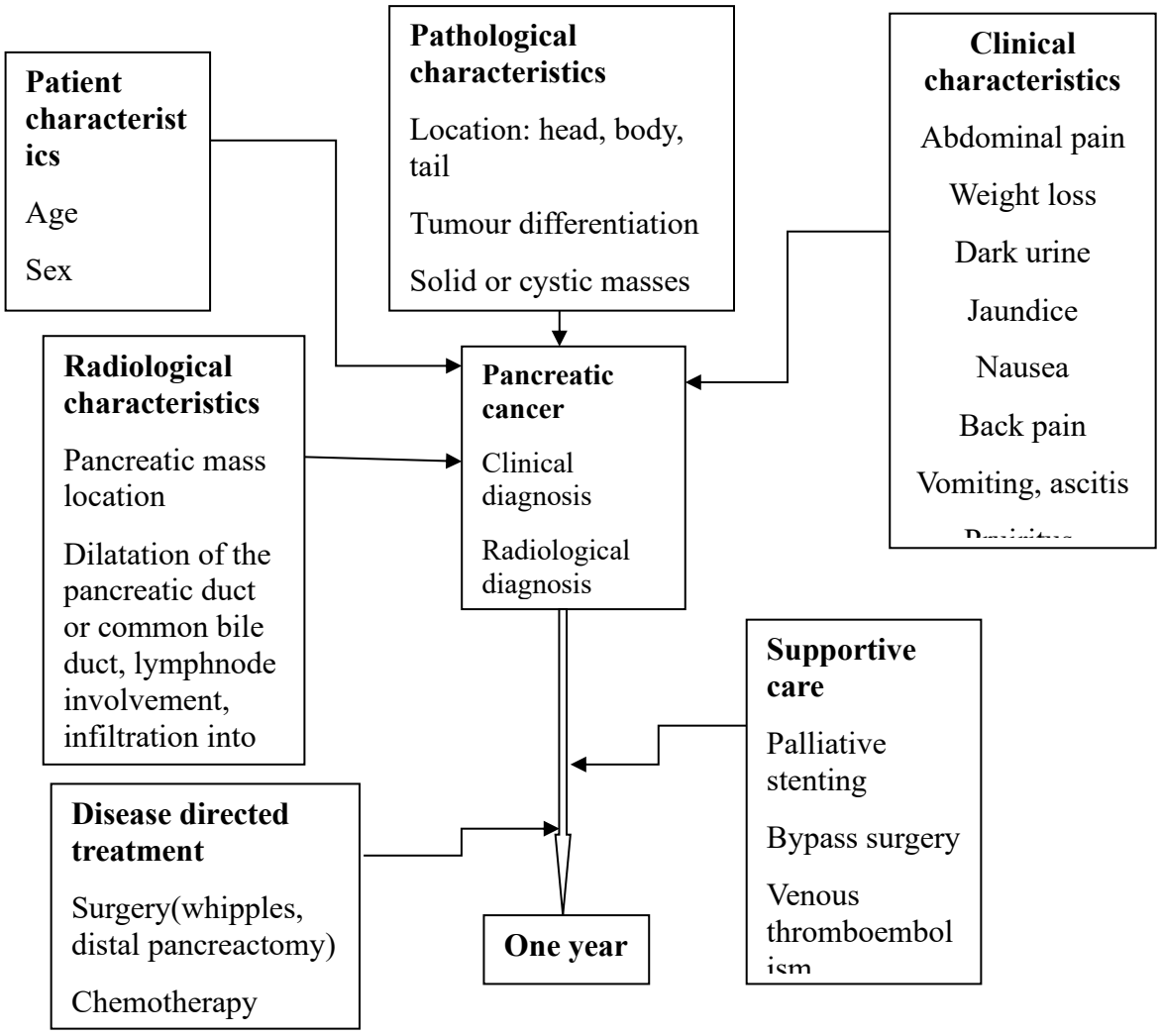


Figure 1 shows the relationship between the sociodemographic and tumor characteristics of pancreatic cancer, treatment modalities, and disease outcomes in terms of mortality or survival. Age, sex, alcohol use, smoking, body mass index, and clinical characteristics affect the tumor characteristics, affecting the management plan and disease outcome. Our study will describe the clinicopathological characteristics and mortality rates within a year of diagnosis of pancreatic cancer at the Uganda Cancer Institute using a retrospective study design.

1.8 Narrative for the conceptual framework

This conceptual framework illustrates the relationship between patient Sociodemographic characteristics (e.g, age, sex, smoking, alcohol use), clinical features (e.g, symptoms, examination findings), pathological characteristics (e.g, tumor size, histological type), and radiologic findings of pancreatic cancer. These are required in the diagnosis of pancreatic cancer. These factors influence treatment modalities and ultimately disease outcomes (mortality or survival). The framework guides this retrospective study in examining how these variables interact to affect one-year mortality at UCI.

CHAPTER TWO: LITERATURE REVIEW

2.1 Overview of Pancreatic Cancer

Pancreatic cancer is the sixth leading cause of cancer-related mortality globally (Sung et al., 2021). There's a higher incidence of pancreatic cancer in high-income countries compared to low- and middle-income countries (Pourshams et al., 2019). The burden of pancreatic cancer in sub-Saharan Africa is not well documented, although anecdotal observations report an increasing trend of disease among people in the region (Obayo et al., 2017).

The risk of pancreatic cancer increases with age, with more than 80% of the cases occurring between 60 and 80 years, albeit with a peak incidence between 70 and 80 years. Pancreatic cancer is rare before the age of 40 unless there are associated genetic risk factors such as Peutz-Jeghers syndrome (Fernandez-del Castillo & Jimenez, 2017; Pourshams et al., 2019; Sanchez & Cheung, 2015). The disease has a predilection for males (Fernandez-del Castillo & Jimenez, 2017; Pourshams et al., 2019; Sanchez & Cheung, 2015).

Other risk factors for pancreatic cancer include cigarette smoking, alcohol, diet, high-calorie intake, obesity, physical inactivity, exposure to certain chemicals such as beta-naphthylamine, benzamine, dichlorodiphenyltrichloroethane, and diseases such as diabetes mellitus and chronic pancreatitis (Fernandez-del Castillo & Jimenez, 2017; Pourshams et al., 2019; Sanchez & Cheung, 2015)

Surgical resection offers the only potential cure; however, less than 20% of patients are candidates for surgery at the time of diagnosis (Fernandez-del Castillo & Jimenez, 2017). Routine screening is futile on low-risk individuals, and there's no low-cost, affordable test with a high sensitivity and specificity currently (Fernandez-del Castillo & Jimenez, 2017).

The prognosis of pancreatic cancer is poor, owing to the early systemic spread and locally aggressive tumor growth(Allen et al., 2017; Fernandez-del Castillo & Jimenez, 2017; Pourshams et al., 2019; Ryan & Mamon, 2016; Sanchez & Cheung, 2015). By presentation, up to 60% of patients have distant metastatic disease, 25-30% have a regionally localized disease, and 10-15% have a truly localized disease (Kolbeinsson et al., 2023).

2.2 Epidemiological Characteristics of Pancreatic Cancer

Globally, pancreatic cancer's incidence is higher in high-income countries but is increasing in low and middle-income countries due to urbanization and lifestyle changes (Moraa & Degu, 2021; Muchiri et al., 2024; Pourshams et al., 2019).

The disease is rare before age 45years with peak incidence at 65-69 years for males and 75-79 years for females (Pourshams et al., 2019). A Kenyan study reported a younger median age of 58.5 years, suggesting regional differences (Muchiri et al., 2024; Pourshams et al., 2019). In Uganda, epidemiological data are limited.

Pancreatic cancer has a slight male predominance globally with a predilection towards people of African ancestry, though some African studies report a higher female predominance (Moraa & Degu, 2022; Muchiri et al., 2024; Siegel et al., 2024).

Modifiable risk factors for pancreatic cancer, smoking (relative risk 1.5), high fasting plasma glucose (8.9%), and high body mass index (increases risk 1.72 fold)(Michaud et al., 2001; Pourshams et al., 2019). Other factors include physical inactivity, alcohol consumption, and genetics (Fernandez-del Castillo & Jimenez, 2017). Additionally, overweight and obese individuals may develop pancreatic cancer at a younger age and have poorer survival rates (Li et al., 2009; Yuan et al., 2013).

The relationship between diet and pancreatic cancer remains elusive; however, a Western dietary pattern, characterized by a high intake of saturated fat and processed meats, has been linked to an increased risk in some studies (Larsson et al., 2014; Nöthlings et al., 2005; Silverman et al., 1998; Thiébaut et al., 2009), but not all (Michaud et al., 2003; Michaud et al., 2005; Rohrmann et al., 2013). Some case-control studies suggest a protective effect from consuming fresh fruits and vegetables, but this has not been observed in prospective studies (Coughlin et al., 2000; Gold et al., 1985; Howe et al., 1990; Norell et al., 1986). Studies about diet and the risk of developing cancer are warranted in a sub-Saharan African population.

Coffee and alcohol consumption have shown conflicting results regarding their impact on pancreatic cancer risk (Fernandez-del Castillo & Jimenez, 2017). Pooled analyses suggest a small effect of alcohol consumption limited to heavy drinkers, but this is confounded by smoking

(Lucenteforte et al., 2012; Michaud et al., 2010). Coffee intake has also shown inconsistent results, with a meta-analysis finding no significant association after adjusting for smoking (Turati et al., 2012).

Aspirin and NSAID use have been studied for their potential inhibitory effect on pancreatic tumorigenesis, but the data are conflicting (Anderson et al., 2002; Bradley et al., 2010; Cook et al., 2005; Gridley et al., 1993; Jacobs et al., 2004; Langman et al., 2000; Schernhammer et al., 2004; Schreinemachers & Everson, 1994; Streicher et al., 2014). Some studies suggest a possible increased risk with extended regular aspirin use (Schernhammer et al., 2004), while others have not found any link, even with high-frequency use (Jacobs et al., 2004).

At diagnosis, 54-60% of patients have metastatic disease, 25-30% have locally advanced disease, and only 10-15% have respectable disease (Fernandez-del Castillo & Jimenez, 2017; Muchiri et al., 2024).

2.3 Clinicopathological Characteristics of Pancreatic Cancer

2.3.1 Clinical Characteristics of Pancreatic Cancer

Pancreatic cancer presents with nonspecific symptoms complicating early diagnosis(Park et al., 2021). A significant number of patients present with an unrespectable (locally advanced) or metastatic disease (Park et al., 2021). Walter *et al.* conducted a prospective study among 391 patients with suspected pancreatic cancer (Walter et al., 2016). The authors compared 119 participants who later had a diagnosis of PDAC with 47 who had other cancers and 225 who did not have pancreatic cancer. No initial symptoms were identified that could differentiate between participants who had PDAC from those who didn't. For instance, 28%, 27%, and 27% of participants with PDAC and 31%, 39%, and 22% of those without PDAC reported decreased appetite, indigestion, and a change in bowel habits, respectively.

About 70% of pancreatic cancers originate from the head of the pancreas, presenting with biliary obstruction, manifesting as dark urine, jaundice, anorexia, fatigue, weight loss, and pancreatic insufficiency in 49%, 49%, 48%, 51%, 55%, and 25%, respectively (Walter et al., 2016). Patients with pancreatic cancer in the body and tail of the pancreas present with abdominal pain, back pain, anorexia, weight loss, and fatigue (Park et al., 2021; Walter et al., 2016). Features of biliary

obstruction are red-flag signs of an advanced disease among these patients. Pancreatic cancer can manifest as new-onset or worsening diabetes mellitus, and rarely as acute pancreatitis (Aslanian et al., 2020).

2.3.2 Pathological Characteristics of Pancreatic Cancer

There are several forms of pancreatic cancer, among which include: pancreatic ductal adenocarcinoma, mucinous neoplasm, intraductal papillary mucinous neoplasm, pancreatic neuroendocrine neoplasms, solid-pseudopapillary neoplasm of the pancreas, and acinar cell carcinoma (Sanchez & Cheung, 2015).

2.3.2.1 Pancreatic ductal adenocarcinoma

Pancreatic ductal adenocarcinoma is the most prevalent form of pancreatic cancer, comprising 90-95% of all pancreatic cancers(Becker et al., 2014; Cascinu et al., 2010), and its incidence shows a geographical disparity: more reported in the HIC than in the LMICs (Pourshams et al., 2019). The predilection of PDAC lies within the pancreatic head, although its emergence in the body or tail is not uncommon (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). Tumor size demonstrates remarkable variability, encompassing a spectrum from microscopic lesions to formidable masses exceeding 10 centimeters in the greatest dimension (Sanchez & Cheung, 2015). Notably, in the head of the pancreas, PDAC can impede bile duct flow and infiltrate neighboring organs (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). It is noteworthy that differentiating PDAC from fibrotic regions associated with chronic pancreatitis solely based on gross examination can present a significant challenge (Sanchez & Cheung, 2015).

2.3.2.2 Mucinous cystic neoplasms

Mucinous cystic neoplasms (MCNs) are epithelial neoplasms characterized by the production of mucin and the presence of a distinctive ovarian-type stroma (Zamboni et al., 1999). The neoplastic epithelial cells form cysts filled with mucinous fluid (Zamboni et al., 1999). MCNs are further classified based on the degree of architectural and cytological atypia into three categories: low-grade dysplasia, moderate dysplasia, and high-grade dysplasia (Sanchez & Cheung, 2015). Notably, MCNs exhibit a strong female predominance, occurring almost exclusively in women (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). In cases where an invasive cancerous component is

present within the MCN, the lesion is designated as MCN with associated invasive carcinoma (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015).

2.3.2.3 Intraductal papillary mucinous neoplasm

Intraductal papillary mucinous neoplasms (IPMNs) represent the most prevalent and well-characterized type of intraductal pancreatic neoplasm (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). Noninvasive IPMNs are further categorized into distinct groups based on the severity of architectural and cytological dysplasia: low-grade dysplasia, moderate dysplasia, and high-grade dysplasia (also known as intraductal papillary mucinous carcinoma in situ) (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). IPMNs arise within the pancreatic ductal system, either the main pancreatic duct or its branches, and typically exhibit a papillary growth pattern (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015).

2.3.2.4 Pancreatic neuroendocrine neoplasms

Pancreatic endocrine neoplasms (PENs) are tumors characterized by predominant neuroendocrine differentiation (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). The majority exhibit well-differentiated features and are considered low-grade malignancies (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). The classification system categorizes PENs into two main groups: well-differentiated neoplasms (further subdivided into low-grade and intermediate grade) and poorly differentiated neuroendocrine carcinomas (high-grade) (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015).

2.3.2.5 Solid-pseudopapillary neoplasm of the pancreas

It is a low-grade malignant epithelial neoplasm, comprising poorly cohesive polygonal epithelial cells that form solid and pseudopapillary structures, with uniform nuclei and nuclear grooves (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015). Cancer occurs more in women than men (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015).

2.3.2.6 Acinar cell carcinoma

Acinar cell carcinoma has been reported in about two percent of pancreatic cancer cases (Sanchez & Cheung, 2015), occurring in people between the ages of seventy and eighty years. It affects more males than females (Haeberle & Esposito, 2019; Sanchez & Cheung, 2015).

2.3.3 Radiological characteristics of pancreatic cancer

A variety of imaging techniques can be used in the initial diagnostic assessment of pancreatic lesions. These include: abdominal ultrasound scan, multidetector computed tomography (MDCT), magnetic resonance imaging (MRI), endoscopic ultrasound, and fluorodeoxyglucose positron emission tomography. MDCT is the standard diagnostic test. EUS is the most sensitive nonoperative imaging test for the detection of malignant pancreatic lesions, with a reported sensitivity between 87%-100%(Lin et al., 1989; Wang et al., 2013). This is superior to transabdominal ultrasound with reported sensitivity between 64%-91%(Palazzo et al., 1993). It is also considered superior to a conventional CT scan (Wang et al., 2013). EUS is particularly useful for the identification of small tumors that are not visualized by other imaging modalities (making it an excellent screening tool), obtaining tissue for FNA or FNB to confirm diagnosis and staging.

PET scans are particularly useful in determining the presence of metastases

2.4 Staging of Pancreatic Cancer

Pancreatic cancer is staged using the American Joint Committee on Cancer (AJCC) tumor/node/metastasis (TNM) classification and staging system, 8th Edition 2017(Tempero et al., 2021). Pancreatic cancer is categorized as resectable, borderline resectable, locally advanced, or metastatic. Resectable disease is treated with surgical resection and adjuvant chemotherapy, while borderline and locally advanced disease is treated with neoadjuvant chemotherapy followed by surgical resection. Metastatic disease is treated with chemotherapy and supportive care.

Table 1 outlines the TNM classification, and Table 2 presents the anatomical staging.

Table 1: TNM classification of pancreatic cancer

Primary tumor (T)	**Description**
TX	Primary tumors cannot be assessed
T0	No evidence of a primary tumor
Tis	Carcinoma in situ; includes high-grade pancreatic intraepithelial neoplasia, intraductal papillary mucinous neoplasm with high-grade dysplasia, intraductal tubulopapillary neoplasm with high-grade dysplasia, and mucinous cystic neoplasm with high-grade dysplasia.
T1	Tumor limited to the pancreas, ≤2 cm in greatest dimension T1a - Tumor ≤0.5 cm in greatest dimension T1b - Tumor >0.5 cm and < 1 cm in greatest dimension T1c - Tumor 1–2 cm in greatest dimension
T2	Tumor limited to the pancreas, >2 cm and ≤4 cm in greatest dimension.
T3	Tumor >4 cm in greatest dimension
T4	Tumor involves the celiac axis, superior mesenteric artery, and/or common hepatic artery, regardless of size.
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N2	Metastasis in ≥4 regional lymph nodes
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

Table 1: TNM Classification for Pancreatic Cancer

Table 2: Anatomical staging

Stage	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T2	N0	M0
IIA	T3	N0	M0
IIB	T1,T2,T3	N1	M0
III	T1,T2,T3	N2	M0
III	T4	Any N	M0
IV	Any T	Any N	M1

2.5 Treatment of Pancreatic Cancer

The only modality of treatment for pancreatic cancer that offers a glimmer of hope is surgery; however, only 20% of the patients may be promised a 'cure' at diagnosis(Jiang et al., 2022). Regardless of the mode of surgery, most patients get metastases, or their cancer becomes locally advanced, and this often requires radical resection (Conroy et al., 2016; Van der Gaag et al., 2010). It is imperative to devise alternative treatments by thoroughly classifying the tumor as resectable, borderline resectable, locally advanced, or metastatic pancreatic cancer (Conroy et al., 2016).

Conventionally, pancreatoduodenectomy is employed for removing tumors that involve the head of the pancreas (Jiang et al., 2022) and distal pancreatectomy with or without splenectomy for tumours in the body or tail of the pancreas (Jiang et al., 2022). For locally advanced tumors, total pancreatectomy may achieve radical resection. The overall 5-year survival rate after surgery is less than 20%, but this can be slightly improved with adjuvant chemotherapy (Conroy et al., 2016).

Because the postsurgical recurrence rates of pancreatic cancer are high, patients may often benefit from adjuvant chemotherapy, albeit not drastically improving the survival rate due to low vasculature and a build-up of an immunosuppressive cancer-associated microenvironment around the pancreas (Brunner et al., 2019; Conroy et al., 2016). Chemotherapeutic drugs that are often used include gemcitabine, 5-Fluorouracil, cisplatin, doxorubicin, irinotecan, oxaliplatin, and

leucovorin (Manji et al., 2017; Miura et al., 2010; Oettle & Riess, 2002; Rombouts et al., 2016). These may be used in combination according to the international guidelines.

It is widely known that pancreatic cancer lesions induce a build-up of an immunosuppressive cancer-associated microenvironment, which impedes drug penetration and suppresses immune reactions by augmenting immunosuppressive cytokines such as interleukin-6 and interleukin-10 (Looi et al., 2019; Manji et al., 2017). Immunotherapy has emerged as a promising field with drugs such as Ipilimumab (Graziani et al., 2011), nivolumab, and pembrolizumab (Mace et al., 2016) being approved or tried for the treatment of pancreatic cancer. These may break the immunosuppressive barrier and improve the overall survival rate among patients with pancreatic cancer (Jiang et al., 2022).

2.6 Prognosis of Pancreatic Cancer

In a 2024 retrospective cohort study, Muchiri et al. reported a 1-year survival rate of 32% among patients with pancreatic cancer at a tertiary hospital in Kenya (Muchiri et al., 2024). Despite achieving complete surgical resection, a significant proportion of patients with pancreatic adenocarcinoma succumb to their disease (Allen et al., 2017). Nodal status reigns supreme as the most impactful prognostic factor in this setting (Allen et al., 2017). The stark difference in five-year survival rates between node-negative (approximately 30%) and node-positive disease (approximately 10%, even with solitary metastasis) underscores this primacy (Allen et al., 2017; Kang et al., 2014). Notably, roughly two-thirds of newly diagnosed patients present with positive lymph nodes, translating to a poorer overall prognosis (Kang et al., 2014). This observation serves as a cornerstone for the rationale behind neoadjuvant chemotherapy in patients with resectable or borderline-resectable disease (Ryan & Mamon, 2016).

While overall five-year survival rates for pancreatic adenocarcinoma remain sobering, the concept of "conditional survival" offers a more dynamic perspective (Ryan & Mamon, 2016). This concept estimates the probability of surviving a specific timeframe given prior survival duration (Mayo et al., 2012). A retrospective analysis of patients undergoing curative-intent surgery highlights the significance of conditional survival (Mayo et al., 2012). This study demonstrated a remarkable improvement in two-year conditional survival at three years (66%) compared to the five-year actuarial survival rate of 18% (Mayo et al., 2012). Interestingly, patients with high lymph node

ratios or positive margins exhibited the greatest gains in conditional survival with increasing time elapsed since treatment, suggesting the potential for long-term disease control in a subset of patients (Mayo et al., 2012).

Several additional factors beyond tumor stage and nodal status influence postoperative outcomes (Ryan & Mamon, 2016). These include surgical margin status, tumor differentiation, lymphatic invasion within the tumor, pre-and postoperative serum CA 19-9 levels, and cigarette smoking status (Benassai et al., 2000; Cameron et al., 2006; Chang et al., 2009; Franko et al., 2013; Geer & Brennan, 1993; Helm et al., 2009; Kinsella et al., 2008; Meyer et al., 2000; Millikan et al., 1999; Pelucchi et al., 2014; Raut et al., 2007; Sohn et al., 2000; Yeo et al., 1997; Yuan et al., 2017). Importantly, the CONKO-001 trial examining adjuvant gemcitabine demonstrates that long-term survival is achievable even in the presence of positive nodes or involved margins, with 15% of patients achieving five-year survival (Sinn et al., 2013).

The prognostic significance extends beyond the simple presence or absence of lymph node metastasis (Ryan & Mamon, 2016). The number of positive nodes plays a crucial role, with the AJCC TNM staging system incorporating this factor for more refined risk stratification (Allen et al., 2017). Similarly, the total number of lymph nodes examined during surgery impacts prognosis. Data suggest that analyzing at least fifteen lymph nodes is essential for accurate staging of node-negative disease, mirroring observations in other gastrointestinal malignancies (Tomlinson et al., 2007).

Validated nomograms incorporating various clinicopathological and surgical variables have been developed to predict a patient's three-year post-operative pancreatic cancer mortality risk (Brennan et al., 2004). These tools may offer valuable prognostic information to guide clinical decision-making, although most currently available nomograms utilize the seventh edition AJCC criteria and do not integrate the latest (eighth edition) staging system (Brennan et al., 2004; Ferrone et al., 2005; Strijker et al., 2020; Tol et al., 2015).

CHAPTER THREE: METHODOLOGY

3.1 Study Design

The study was a retrospective cross-sectional study at the Uganda Cancer Institute (UCI) of medical records of pancreatic cancer patients.

3.2 Study Site

The study was conducted at UCI. UCI is a public, specialized, tertiary care health facility that's affiliated with Makerere University College of Health Sciences and Mulago National Referral Hospital. It is located along Upper Mulago Hill Road, about 4.5 km north of Kampala's central business district. With an 80-bed capacity, UCI attends to more than 800 patients monthly. It is East Africa's Centre of Excellence for Oncology that receives patients from other neighbouring countries, which include Congo, South Sudan, Rwanda, Eritrea, among others. Among the patients who receive care at UCI are those with pancreatic cancer. These patients are often referred from Mulago National Referral Hospital, regional referral hospitals, private and not-for-profit hospitals, and District hospitals. Such treatment employs a multidisciplinary team of experts from UCI, Mulago National Referral Hospital, and Makerere University, College of Health Sciences that includes medical oncologists, surgical oncologists, medical pathologists, radiologists, radiotherapists, laboratory technologists, and palliative care specialists. This makes it ideal for this study.

3.3 Study Duration

Medical records of patients who had pancreatic cancer over five years (from 1st July 2018 to 30th June 2023) were reviewed. Data collection occurred over 4 weeks in February and March 2025.

3.4 Study Population

3.4.1 Target Population

Patients diagnosed with pancreatic cancer in Uganda.

3.4.2 Accessible Population

Patients with a histopathologic and/or radiological diagnosis of pancreatic cancer managed at UCI between 1st July 2018 and 30th June 2023.

3.4.3 Sample Population

Medical records of patients above 18 years with a confirmed histopathologic and/or radiologic diagnosis of pancreatic cancer at UCI between 1st July 2018 and 30th June 2023.

3.5 Eligibility Criteria

3.5.1 Inclusion Criteria

- Medical records of patients who had a histopathological and/or radiological diagnosis of pancreatic cancer.

3.5.2 Exclusion Criteria

- Medical records with incomplete data (particularly lacking key variables)—such as missing age, sex, history, and examination findings, histological or radiological confirmation of pancreatic cancer—and those for which such information could not be retrieved from any other data tools were excluded from the study.

3.6 Sample Size Determination

All eligible medical records of patients with histopathological and radiological diagnosis of pancreatic cancer were retrieved between 1st July 2018 and 30th June 2023. The sample size was estimated as follows.

Objective one: Since the accessible population was finite and estimated at around 195 patients, the Finite Population Correction formula was used to estimate the sample size.

$$n = \frac{N * Z_{\frac{\alpha}{2}}^{2} * P * (1 - P)}{d^2 * (N - 1) + Z_{\frac{\alpha}{2}}^{2} * P * (1 - P)}$$

Where n = calculated sample size, $Z_{\frac{\alpha}{2}}$ = normal deviation of 1.96, which gives a 5% level of significance. P = 73% the prevalence of abdominal pain (the most common clinic pathological characteristics) among patients with pancreatic cancer in Kenya (Muchiri et al., 2024), N = 195 is the total population size, and d = maximum allowable error (precision) of 5%.

$n = \frac{225 \times 1.96^2 \times 0.73 \times 0.27}{d^2 \times (225-1) + 1.96^2 \times 0.73 \times 0.27} = 119$

Adjusting for missing data

The study anticipated some missing data from some records selected for the study. Therefore, the sample size was adjusted using the formula:

$$adjusted\ Sample\ size(w) = \frac{calculated\ sample\ size}{1 - loss\ to\ missing\ data\ rate}$$

Considering a loss to follow-up rate of 10%, the sample size becomes: $w = \frac{119}{1-0.1} = 133$

After adjusting for missing data in the records, the sample size for objective one was 133.

Objective two: Since the accessible population is finite and estimated at around 195 patients, the Finite Population Correction formula will be used to estimate the sample size.

$$n = \frac{N * Z_{\frac{\alpha}{2}}^{2} * P * (1 - P)}{d^2 * (N - 1) + Z_{\frac{\alpha}{2}}^{2} * P * (1 - P)}$$

Where n = calculated sample size, $Z_{\frac{\alpha}{2}}$ = normal deviation of 1.96, which gives a 5% level of significance. P = 68% the median mortality rate among patients with pancreatic cancer in Kenya (Muchiri et al., 2024), N = 195 is the total population size, and d = maximum allowable error (precision) of 5%.

$n = \frac{195 \times 1.96^2 \times 0.68 \times 0.32}{d^2 \times (1955-1) + 1.96^2 \times 0.68 \times 0.32} = 124$

Adjusting for missing data

The study anticipated some missing data from some records selected for the study. Therefore, the sample size was adjusted using the formula:

$$adjusted\ Sample\ size(w) = \frac{calculated\ sample\ size}{1 - loss\ to\ missing\ data\ rate}$$

Considering a missing data rate of 10%, the sample size became: $w = \frac{124}{1-0.1} = 138$

After adjusting for missing data in the records, the sample size for objective two was 138.

Objective three: Due to paucity of information about the relationship between clinic pathological characteristics and mortality rate within a year of diagnosis in sub-Saharan Africa, the sample size was estimated using Stata software for simpler comparisons of survival curves reported by Machir et al. (2024). Stata has built-in functions for sample size calculations. These tools often allow calculations with fewer parameters to consider. For this study calculation requires input of a hazard ratio of 0.2 (Muchiri et al., 2024) and specifying a significance level of 0.05 and 80% power. Therefore, the sample size for objective three will be estimated at 106 using this approach.

Adjusting for missing data

The study anticipated some missing data from some records selected for the study. Therefore, the sample size was adjusted using the formula:

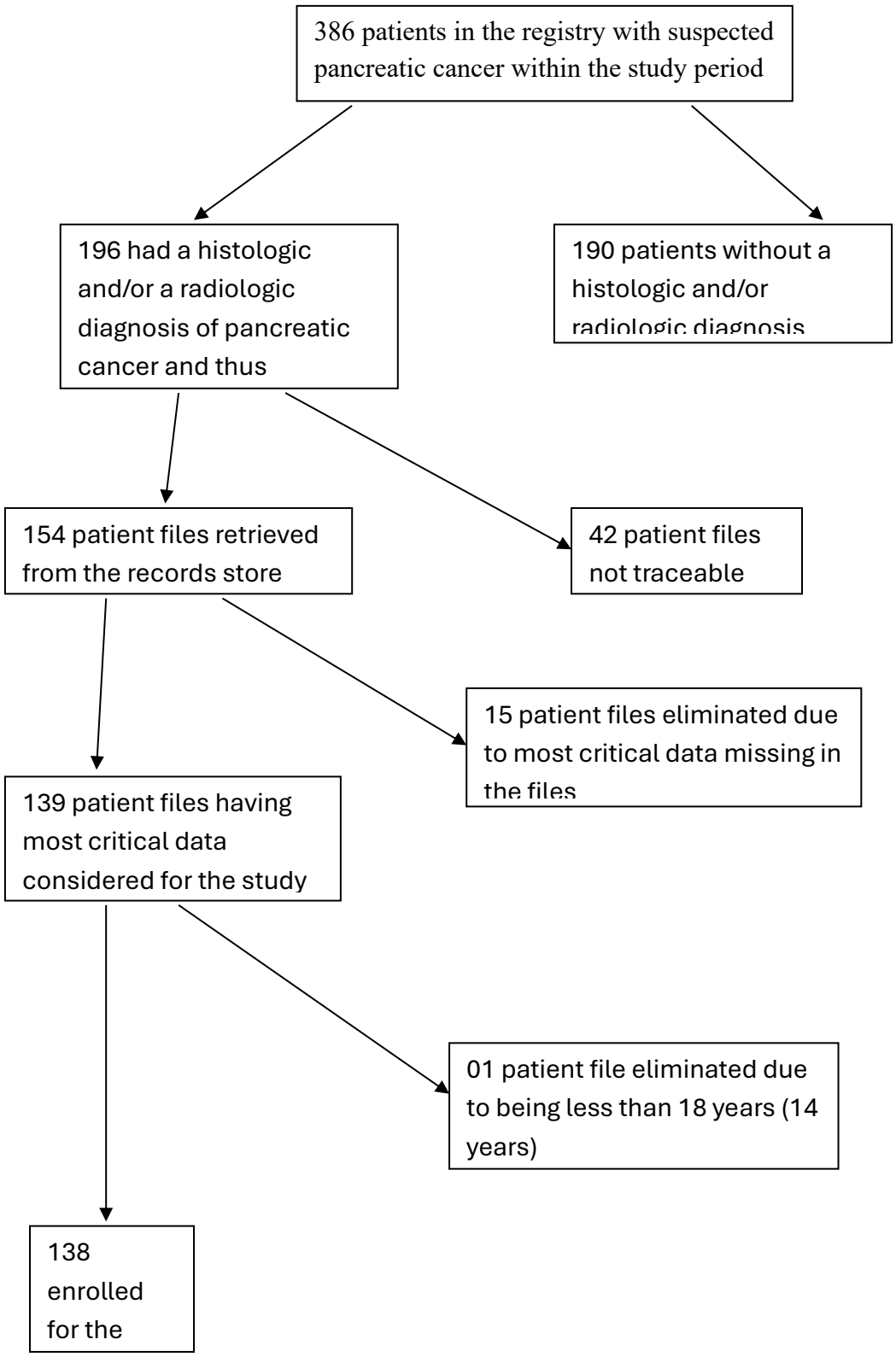
$$adjusted\ Sample\ size(w) = \frac{calculated\ sample\ size}{1 - loss\ to\ missing\ data\ rate}$$

Considering a missing data rate of 10%, the sample size became: $w = \frac{106}{1-0.1} = 118$

After adjusting for missing data in the records, the sample size for objective three was 138.

Therefore, the effective sample size for this study was 138 patients with pancreatic cancer since this was the largest sample size estimated.

Figure 1: Diagrammatic representation of sampling



3.7 Sampling Method

Consecutive sampling of medical records of patients with a histopathologic and/or radiologic diagnosis of pancreatic cancer was employed.

3.8 Study Variables:

3.8.1 Dependent variable

- Mortality within a year of diagnosis from pancreatic cancer

3.8.2 Independent variables

- Sociodemographic characteristics – age, sex, body mass index, smoking, and alcohol use.
- Clinical characteristics – symptoms and their duration at initial diagnosis, date at diagnosis or enrollment into care, tumor location, tumor grade, histological type, TNM staging, radiological characteristics, and comorbidities such as HIV and Diabetes Mellitus.
- Treatment modalities – surgery (Whipple, bypass, local resection, palliative stenting, distal pancreactomy), chemotherapy – adjuvant, neoadjuvant, and/or palliative chemotherapy.

3.9 Data Collection Procedure

A pre-coded structured data extraction tool was used to collect data on sociodemographic details, clinical presentation, physical examination findings, radiologic and pathologic characteristics. Charts of confirmed pancreatic cancer patients managed at UCI between 1st July 2018 and 30th June 2023 were retrospectively reviewed. Patients numbers of patients seen with pancreatic cancer within the study period were retrieved from the UCI Database. The files were retrieved from the records offices. The required information was retrieved from each patient's chart, including age, sex, history of alcohol use or smoking, tumour location, histological type, grade (TNM), stage, and disease outcomes. The patient's initial laboratory results when they were enrolled into care were also extracted from the files into the data extraction tool. Treatment details, including surgical procedures, chemotherapy, and radiotherapy, were also collected. Phone calls were made to patients who were no longer in contact with UCI staff, either through the patients themselves or their next of kin, to ascertain survival status. Verbal consent was sought from these patients or their next of kin before the interview was carried out. The dates were recorded and archived using a telephone script.

In cases of grief during telephone interviews with individuals who had lost their loved ones, a supportive atmosphere was ensured. The interviewers listened actively, allowed participants to express their feelings, showed empathy, and exercised patience. Participants were given the option to pause and resume the conversation later, and counseling services were suggested in extreme cases.

Data was collected and stored using the Epidata client.

3.10 Data Management

3.10.1 Data Analysis

The retrieved and aggregated data were checked, organized, coded, and stored using the Epidata client. The data were then exported to STATA 16.0 for analysis. Data cleaning and validation were performed before analysis. Data were double-entered by two trained research assistants.

The descriptive statistics of the socio-demographics, clinicopathological, and other baseline characteristics of the participants were done using frequencies and proportions for categorical variables and means and standard deviations for normally distributed continuous variables. For the cases of non-normally distributed continuous variables, medians and interquartile ranges were used.

Cumulative survival curves that showed the cumulative proportion of patients dying at fixed time intervals and the corresponding life table of cumulative survival were also drawn.

The association between the clinicopathologic characteristics was done using bivariate binary logistic regression, where the odds ratios of association were reported and their corresponding p-values. Associations with p-values less than 0.05 were considered significantly associated.

3.10.2 Quality Control

The data collection tool (data extraction tool) was pre-coded and pre-tested on ten patients' files to ensure that it captured all the required information. Each completed data extraction tool was manually checked by the principal investigator for completeness before being entered into EpidataClient. Each data point was double-entered, and comparisons were made to minimize errors during data entry, storage, and exportation.

3.11 Ethical Considerations

Permission to conduct the study was sought from the Department of Surgery and the School of Medicine Research and Ethics Committee (SOMREC), followed by administrative clearance from the Uganda Cancer Institute.

The study was conducted in accordance with the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. A waiver of informed written consent was obtained from the institutional review board owing to the retrospective nature of the study design. Verbal consent was sought for the phone interviews.

3.13 Dissemination of Results

The book will be submitted to the Department of Surgery, School of Medicine at Makerere University upon approval. Copies will also be sent to Makerere University Albert Cook library, the Main Library, and Uganda Cancer Institute. Manuscripts will also be written and published in peer-reviewed journals. Posters will be prepared for presentations at journal clubs and conferences, locally and internationally.

CHAPTER FOUR: RESULTS

4.1 Overview

This chapter presents findings from a retrospective cross-sectional study of 138 pancreatic cancer patients. Results address three objectives: (1) describe the clinicopathological characteristics, (2) determine the one-year mortality rate, and (3) evaluate associations between clinicopathological characteristics and one-year mortality. Data were analyzed using STATA 16.0, with descriptive statistics (frequencies, percentages, means, and median) and logistic regression (odds ratio), 95% confidence intervals, and p-value. Missing data were excluded from specific analyses, as noted. Loss to follow-up was excluded from the mortality rate calculation.

4.2 Objective 1; the clinicopathological characteristics of pancreatic cancer

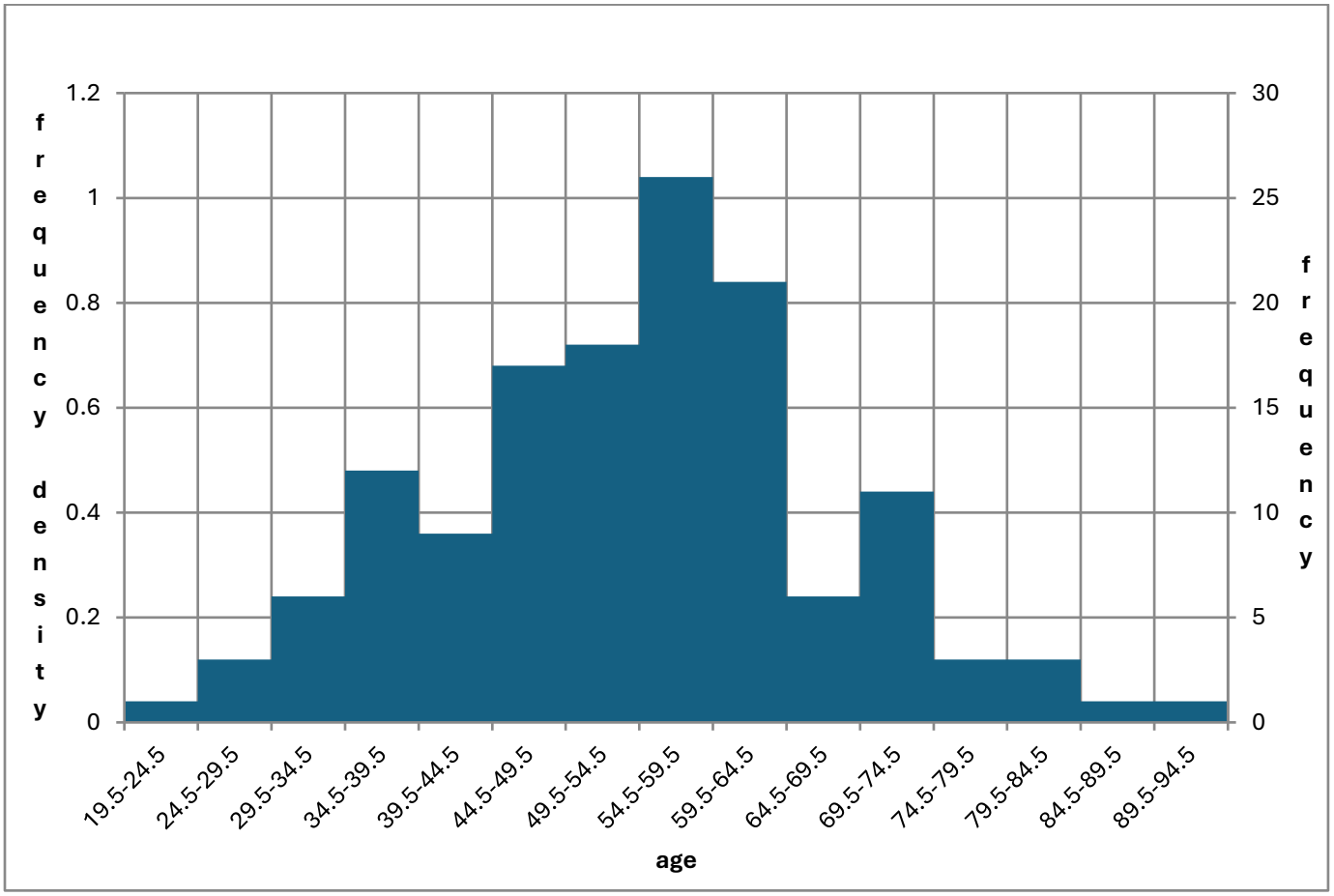
Table 3: Sociodemographic, clinical, radiological, and histological characteristics of pancreatic cancer study participants

Variable	Categories	Frequency and proportion N (%)
Sociodemographic and clinical characteristics		
Age	Mean (SD) = 54.2 (13.1)	
Sex	Male Female	64 (46.4) 74 (53.6)
Smoking	No Yes No history in file/missing	108 (81.8) 24 (18.2) *06
Alcohol use	No Yes No history in file/missing	83 (63.8) 47 (36.2) *08
Co morbidities	HIV Diabetes Mellitus Hypertension No comorbidities Not reported/missing	14 (12.7) 28 (25.5) 14 (12.7) 54 (49.1) *28
Treatment modalities	Whipple and distal pancreatectomy Bypass Stenting Non-surgical intervention	22(15.9) 20(14.5) 3(2.2) 93(67.4)
Radiological Characteristics, histological,		
Type	Pancreatic ductal adenocarcinoma Intraductal papillary mucinous neoplasm Pancreatic neuroendocrine neoplasms Acinar cell carcinoma Solid pseudopapillary neoplasm Radiologic diagnosis only (no histology)	121(93.8) 03(2.3) 01(0.8) 02 (1.6) 02 (1.6) *09
Histological grade	Low grade(well differentiated) Moderately differentiated High grade(poorly differentiated) Not graded	8 (9.8) 48 (58.5) 26 (31.7) *56
Location	Head Body Tail Mixed Not specified(had a histological diagnosis but no radiology results)	88 (68) 28 (21.5) 8 (6.2) 6 (4.6) *8
TNM stage	I IIB III IV Inaccessible or incomplete data for staging/missing	10(9.6) 20(19.2) 09(8.7) 19(18.3) 46(44.2) *34

* Not included in the denominator since such information couldn't be obtained from the files

The majority of the participants were female (53.6%), did not smoke (81.8%), and did not abuse alcohol (63.9%); the majority received non-surgical intervention (67.4%). The majority of the participants were managed non surgically (67.4%). The majority of the tumors were Adenocarcinoma (93.8%), Intraductal papillary mucinous neoplasms (2.3%), acinar cell carcinomas (1.6%), and solid pseudopapillary (1.6%) had moderately differentiated tumors (58.5%), had the tumors located in the head of the pancreas (68.0%). The majority presented in stage IV disease with most metastases (Table 3).

Figure 2: Showing the age distribution of the study participants.



The mean age of the study participants was 54.2 years. The youngest patient was 24 years and the oldest patient was 90 years old. The majority of the participants were between the ages of 54.5-59.5. (Figure 3)

Table 4: Laboratory findings and tumor Markers of the study participants

Tumour Marker	Mean (SD)	Median (IQR)
CA 19-9	3709.3 (15553.0)	55.1(5.52- 1000)
CEA	97.7 (435.7)	5.2 (2.3-25.5)
CA 125	416.7 (940.7)	73.2 (14.7-225.5)
LFTs		
Bilirubin (micromole/L)	91.7(151.7)	14.5(6.8- 103.2)
Albumin (g/dl)	31.5(10.7)	32(27- 38.4)
AST (U/l)	103.3(270.4)	37.8(21.4- 95.6)
ALT (U/l)	60.8(65.6)	30.9 (16.7- 84.1)
RFTs		
Creatinine (micromole/l)	93.8 (128.8)	64 (54.3- 84.9)
Urea (mmol/l)	5.8(7.0)	3.5(2.3- 5.9)
CBC		
Hb (g/dl)	12.1 (9.0)	11.5(10.1- 12.6)
Platelet Count (*1000/microlitre)	308.8(142.5)	282(223-378)

The mean and median levels of the study participants for the laboratory findings and tumour markers are shown in Table 4. The mean CA 19-9, CEA, and CA 125 were high at 3709.3(SD 15553), 97.7(SD 435.7), and 416(940.7), respectively. These were means for only patients who had these tumour markers in their files. The mean albumin level of the participants was below the reference ranges as noted above.

Table 5: Clinical characteristics/ presentation of the study participants

Variable	Frequency (proportion) N (%)	Duration of occurrence Mean (SD)	Duration of occurrence Median (IQR)
Mid Epigastric pain			
No	20(15.1)		
Yes	118 (84.9)	5.4(5.2)	3.5(2-7)
Back Pain			
No	114(82.6)		
Yes	24(17.4)	5.5(4.8)	3(2-9.5)
Bloating			
No	129(93.5)		
Yes	9(6.5)	10.6(16.9)	4(1-12)
Loss of appetite			
No	74(53.6)		
Yes	64(46.4)	3.6(2.7)	3(2-5)
Early Satiety			
No	113(81.9)		
Yes	25(18.1)	3.0(3.0)	2(1-4)
Nausea and vomiting			
No	80(60.1)		
Yes	55(39.9)	2.8(2.4)	2(1-3.5)
Fever			
No	129 (93.5)		
Yes	9 (6.5)	2.3 (1.9)	2(1-3)
Tenderness			
No	121(87.7)	2.5 (2.9)	1(1-3)
Yes	17(12.3)		
Jaundice			
No	69(50)		
Yes	69(50)	2.7(2.2)	2(1-3)
Weight loss			
No	65(47.1)		
Yes	71(52.9)	4.1(3.3)	3(2-6)
Pale coloured stools			
No	130(94.2)		
Yes	8(5.8)	2.9(2.3)	3(1-4)
Diarrhoea			
No	127(91.7)		
Yes	11(8.3)	3.2(3.4)	2(0.75-5)
Dark/ Tea coloured urine			
No	121(87.7)		
Yes	17(12.3)	2.2(1.7)	2(1-3)
Itchy skin			
No	88(67.2)		
Yes	43(32.8)	2.6(1.9)	2(1-3)
Fatigue			
No	100(77.5)		
Yes	29(22.5)	2.8 (1.9)	2(1-5)
Epigastric abdominal mass			
No	125(90.6)		
Yes	13(9.4)	13.4(19.6)	5(3-10)

The majority of the participants presented with mid-epigastric pain (84.9%), weight loss (52.9%), and jaundice (50.0%). The symptom/ sign that presented the longest was bloating, which presented with a mean duration of 10.6 months (Table 5).

4.3 Objective 2: mortality rate within a year of diagnosis.

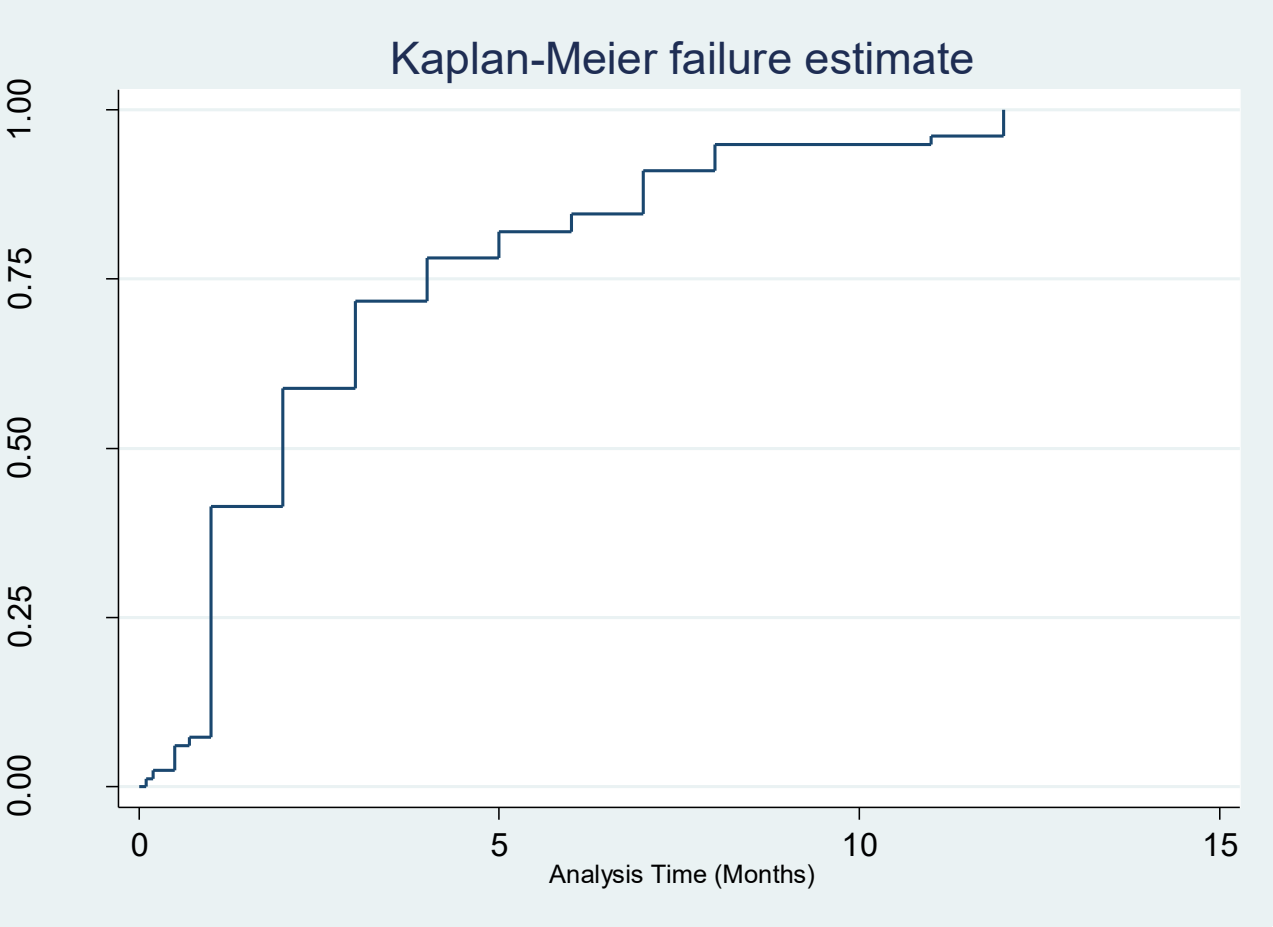
The one-year mortality rate was 69.5 %(n=82/118), equivalent to 695 deaths per 1000 patients per year. 20 of the 138 patients could not have their status established due to loss to follow-up and, therefore not considered in the denominator. A life table analysis (Table 6) showed the highest mortality between months 1 and 2, with the cumulative failure probability rising from 0.0732 to 0.4169. The Kaplan-Meier failure curve(Figure 4) illustrates a sharp increase in mortality from 0.10 to 0.35 between months 1 and 2, followed by a slower rise to 0.75 by month 5, stabilizing thereafter.

Table 6: Life table for cumulative mortality of pancreatic cancer patients

Interval		Beg. Total	Deaths	Lost	Cum. Failure	Std. Error	[95% Conf.	Int.]
0	1	82	6	0	0.0732	0.0288	0.0336	0.1556
1	2	76	28	1	0.4169	0.0546	0.3187	0.5314
2	3	47	14	1	0.5925	0.0547	0.4880	0.6998
3	4	32	10	0	0.7198	0.0503	0.6190	0.8132
4	5	22	5	0	0.7835	0.0462	0.6877	0.8662
5	6	17	3	0	0.8217	0.0430	0.7304	0.8965
6	7	14	2	0	0.8472	0.0405	0.7595	0.9159
7	8	12	5	0	0.9108	0.0321	0.8356	0.9607
8	9	7	3	0	0.9491	0.0248	0.8848	0.9834
11	12	4	1	2	0.9660	0.0216	0.9038	0.9925
12	13	1	1	0	1.0000	.	.	.

The highest number of deaths in this study occurred between months one and two. (Table 6)

Figure 3:Kaplan Meier failure estimate



The curve shows the cumulative probability of mortality over 12 months with a sharp increase between months 1 and 2 (0.10 to 0.35), a gradual rise to 0.75 by month 5, and stabilization thereafter.

4.4 Objective 3: The association between the clinicopathological characteristics of pancreatic cancer and mortality rate within a year of diagnosis

Table 7: Bivariate associations between clinic pathologic characteristics and mortality of participants

Variable	Categories	Died	Lost to follow-up	Lived	Odds ratio	p value
Comorbidities	HIV	11(16.7)	0(0.0)	3(9.4)	Reference	
	Diabetes	11(16.7)	6(50.0)	11(34.4)	0.273	0.095
	Hypertension	9(13.6)	1(8.3)	4(12.5)	0.614	0.582
	Others	35(53.0)	5(41.7)	14(43.8)	0.682	0.597
Presence of metastases	No	19(23.2)	9(45.0)	5(13.9)	Reference	
	Yes	63(76.8)	11(55.0)	31(86.1)	0.538	0.254
Histological grade (differentiation)	Low/ well	4(8.5)	0(0.0)	4(20.0)	Reference	
	Moderately	26(55.3)	10(66.7)	12(60.0)	2.167	0.327
	High/ poor	17(36.2)	5(33.3)	4(20.0)	4.250	0.108
Pancreatic mass location	Head	50(67.6)	15(83.3)	23(71.9)	Reference	
	Body	20(27.0)	1(5.6)	7(21.9)	1.314	0.589
	Tail	4(5.4)	2(11.1)	2(6.3)	0.920	0.926
TNM staging	I	5(7.9)	1(7.1)	4(15.4)	Reference	
	IIA	12(19.1)	3(21.4)	5(19.2)	1.920	0.446
	IIB	6(9.5)	1(7.1)	2(7.7)	2.400	0.407
	III	8(12.7)	3(21.4)	7(26.9)	0.914	0.916
	IV	32(50.8)	6(42.9)	8(30.8)	3.200	0.135
Age					1.027	0.117
CA 19-9					1.000	0.780
CEA					1.020	0.149
CA 125					1.000	0.491
Albumin	Normal(>35g/l)	17(27.9)	6(42.9)	14(53.9)	Reference	
	Low (≤ 35g/l)	**44(72.1)**	**8(57.1)**	**12(46.2)**	**3.020**	**0.023**
Bilirubin	Normal (< 20 µmol/l)	28(51.9)	7(53.9)	16(61.5)	Reference	
	High (≥ 20µmol/l)	26(48.2)	6(46.2)	10(38.5)	1.486	0.416
CA 19-9	Normal (< 37 units/ml)	19(35.2)	7(58.3)	16(61.5)	Reference	
	High (≥ 37 units/ml)	**35(64.8)**	**5(41.7)**	**10(38.5)**	**2.947**	**0.029**

Albumin and CA 19-9 levels were significantly associated with mortality. The odds of dying within one year among pancreatic cancer patients with low albumin levels were 3.02 times the odds of dying within one year among pancreatic cancer patients with normal albumin levels. Similarly, the

odds of dying within one year among pancreatic cancer patients with high CA 19-9 levels are 2.947 times the odds of dying within one year among pancreatic cancer patients with normal CA 19-9 levels. (Table 7).

Table 8: Bivariate associations between clinical signs and symptoms with mortality rate

Variable	Mortality status		Chi-square P-value
	Died N (%)	Alive/lost to follow up N (%)	
Epigastric pain			
No	12(14.6)	9(16.1)	
Yes	70(85.4)	47(83.9)	0.817
Back pain			
No	66(82.5)	45(83.3)	
yes	14(17.5)	9(16.7)	0.900
Bloating			
No	76(92.7)	52(94.6)	
yes	6(7.3)	3(5.4)	0.666
Loss of appetite			
No	36(43.9)	36(66.7)	
yes	46(56.1)	18(33.3)	0.009
Early satiety			
No	63(76.8)	50(89.2)	
Yes	19(23.2)	6(10.7)	0.062
Nausea and vomiting			
No	42(51.8)	38(70.4)	
Yes	39(48.2)	16(29.6)	0.032
Fever			
No	73(92.4)	52(94.5)	
yes	6(7.6)	3(5.5)	0.626
Tenderness			
No	66(84.6)	48(90.6)	
yes	12(15.4)	5(9.4)	0.320
Jaundice			
No	38(46.3)	29(53.7)	
Yes	44(53.7)	25(46.3)	0.401
Weight loss			
No	30(38.5)	32(58.2)	
Yes	**48(61.5)**	**23(41.8)**	**0.025**
Pale coloured stools			
No	65(91.6)	53(96.4)	
yes	6(8.4)	2(3.6)	0.272
Diarrhea			
No	71(93.4)	50(89.3)	
Yes	5(6.6)	6(10.7)	0.396
Dark coloured urine			
No	62(79.5)	53(98.2)	
Yes	**16(20.5)**	**1(1.8)**	**0.002**
Itchy skin			
No	50(64.9)	38(70.4)	
Yes	27(35.1)	16(29.6)	0.514
Fatigue			
No	58(76.3)	42(79.3)	
Yes	18(23.7)	11(20.7)	0.695
Epigastric abdominal mass			
No	63(87.5)	49(92.5)	
Yes	9(12.5)	4(7.5)	0.370

There is a significant association between loss of appetite, weight loss, nausea and vomiting, and dark or tea coloured urine and mortality among pancreatic cancer patients. There is no significant association between the other symptoms and mortality among pancreatic cancer patients.

CHAPTER FIVE: DISCUSSION

5.1 The Clinicopathological Characteristics of Pancreatic Cancer

The study found that the mean age of the patients was 54.2 years (Table 3). This is relatively similar to findings from studies done in Kenya, Malawi, and Zambia, which found a mean age of 58.5, 52.1, and 55.7 years, respectively (Asombang et al., 2017; Kendig et al., 2013; Muchiri et al., 2024), thus showing a possible regional pattern. However, this is slightly younger than what is typically observed in HICs, where pancreatic cancer commonly affects individuals over the age of 65 years (Institute, 2020; Pourshams et al., 2019; Riall, 2009). The relatively younger age observed in this study may be due to a high prevalence of genetic mutations since early-onset pancreatic cancer is often associated with genetic mutations or environmental factors like chronic pancreatitis (Ben-Aharon et al., 2019; Fernandez-del Castillo & Jimenez, 2017; Pourshams et al., 2019). However, the presence of genetic factors in our patients needs more genetic studies to establish this.

There were more females (53.6%) as compared to males (46.4%) with pancreatic cancer in this study (Table 3). These results were similar to the study done by Muchiri et al in Kenya, where 53% and 47% of patients were female and male, respectively(Muchiri et al., 2024). However, studies done in Europe, the USA, Asia, South Africa, and Zambia show more predilection for males than females (Asombang et al., 2017; Fernandez-del Castillo & Jimenez, 2017; Moshayedi et al., 2022; Pourshams et al., 2019; Sanchez & Cheung, 2015). Potential explanations include lifestyle differences(e, smoking patterns, obesity), biological differences between different genders in different regions, and health-seeking behaviours in different sexes(Lowenfels & Maisonneuve, 2004). Furthermore, even where we have more males affected than females, some studies have shown the increase in incidence among females to be higher than in men. This has been mostly attributed to lifestyle changes(smoking patterns, obesity) (Abboud et al., 2023; Lowenfels & Maisonneuve, 2004).

The commonest clinical symptoms (table 5) reported in this study included mid-epigastric pain (84.9%), weight loss (52.9%), jaundice (50%), and loss of appetite (46.4%). These findings were relatively similar to those in Kenya, where abdominal pain was the most common presenting feature at 73%, and jaundice at 68%(Muchiri et al., 2024). The median duration of these symptoms was an average of 3months, which is similar to the studies done in Kenya(Muchiri et al., 2024).

Bloating, although less common (6.5%), had the longest average symptom duration, indicating that it might be underappreciated by patients and clinicians alike. All these findings also align with global data, which notes that non-specific gastrointestinal symptoms are common and contribute to diagnostic delays(Park et al., 2021; Walter et al., 2016). The presence of abdominal pain usually in the epigastrium radiating to the back, jaundice, and weight loss should raise a high index of suspicion, as noted in our study and other studies(Freelove & Walling, 2006).

Most tumours (68%) were located in the head of the pancreas (Table 3). Other sites consisted of 21.5% in the body, 6.2% in the tail, and 4.6 mixed tumours (tumours in more than one part of the pancreas). These results are generally consistent with findings reported by Park et al, van Erning et al, which noted the pancreatic head being the most predominant location for pancreatic tumours at 60- 81%, 19% involving the body and tail(Park et al., 2021; van Erning et al., 2018). The predominance of tumours in the head of the pancreas may facilitate earlier diagnosis in some cases, since they may lead to earlier symptoms like jaundice due to obstruction of the common bile duct, although many patients still present at advanced stages.

The most common histological type was Pancreatic Ductal Adenocarcinoma (PDAC), accounting for 93.8% of cases, which is consistent with global data recognizing PDAC as the predominant form of pancreatic cancer(Kang et al., 2021). For this reason, the term pancreatic cancer is often used to refer to pancreatic adenocarcinoma, and the two are often used interchangeably in literature. PDAC has the worst prognosis of all the histological variants due to its aggressive nature and resistance to therapy (Schawkat et al., 2020). Although several histology report forms didn't have the histological grade, of those that had, most were moderately differentiated at 58.5%), followed by poorly differentiated tumours at 31.7%. This differs from a study done in Kenya (Muchiri et al., 2024), which found more well-differentiated tumours as compared to poorly differentiated and moderately differentiated tumours. The reasons for these differences are possibly due to differences in histological reporting or tumour biology.

Biochemically, the study found median levels of CA 19-9 of 51.1(table 4). Only 92 patients of the 138 had CA 19-9 levels in their files, of which 54.3% had elevated levels of this tumour marker. CA 19-9 is a tumour marker commonly associated with pancreatic cancer. These tumor markers are often used for prognosis and follow-up of treatment. Generally, normal CA19-9 levels may correlate with early pancreatic cancer(Ballehaninna & Chamberlain, 2012). However, CA 19-9 is

not cancer-specific, may be elevated in other hepatobiliary diseases, and may remain low even in advanced disease in a group of patients that do not express the CA 19-9 (Rawla et al., 2019). This highlights the importance of combining biochemical, clinical, and imaging findings for accurate diagnosis of this malignancy.

5.2. The Mortality Rate

The mortality rate within a year of diagnosis was found to be 69.5%, equivalent to 695 deaths per 1,000 patients. This high mortality rate underscores the aggressive nature of pancreatic cancer and the late presentation of patients with this malignancy, since late presentation is associated with high mortality of these patients (Scarpa et al., 2010). Despite available treatment modalities, including chemotherapy and surgical interventions such as Whipple's procedure, distal pancreatectomy, the prognosis remains poor. This mortality rate is similar to that from findings from, who reported a one-year survival rate of only 32% among patients from Kenyatta hospital, Kenya. These results reinforce global observations by Sung et al. (2021) that place the five-year survival rate for pancreatic cancer at below 10%. The greatest number (nearly 60%) of deaths occurred within the first 3 months after diagnosis, with the highest loss to follow-up also noted within the same period. Studies by Muchiri et al in Kenya and Hariharan et al in 51 countries in Europe, America, and Asia found a median survival of 3-5 months for advanced metastatic disease and 6-10 months for locally advanced disease (Hariharan et al., 2008; Muchiri et al., 2024). The high mortality may be attributed to multiple factors, including delayed diagnosis due to the nonspecific symptoms, lack of specialized care in peripheral health units, poor access to diagnostic imaging, and late-stage presentation. Considering all patients for we were able to establish a TNM staging (Table 3), 44.2% and 18.3% of these patients presented in stage IV and stage III, respectively. Only 15.9% of patients underwent curative surgery (whipple/distal pancreatectomy), similar to the global 15-20% resectability rate (Jiang et al., 2022). Limited diagnostic resources and insufficient awareness among the population may contribute significantly to diagnostic delays.

This finding carries significant implications for public health policy and clinical management. There is a critical need to establish national pancreatic cancer assessment and referral guidelines to identify cases earlier. Additionally, investment in specialized cancer care infrastructure and public education campaigns could contribute to improved survival rates

5.3 The Association between Clinicopathological Characteristics and One-Year Mortality Rate

Our study found weight loss, nausea and vomiting, loss of appetite, tea coloured urine (Table 8), low serum albumin levels (OR=3.02, p=0.023), and elevated CA 19-9 levels (OR=2.95, p=0.029) (Table 7) were significantly associated with mortality within a year of diagnosis. This is consistent with other studies that have described low albumin levels as predictors of mortality of not only cancer of the pancreas but also other malignancies(Gupta & Lis, 2010; Siddiqui et al., 2007). The low serum albumin levels usually stem from a number of factors, among which include poor nutritional status, dysfunctional protein metabolism, and tumor burden. Albumin plays a role in the body's immune response and immune function. Low levels, therefore, impair the immune response, making these patients susceptible to infections and thus contributing to worse outcomes. The low serum albumin levels are accompanied by weight loss, which has also been noted in our study as one of the significant associations to mortality, with a chi-square P-value of 0.025. CA 19-9's prognostic value is well established, with elevated levels indicating advanced disease. The higher the levels, the more likely the disease is advanced and thus the higher the association with mortality (Ballehaninna & Chamberlain, 2012; Usón Junior et al., 2018). The lack of association with age, comorbidities, or TNM stage may stem from the small sample size or incomplete staging data, reducing statistical power. The non-significant association with metastases (p=0.254) likely reflects missing staging data, as 76.8% of deceased patients had metastases.

5.4 Limitations of the study

This being a retrospective study, incomplete data in the patients' files were one of the major limitations. The missing data were random for different variables. Files with many missing variables were not considered for the study.

Though carried out in an oncology center, the results may not reflect outcomes in peripheral facilities, reducing generalizability. There are patients with cancer of the pancreas who may not reach UCI for management, thereby reducing the external validity of the study.

The study relied exclusively on medical records from the Uganda Cancer Institute. Some files could not be traced for the study, thus having a small sample of files to pick from for this study. This prevented randomization of the study to minimize bias and validity of the study.

Loss to follow-up may have led to bias in the mortality rate calculation. These participants couldn't be traced by their telephone contacts or through their next of kin as registered at UCI.

The retrospective study provided an analysis of cancer of the pancreas for the last five years, but did not assess the current situation. To address this gap, future prospective cohort studies to better understand the clinicopathological characteristics of cancer of the pancreas and their association with mortality.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

This retrospective chart review of 138 pancreatic cancer patients at UCI (July 2018-june 2023) revealed a high mortality rate within a year of diagnosis of 69.5% with 59.4% of deaths occurring within 3 months. Patients had a mean age of 54.2 years, with a slight female predominance (53.6%). Mid-epigastric pain (84.9%), weight loss (52.9%), and jaundice (50.0%) were common. The tumors were most commonly located in the head of the pancreas (68.0%) and were largely of the Pancreatic Ductal Adenocarcinoma (PDAC) type (93.8%). Most patients presented with stage IV disease (44.2%), reflecting diagnostic delays or aggressiveness of the tumour. Weight loss, nausea and vomiting, loss of appetite, low serum albumin levels (OR=3.02), and elevated CA 19-9 (OR=2.95) were significantly associated with mortality, highlighting their prognostic value. These values emphasize pancreatic cancer's aggressive nature in Uganda, driven by late presentation, limited resectability (15.9%), and resource constraints. These findings suggest the need for more robust, multicentre studies to confirm and explore these trends further.

6.2 Recommendations

Based on the above conclusions, the following recommendations are made:

1. **To the Ministry of Health and Uganda Cancer Institute:** Initiate early detection strategies of the clinicopathological characteristics of pancreatic cancer patients to promote early diagnosis. Train primary health providers to recognise early symptoms (e.g, Epigastric pain, weight loss, late onset Diabetes Mellitus and refer promptly. (within 12 months)
2. **To Oncologists and Clinical Researchers:** Conduct prospective cohort studies or molecular profiling of pancreatic cancer cases to explore underlying factors contributing to the high one-year mortality rate, early age of onset within the region, and also address single-center limitations (ongoing, within the next 2–3 years).
3. **To Hospital Administrators and Clinicians:** Introduce risk stratification protocols for clinical use that incorporate weight loss, low serum albumin levels, high CA19-9 levels, loss of appetite, nausea, and vomiting to identify high-risk patients at diagnosis. These patients could be prioritized for aggressive management or palliative care planning. That

can help identify high-risk patients who might benefit from more aggressive management, only achievable if patients present at an early stage of resectable disease (begin within 6 months).

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APPENDICES

APPENDIX I: DATA COLLECTION TOOL

TITLE: CLINICOPATHOLOGICAL CHARACTERISTICS OF PANCREATIC CANCER AND THE ASSOCIATED MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE: A FIVE-YEAR RETROSPECTIVE CHART REVIEW STUDY

Review Date...../...../..... questionnaire ID .....

Data reviewer: .....

SECTION A: SOCIO-DEMOGRAPHIC DATA

Age in years .....

Sex 1 = male 2 = female

Tribe.....

Occupation.....

Date of first interfence with a tertiary health unit.....

Date of diagnosis or first review.....

Status within a year of diagnosis 1. Demise 2 loss to follow up 3 alive

Address (village/subcounty) .....

History of smoking 1=Yes 2=No

Duration of smoking .....

Types of smoke 1.cigarettes 2. cigars 3. Tobacco

Estimated number of cigarettes per day .....

History of alcohol consumption 1=Yes 2=No

Duration of alcohol intake.

Type of alcohol taken

1. beer 2. Whisky 3. Spirits 4. wines 5.Others specify.....

Estimated amount per day.....

Family history of pancreatic cancer 1= Yes 2=NO

Family history of other malignancies 1 yes 2 No specify.....

Other comorbidities 1. HIV 2. DM 3. HTN 4. others specify.....

SECTION B: PATIENTS' CLINICAL PARAMETERS AT ADMISSION

Clinical characteristic	Comment		Duration of symptoms
Abdominal pain (Please specify), mid epigastric pain	Yes (Tick as appropriate)	No	
Back pain			
Bloating			
Loss of appetite			
Early satiety			
Nausea and/or vomiting			
Temperature			
Tenderness (please specify the site)			
Jaundice			
Weight loss			
Pale stools (clay-colored stools)			
Diarrhea			
Dark urine or tea colored urine			
Itchy skin /pruritus			
Fatigue			
Epigastric or abdominal mass			
Venous thrombosis			
Ascites (abdominal distention)			
Others (specify)			

SECTION C: MANAGEMENT (Please specify the type or surgery, chemotherapy, or radiotherapy; if none received, fill 'NONE')

SURGERY	Whipple's surgery	
	Bypass surgery	
CHEMOTHERAPY	REGIMEN	NUMBER OF CYCLES
RADIOTHERAPY		
OTHERS (Specify)		

SECTION D: OUTCOME WITHIN A YEAR OF DIAGNOSIS (Survival in months)

.....

.....

.....

For those study participants with unknown survival or mortality within a year of diagnosis, please turn to telephone script to establish.

ONLY PROCEED AFTER OBTAINING VERBAL CONSENT

TELEPHONE SCRIPT

Participant being talked to; **A patient** **B Next of Kin**

If ok to continue

******(in cases where the participant talked to is the patient)*****

Can i confirm your age and gender

.....

When were you diagnosed with pancreatic cancer?

.....

I would request to know how you doing currently

.....
.....
.....

Do you have any concerns? We request to know the reason as to why you haven't been able to come for review within this specific period

.....
.....
.....

In case of concerns. advise the patient accordingly

*******in case the interviewee is the next of kin**********

Can i confirm your relationship to the patient....(name mentioned matches with what is in the patient's file)

If No. Ask the participant if they have had any patient managed with cancer of the pancreas in Uganda Cancer institute and how they are doing currently. Advise accordingly. Thanks for your participation. End call

If yes

Confirm age and sex of the patient

.....

When was your loved one diagnosed with pancreatic cancer?

.....

How would you describe their health status within the first year of diagnosis?

.....
.....
.....

In case of death

I am deeply sorry for your loss. My thoughts are with you. May the deceased's soul rest in eternal peace.

May I please confirm date of death or year if known and what happened.....
.....
.....

Do you have any wuestions for me at this time? Answer any questions the participant may have

Conclusion

Thank you so much for your valuable time. Your input is crucial for my research. Have a wonderful day

APPENDIX II: VERBAL CONSENT

Verbal Consent

ly: **CLINICOPATHOLOGICAL**
)F CANCER OF THE PANCREAS AND THEIR ASSOCIATION WITH MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE.

Participant name: **Person calling:**

Date Called: Click here to enter a date. **Time Called:**

Introduction

Hello, my name is Dr. Wamala Pius. I am a general surgery resident at Mulago National referral Hospital under Makerere University and I am calling you from the Uganda Cancer Institute. Could I please speak to.....?

Is now a good time to talk?

If no: Is there a better time to call back? Date/time.....

If yes: You are receiving this call because you/your patient was or is managed at Uganda Cancer Institute and Your contact information was obtained from our medical record as possible candidate for a research study aimed at describing CLINICOPATHOLOGICAL CHARACTERISTICS OF CANCER OF THE PANCREAS AND THEIR ASSOCIATION WITH MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE.

Your participation is completely voluntary. This means that you do not have to participate in this survey unless you want to. The research survey will take 10 minutes Are you willing to hear more about the study?
☐Yes ☐No

(If yes, continue. If no, thank them for their time and end the call.)

Study Information

The study aims to describe the **clinicopathological characteristics of cancer of the pancreas and their association with mortality rate within a year of diagnosis at uganda cancer institute**. Cancer of the pancreas is the 6th leading cause of cancer related deaths globally. Though more common in the high income countries, the burden of pancreatic cancer in LMIC and MICs is increasing.

Purpose of the study

This study is to describe the clinicopathological characteristics of pancreatic cancer and the associated mortality rate within a year of diagnosis at Uganda Cancer Institute. The study findings will provide an intricate understanding of the clinical presentation, disease status at presentation, treatment modalities, and disease outcome among the Ugandan population. They will also highlight the burden of pancreatic cancer in Uganda and sub-Saharan Africa at large.

We estimate that approximately ..... participants will be enrolled in this study from Uganda Cancer Institute

Research Activities

As part of our formal study, We are conducting a one-on-one telephone survey involving a pretested questionnaire to evaluate survival status within a year of diagnosis of pancreatic cancer.

I hope that you will do your best to answer all the questions, as it is helpful to have the most complete survey possible. However, if you find some of the questions difficult or sensitive/uncomfortable in nature and do not wish to answer or require more elaboration of the question, please let me know.

Confidentiality:

You also need to understand that all information that I receive from you by phone, including your name and any other identifying information will be strictly confidential to the extent provided by the law and will be kept under lock and key. Your identity will be coded and will not be associated with any published results

All information collected about you will be "de-identified" by replacing your identifiable information (i.e., name) with a "study number". Only the "study code key" can connect the information collected about you to your identity. The study code key will be safeguarded by PI under lock and will not be available to anyone else.

However, to monitor the confidentiality of this research study, a representative from the Makerere University School of Medicine Research and Ethics Committee may have access to private information that identifies you.

Risks/Disconforts

There is no expected risk to you for helping us with this study.

Benefits and Alternatives:

There may not be any direct benefits from this study be it financial or otherwise. However, the results will be useful in developing evidence-based strategies that will inform clinicians and future patients.

Alternatives:

Your participation in this study is not mandatory and you may end participation at any time without prejudice and without affecting the future relationship with your health care provider at UCI or your medical care.

Reimbursement/compensation for participating in the study:

There is no monetary reimbursement or compensation of any kind.

Questions about the study:

If you have any questions about the study, please contact the principal investigator Dr. Wamala Pius on Tel. number 0700783180 or email address: pchwamala@gmail.com.

Questions about participants' rights:

In case you have questions about your rights as research participants you can contact the chairperson School of Medicine Research and Ethics committee (SOMREC) Assoc. Prof. Ponsiano Ocama, Tel: +256772421190. The chairperson will have answers to any questions you might have.

Statement of voluntariness:

Your participation in the proposed study is voluntary. You also have a right to withdraw from the study at any time without penalty.

Dissemination of results:

You will get feedback on the findings and progress of the study from the PI.

Ethical approval:

This study has been accredited and approved by the Makerere University School of Medicine Research and Ethics Committee and the Ethics Committee of the Uganda Cancer Institute.

In case you have any questions at a later date in the study? You can also call Principal Investigator about the research, use of your health information or the research study.

Consent

Are you ready to decide if you want to participate or not? If you need time to think about the study or want to talk about it with someone else, we can arrange to talk at a different time.

(If the participant/parent wants additional time or wants to talk again, ask about the best time to call back)- date/time:

Do you want to participate in this study?

☐Yes ☐No

If no: Thank you for your time. Goodbye.

If yes: Please confirm that you have been informed regarding the information about this study and are giving your consent to be a part of it.

☐ Verbal Consent

APPENDIX III: LETTER FROM THE DEPARTMENT TO IRB

MAKERERE UNIVERSITY

P.O. Box 7072 Kampala, Uganda
E-mail: surgery@chs.mak.ac.ug

Phone: 256 0414 532374
Telegrams: "MEDMUK"

COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
DEPARTMENT OF SURGERY

25th June 2024

The Chairman
SOMREC
College of Health Sciences

Dear Sir,

RE: PROPOSAL SUBMISSION TO IRB

This is to confirm that Dr. Wamala Pius's research proposal titled **"Clinicopathological characteristics and mortality rates within a year pot diagnosis of pancreatic cancer in patients at Uganda Cancer Institute: A 5 year retrospective chart review study"** was presented at the Department of Surgery.

He was cleared at the department level and given permission to go on and submit it to IRB for further consideration.

Any assistance rendered to him will be highly appreciated.

Yours,

Prof. Moses Galukande
Head
Department of Surgery

MAKERERE UNIVERSITY DEPT. OF SURGERY
25 JUN 2024
P. O. BOX 7072 KAMPALA (U)

APPENDIX IV: CLERANCE LETTER FROM IRB

MAKERERE UNIVERSITY
P.O. Box 7072 Kampala, Uganda
E-mail: research9@gmail.com
Phone: 256 414 533541
Fax: 256 414 541036/0414 532204
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
RESEARCH ETHICS COMMITTEE

24/10/2024

To: WAMALA PIUS

0783924321

Type: Initial Review

Re: Mak-SOMREC-2024-1001: CLINICOPATHOLOGICAL CHARACTERISTICS OF PANCREATIC CANCER AND THEIR ASSOCIATION WITH MORTALITY RATE WITHIN A YEAR OF DIAGNOSIS AT UGANDA CANCER INSTITUTE: A FIVE-YEAR RETROSPECTIVE CHART REVIEW STUDY.

I am pleased to inform you that at the **195** convened meeting on **10/09/2024**, the MAK School of Medicine REC (Mak-SOMREC) meeting voted to approve the above referenced application.
Approval of the research is for the period of **24/10/2024** to **24/10/2025.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re-review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **24/10/2025** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.
6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by MAK School of Medicine REC (Mak-SOMREC):

No.	Document Title	Language	Version Number	Version Date
1	Protocol	English	CLEAN COPY OF PROPOSAL FOR REVIEW	2024-10-21
2	COVID-19 & EBOLA risk management plan	ENGLISH	COVID-19 AND EBOLA MANAGEMENT PLAN PDF	2024-10-18
3	VERBAL CONSENT FORM FOR REVIEW	ENGLISH	VERBAL CONSENT PDF	2024-10-18
4	Data collection tools	ENGLISH	DATA EXTRACTION TOOL WITH TELEPHONE SCRIPT	2024-10-18
5	Informed Consent Waiver	English	WAIVER OF CONSENT FOR REVIEW	2024-10-18
6	COVID-19 & EBOLA risk management plan	English	ebola and covid management plan	2024-07-01
7	Data collection tools	English	questionnaire	2024-06-30

Yours Sincerely

MAKERERE UNIVERSITY
SCHOOL OF MEDICINE
INITIAL APPROVAL
VALID UNTIL
24 OCT 2025
RESEARCH & ETHICS COMMITTEE
P.O. BOX 7072,KAMPALA

Prof. Ponsiano Ocama
For: MAK School of Medicine REC (Mak-SOMREC)

APPENDIX V: WAIVER OF CONSENT

MAKERERE UNIVERSITY
P.O. Box 7072 Kampala, Uganda
E-mail: rresearch9@gmail.com
Phone: 256 414 533541
Fax: 256 414 541036/0414 532204

COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE

RESEARCH ETHICS COMMITTEE

October 24, 2024

Dr. Wamala Pius
Department of Surgery

Dear Dr. Wamala,

RE: APPROVAL OF CONSENT WAIVER

In your letter dated 16th October 2024, you requested the committee to waive off consent for the study entitled **"Clinicopathological characteristics of pancreatic cancer and their association with mortality rate within a year of diagnosis at Uganda Cancer Institute: A five-year retrospective chart review study" Mak-SOMREC-2024-1001**. It was noted that the study will involve review of medical records of patients above 18 years of age with a histopathologic and radiological diagnosis of pancreatic cancer at Uganda Cancer Institute between 1st July 2018 and 30th June 2023.

On behalf of the committee, I am glad to inform you that the committee has granted waiver of the informed consent process for this study.

Yours sincerely,

Dr. Aloysius Gonzaga Mubuuke
Vice Chairperson School of Medicine Research and Ethics Committee

APPENDIX VI: ADMINISTRATIVE CLEARANCE FROM UCI

Uganda Cancer Institute

Upper Mulago Hill Road, P.O.Box 3935, Kampala - Uganda. Tel:+256 414 540 410 Website: www.uci.or.ug

04th December, 2024

Dr. Wamala Pius

RE: Permission to Conduct Research at Uganda Cancer Institute.

Thank you for choosing Uganda Cancer Institute for your study titled "**Clinical pathology characteristics of pancreatic cancer and their association with mortality rate within a year of diagnosis at the UCI**". The study was reviewed and accepted to be conducted at UCI. This decision was based on the fact that your study had a primary approval from **(SOMREC)** Please take note of the following as you conduct research at UCI;

i) The conduct and discipline of your study staff will be governed by the rules that govern the conduct and discipline of Public Officers.

ii) Abide by the National Council for Science and Technology (UNCST) regulations for conducting research involving human participants and all relevant regulations. Thus ensure timely renewal of approvals to avoid expiration because we will expect you to avail us proof of renewal to allow you to continue with study conduct after the expiry date.

iii) You are requested to do thorough protocol training for your staff to ensure effective implementation of the study. You should also deliver the updated certificate (s) of human subject's protection for each of your study staff at UCI to the Research and Ethics Review Office before study implementation.

iv) Your contact person or Supervisor and collaborator at UCI is **Dr. Obayo Siraji** and you are expected to work closely with her throughout your conduct of research at UCI.

Research Is Our Resource

v) Schedule a date with the coordinator of research in progress meeting(s) to orient UCI staff about this study before implementation. This helps to solicit for cooperation of staff once the study begins.

This offer can however be terminated in case your behavior or study staff is contrary to the Institute's values and principles.

By copy of this letter, the UCI Clinical head is informed about your study and strongly urged to take action in case of any malpractices observed as you conduct research at UCI.

Sincerely,

Dr. Benjamin Mwesige
Head Research UCI

C.C. Executive Director, UCI

" The Senior Hospital Administrator, U.C.I.

" UCI Clinical Head, UCI

" **Dr. Obayo Siraji (UCI Supervisor)**

APPENDIX VII: BUDGET

Activity	Item	Quantity	Unit cost (Ug.	Total cost (Ug.
Proposal development	Printing	60 pages, 20 copies	100	120,000
Proposal presentation to the department and IRB	Printing	60 pages, 10 copies	100	60,000
Proposal minutes	Printing	5 pages, 5 copies	100	2,500
DATA COLLECTION TOOL				
Questionnaires	Printing	10 pages, 400 copies	100	400,000
STATIONARY				
Binders		60 copies	3,000	180,000
Folders		40	2,000	80,000
Data collectors/records personnel		3	1,200,000	3,600,000
statistics	Statistician	1	1,500,000	1,500,000
Data	Data entry			500,000
Data analysis and reporting	External hard disk	1	500,000	500,000
Miscellaneous				2,000,000
Total				8,942,500

APPENDIX VIII: STUDY TIMELINE

ACTIVITY	MAR 2024	APR 2024	MAY 2024	JUN 2024	JULY 2024	AUG 2024	SEPT 2024	OCT 2024	NOV 2024	DEC 2024	JAN 2025	FEB 2025
Proposal development												
Proposal approval												
Data collection												
Data analysis												
Report writing												
Report submission												
Dissemination of study results												