

ORIGINAL ARTICLE

Surgical management and histopathological patterns of periampullary cancers in Sudanese patients: A single-center prospective study

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Abstract

Background: Histopathological patterns of periampullary cancers (PAC) provide valuable information for clinicians in the selection of effective post-operative therapies and serve as a prognostic marker for patients. Therefore, this study was conducted to determine the surgical management and histopathological patterns of PAC necessary to achieve excellent surgical outcomes.

Methods: This prospective study was conducted from October 2021 to September 2023 at Ibn Sina Specialized Hospital, Khartoum, Sudan. Eighty patients diagnosed with resectable PAC were enrolled.

Results: PAC was more prevalent in male patients (52.5%), with a male: female ratio of 1.1:1.0. The peak incidence occurred between 46 and 60 years, representing 38.75% of patients. The most significant reported comorbidity was cigarette smoking (36.25% of patients). Scleral icterus was found in 47.5% of patients. Pancreatic head cancer was found in 55% of patients. Histopathological analysis revealed adenocarcinoma in 82.5% of patients. R0 resection (tumor-free margins) was the most common resection category (87.5% of patients). Lymphovascular invasion was detected in 37.5% of patients. Malignant lymph node involvement (1–3 nodes) was found 47.5% of patients. Perineural invasion was found in 55%. Finally, the most common histopathological differentiation of PAC was well-differentiated (Grade I) in 67.5% of patients. The mortality rate was 0%.

Conclusions: Updated knowledge regarding the management modalities of PAC is a prerequisite for accurate histopathological assessment and good surgical outcomes. Furthermore, histopathological analysis helps clinicians to

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Abbreviations: CA19-9, cancer antigen 19-9; CBD, common bile duct; CEA, carcinoembryonic antigen; CT, computed tomography; DM, diabetes mellitus; IV, intravenous; LFT, liver function tests; LN, lymph nodes; MDT, multidisciplinary team; MRCP, magnetic resonance cholangiopancreatography; PAC, periampullary cancers; TUS, transabdominal ultrasound.

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select effective postoperative therapies for greater improvement in survival outcomes.

KEYWORDS

adenocarcinoma, cholangiocarcinoma, histopathological patterns, periampullary cancers, Sudan

1 | INTRODUCTION

Periampullary cancers (PAC) are neoplasms that develop in a complex anatomical region within 2 cm of the duodenal papilla. It occurred at the pancreatic head and distal common bile duct (CBD) (pancreatobiliary epithelium). As well as in the ampulla of Vater and second part of the duodenum (simple columnar epithelium), [1, 2]. Worldwide, PAC represents 0.2% of all gastrointestinal cancers and its overall incidence is 0.53/100,000 individuals [3]. In the United States, epidemiological surveillance estimates an incidence of 0.49 per 100,000 individuals [4]. Most patients are diagnosed at late stages, either with locally advanced or metastatic disease, reducing the chance for curative resection [5]. Additionally, PAC is more prevalent in men than in women and is more prevalent in patients older than 50 years (median age, 71 years), [4, 6, 7]. PAC is anatomically distributed as follows: pancreatic head (56.3%), ampulla (19.9%), duodenum (9.7%) and distal CBD (7.6%) [2].

Several studies have identified risk factors for PAC development. Patients diagnosed with chronic pancreatitis between the ages of 45 and 54 years have a 2.3–18.5-fold increased risk, with an annual incidence of 6–12 per 100,000 individuals [8, 9]. Type 2 diabetes mellitus (DM) for >5 years is 1.0–1.5-fold increased risk of PAC with a prevalence of up to 21.3% [2, 10]. Obesity (body mass index of ≥ 40 kg/m²) is a risk factor in 12%–20% of patients [11]. Tobacco smoking is associated with 25% of pancreatic cancer cases [2, 12]. A first-degree relative with PAC increases the risk, and 10% of patients have inherited conditions such as BRCA-1 or BRCA-2 mutations, cystic fibrosis, familial adenomatous polyposis, familial atypical multiple mole melanoma, hereditary non-polyposis colorectal cancer (Lynch syndrome), hereditary pancreatitis, and Peutz–Jeghers syndrome [13]. Moreover, a low socioeconomic status in urban areas is also linked to a higher risk of PAC compared with rural areas (10.2% vs. 4.8%, respectively) [14, 15].

The most common clinical symptom of PAC is painless yellowish discoloration of the sclera, occurring in 20%–90% of patients. Other symptoms include anorexia, nausea, weight loss, and dull epigastric or right hypochondriacal pain aggravated by eating as a result of

pancreatic duct or biliary obstruction. Vomiting, usually considered a late manifestation of PAC, results from duodenal obstruction. Melena or hematemesis can occur as a result of chronic intermittent bleeding, mainly in patients with ampullary cancer [6]. The most common clinical examination finding is jaundiced sclera (56%), followed by pale conjunctiva due to either the malignant process or bleeding [16, 17]. A palpable gallbladder accompanied by mild to moderate hepatomegaly is identified in 14.6% of patients [18]. Ascites is a reflection of hypoalbuminemia in 26% of patients [19, 20]. Clinical signs of distant metastasis are present in 21% of patients [21]. PAC has a silent aggressive nature and is difficult to detect in its early stages because of nonspecific symptoms, leading to rapid spread to nearby structures and reduced chances of radical resection [22, 23].

Several laboratory tests can help in early PAC diagnosis. Liver function tests showed increased alkaline phosphatase and serum bilirubin levels, reflecting a state of obstructive jaundice. Urinalysis and renal function tests are used to evaluate kidney function before intravenous (IV) contrast-enhanced abdominopelvic computed tomography (CT). A complete blood count can be used to evaluate anemia and ongoing infections [17]. Moreover, tumor markers such as cancer antigen 19–9 (CA19-9) have high sensitivity (79%–81%) and specificity (80%–82%) in the detection of symptomatic pancreatic cancers [24]. The CA19-9 level is abnormal in 56%–95% of patients with distal cholangiocarcinoma. A carcinoembryonic antigen (CEA) level of 5 ng/mL has been found to be a helpful indicator of distal cholangiocarcinoma (10%–99%) and pancreatic cancer (44%–88%), [25].

Modern radiology has recently improved the diagnostic assessment of these cancers. Transabdominal ultrasound (TUS) can detect biliary tree dilatation, but it has low sensitivity (67%) and specificity (40%) for PACs, particularly pancreatic cancers [26, 27]. Abdominopelvic CT is superior to magnetic resonance cholangiopancreatography (MRCP) and is considered the most useful and cost-effective test. It determines PAC resectability with high sensitivity (90%) and specificity (72%) [23, 28]. MRCP is also used for detection and staging of PAC with a specificity and accuracy of MRCP were (78.3% and 91.5%), respectively. Furthermore, endoscopic ultrasonography is useful

for evaluation of regional lymphadenopathy and the depth of malignant invasion [29].

Preoperative professional multidisciplinary team (MDT) meetings during the staging process help to determine the potential resectability of PAC. Stage I PAC is < 4 cm in size, has a <5-mm depth of wall invasion, and has no regional lymph node (LN) or distant metastasis. Radical surgical resection is the best treatment option. Stage II PAC does not extend beyond the serosa, has a 5 to 12-mm or greater depth of invasion, and has no LN involvement. Stage III PAC (intraperitoneal metastasis) is > 4 cm in size and extends beyond the serosa into other adjacent organs and LN. Unresectable stage IV PAC invades the major blood vessels and accompanying LN or invades two or more organs [30]. Surgical resection in the form of Whipple's pancreaticoduodenectomy is an ideal treatment strategy. However, despite proper MDT meetings, most patients are not fit for this surgery because they present in the late non-operable stages.

The estimated 5-year survival rate ranges from 60% to 80% in patients with resectable PAC. Involvement of regional LN and positive surgical margins worsen the prognosis in 20%–30% of patients [22, 23, 31]. Moreover, the postoperative overall 5-year survival rate is 64%–80% without LN metastasis and 17%–50% with LN metastasis [32]. Another study revealed overall estimated 5-year survival rates of 49%, 45%, 27%, and 18% for duodenal cancer, ampullary cancer, distal bile duct cancer, and pancreatic cancer, respectively [2]. Furthermore, 20%–40% of patients with PAC are found to have unresectable cancers intraoperatively because of locally advanced or metastatic malignancies that require palliative approaches, such as biliodigestive anastomotic bypass followed by adjuvant chemoradiation therapy [31]. Adjuvant chemoradiotherapy can reduce the risk of metastasis-related death. The most commonly used conventional chemotherapeutic drugs for PAC are 5-fluorouracil or gemcitabine-based regimens. Although they do not significantly improve the median overall survival rate, they inhibit cell proliferation and promote apoptosis. Cyclophosphamide and methotrexate provide effective palliation [1, 33]. Postoperative histopathological analysis of specimens is an excellent predictor of patients' prognosis and chemotherapy response. Patients with well-differentiated cancer, small tumors, negative LN involvement, clear resection margins, and absence of vascular or perineural invasion show better treatment responses [34, 35]. Special attention to the different histopathological types of PAC is needed to differentiate between benign tumors (11.4%) and malignant lesions (88.6%) [36]. The most common subtype is pancreatic adenocarcinoma of the pancreatic head (93%), followed by ampullary adenocarcinoma and neuroendocrine

tumors [37, 38]. The most common malignant subtype of distal bile duct cancer is adenocarcinoma. The main duodenal subtype of PAC is adenocarcinoma [39].

A deep humanitarian crisis followed the eruption of armed clashes on 15 April 2023 between Sudanese armed forces and rapid support forces in Khartoum (the capital of Sudan) and various Sudanese states. This conflict resulted in significant loss of lives and severely compromised healthcare services. Many hospitals went out of service because of lack of medical supplies, fuel shortages for generators, a critical shortage of medical staff, including specialized professionals such as surgeons and anesthesiologists, and escalating violence against health workers, including physical assaults, kidnappings, and killings. These issues have severely disrupted health services in Sudanese states, leading to ongoing outbreak threats, reduced efficiency of medical treatments for chronic diseases such as cancer, and inadequate long-term monitoring. This is the first prospective study in Sudan to describe the surgical management and histopathological patterns in patients with PAC. However, it was limited by its small sample size, the patients' low socioeconomic status, and the ongoing war in Sudan. These factors affected the long-term follow-up and complicated the selection of comparative statistical tests that require larger sample sizes of patients from multiple centers. Moreover, immunohistochemical studies are needed for further tumor histogenesis verification. A thorough review of the literature revealed no specific comparative data on the histopathological patterns of PAC between countries or updated surgical management. Therefore, this study was conducted to determine the surgical management and histopathological patterns of PAC necessary to achieve excellent surgical outcomes.

2 | METHODS

This prospective, observational, descriptive analytic hospital-based study was conducted in the gastroenterological surgical department of Ibn Sina Specialized Hospital, Khartoum, Sudan, from October 2021 to September 2023. The study received no grant funding and was performed in compliance with the guidelines for human studies. Additionally, it was ethically conducted in accordance with the World Medical Association Declaration of Helsinki. Before study commenced, ethical approval was obtained from the local research ethics committee of the Faculty of Medicine and Health Sciences, Omdurman Islamic University (committee meeting number: 186, date: 8 September 2021) to publish this study for the purpose of research and to collect medical data from the international medical websites and

medical literature. Written informed consent was obtained from all enrolled Sudanese patients. No clinical trials were involved in this study.

The following data were collected by questionnaire: demographic characteristics, clinical presentation, provisional diagnosis, investigation modalities, risk factors, surgical indications, and comorbidities. The inclusion criteria were Sudanese patients aged ≥ 15 years, a clinical diagnosis of PAC confirmed by TUS and MRCP, patients with any stage of PAC identified by abdominopelvic CT combined with IV and water-soluble contrasts, and elective treatment with the open classical Whipple's procedure. The exclusion criteria were treatment with the laparoscopic Whipple's procedure, non-operable PAC, iatrogenic hepatobiliary injuries, incomplete records, and any comorbidity precluding general anesthesia.

Postoperatively, histopathological analysis began by serial sectioning of state specimens at 3 to 5- μm -thickness. The gross dimensions of consecutive sections were measured and identified by microscopic histology, with mapping of sections along the largest tumor dimension. Serial sectioning also helped identify >12 LN. Samples were placed in paraffin blocks and paraffin blocks and cut by a microtome into 5- μm -thick slices. One slice was placed on a transparent salt plate for transmission measurement, and another was mounted on glass for hematoxylin–eosin staining to facilitate histopathological examination.

The paraffin-covered samples were deparaffinized with 24 h hexane bath to prevent paraffin absorption. Two expert pathologists assessed the hematoxylin–eosin slides for histopathological grading, cancer origin, perineural invasion, lymphovascular involvement, and LN status. The evaluation findings of the resected margins were recorded as follows: gastric/duodenal margins, ampulla of Vater, cystic duct margin, pancreatic neck margin, pancreatic uncinate margin, superior mesenteric vein/portal vein.

The patients' clinical details were entered into a spreadsheet (Excel 2016 for Windows). These data were statistically analyzed using SPSS version 26 (IBM Corp.). Descriptive statistical analytic tests were conducted. The statistical results were considered significant at $P < 0.05$.

3 | RESULTS

Eighty patients were diagnosed with operable PAC and underwent the elective open classical Whipple's procedure. PAC were more common in 42 males (52.5%) than in 38 females (47.5%) with a male: female ratio of approximately (1.1:1.0). The peak incidence occurred at 46–60 years of age, representing 31 (38.75%) patients (Table 1). The comorbidities significantly associated with

TABLE 1 Demographic data of patients diagnosed with periampullary cancers.

Sex	Frequency	Percentage (%)
Male	42	52.5
Female	38	47.5
Age (years)		
15–30	4	5
31–45	14	17.5
46–60	31	38.75
61–75	28	35
>75	3	3.75

a high risk of PAC were cigarette smoking in 29 (36.25%) patients, type 2 DM in 22 (27.5%) patients, morbid obesity (body mass index of $\geq 40 \text{ kg/m}^2$) in 16 (20%) patients and alcohol intake in 13 (16.25%) patients.

The most common presenting symptoms were scleral icterus with darkly colored urine and itching in 38 (47.5%) cases, followed by severe weight loss/anorexia in 21 (26.25%) patients, vague epigastric pain in 13 (16.25%) patients, and melena in 8 (10%) patients. None of the patients in this study had previous hematemesis or a family history of PAC. Abdominal examination revealed the following clinical signs: deeply jaundiced sclera in 38 (47.5%) patients, a palpable gallbladder in 22 (27.5%) patients, ascites in 13 (16.25%) patients and pale conjunctiva in 7 (8.75%) patients. Fifty-one patients resided in rural areas, while 29 (36.25%) resided in urban areas. No patient had a clinical presentation of distant metastasis.

All patients underwent preoperative laboratory tests, including liver function tests and measurement of tumor markers (CA19-9, CEA). Laboratory tests revealed abnormal values of direct bilirubin ($>2.5 \text{ mg/dL}$) in 59 (73.75%) patients. Also, alkaline phosphatase ($>147 \text{ IU/L}$) in 62 (77.5%) patients, alanine transaminase ($>36 \text{ U/L}$) in 11 (13.75%) patients, and aspartate transaminase ($>33 \text{ U/L}$) in 7 (8.75%) patients. Serum albumin ($<3.4 \text{ g/dL}$) in 26 (32.5%) patients. The bleeding profile was abnormal in 12 (15%) patients. Renal function tests showed no biochemical evidence of acute kidney injury in any patient. Regarding tumor markers, serum CA19-9 was markedly elevated ($>37 \text{ U/mL}$) in 42 (52.5%) patients and serum CEA ($>2.5 \text{ ng/mL}$) in 19 (23.75%) patients.

All patients also underwent preoperative diagnostic radiological modalities for PAC. TUS revealed a dilated biliary tree in all patients. Contrast-enhanced abdominopelvic CT showed variable PAC staging as follows: local stage in 74 (92.5%) patients, locally advanced stage in 6 (7.5%) patients, and absence of metastatic stage in all patients. In an effort to improve the survival rate and

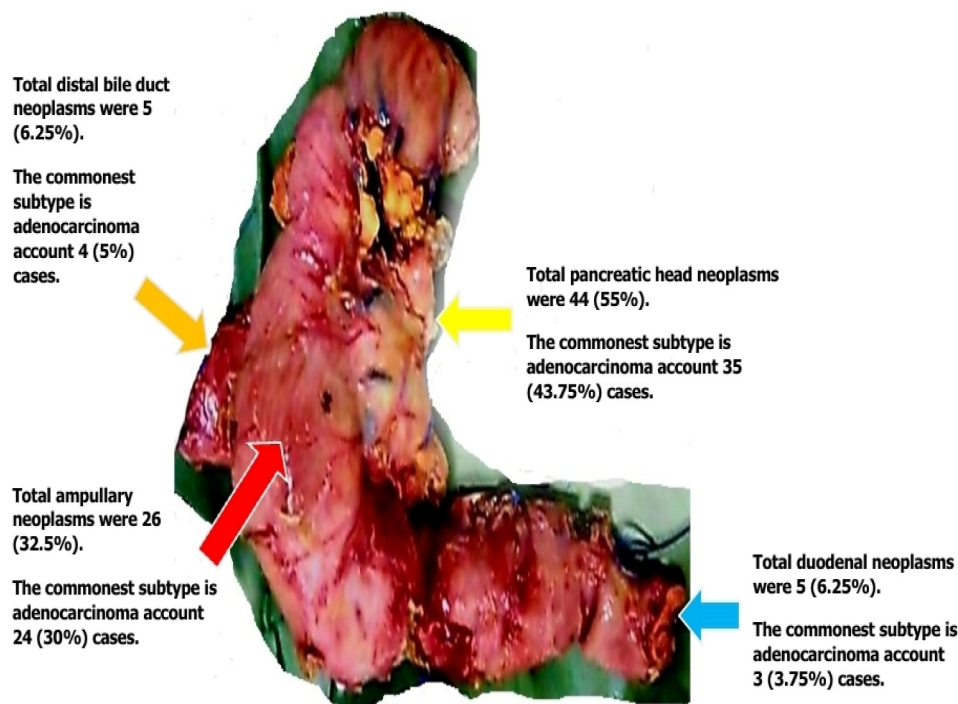


FIGURE 1 Postoperative specimen for microscopic histopathological analysis of periampullary cancers.

achieve clear surgical margins, preoperative MDT meetings were performed for all patients. MRCP was performed for all but 28 (35%) patients because of its high cost. Fifty-two patients (65%) who underwent MRCP had variable radiological signs of a dilated biliary tree and site of obstruction among the various subtypes of PAC.

All patients underwent the classical Whipple's procedure. Complete resection was achieved in 75 (93.75%) patients and borderline resection in 5 (6.25%) patients. No patient had unresectable tumors. The PACs were arranged anatomically as follows: pancreatic head cancer in 44 (55%) patients, ampullary cancer in 26 (32.5%) patients, duodenal cancer in 5 (6.25%) patients, and distal cholangiocarcinoma in 5 (6.25%) patients.

Postoperative microscopic histopathological analysis of the resected specimens revealed that the most common malignant lesion was pancreatic head cancer in 44 (55%) patients, followed by ampullary cancer in 26 (32.5%) patients, duodenal cancer in 5 (6.25%) patients, and distal bile duct cancer in 5 (6.25%) patients. Moreover, adenocarcinoma was the most commonly reported malignant subtype, affecting 66 (82.5%) patients distributed as the follows: 35 (43.75%) patients in the pancreatic head, 24 (30%) patients in the ampulla of Vater, 4 (5%) patients in the distal bile duct and 3 (3.75%) patients in the duodenum (Figure 1). The resected margins were classified as R0 (tumor-free margins) in 70 (87.5%) patients, R1 (micro-residual margins) in 10 (12.5%) patients, and R2

(macro-residual margins) in none. Lymphovascular invasion was present in 30 (37.5%) patients and absent in 50 (62.5%) patients. The number of cancerous LNs was 0 in 35 (43.75%) patients, 1–3 in 38 (47.5%) patients and >4 in 7 (8.75%) patients.

Perineural invasion was present in 44 (55%) patients and absent in 36 (45%) patients. The PAC showed variability as follows: well-differentiated cancers (Grade I) were present in 54 (67.5%) patients, moderately differentiated cancers (Grade-II) in 19 (23.75%) patients, and poorly differentiated cancers (Grade-III) in 7 (8.75%) patients (Table 2). The mortality rate was 0%. The results of this study were statistically significant ($P < 0.05$).

4 | DISCUSSION

Early diagnosis of PAC is challenging, often preventing radical resection because of its nonspecific symptoms and silent aggressive nature; this may lead to rapid spread into surrounding structures [22, 23]. Moreover, few Sudanese hospital-based studies have provided accurate updates on the surgical management and histopathological patterns of PAC. Such studies are valuable for clinicians in selecting effective postoperative therapies to improve patients' survival outcomes. Therefore, the aim of this study was to determine the surgical management and histopathological patterns of PAC necessary to achieve excellent surgical outcomes.

TABLE 2 Postoperative histopathological characteristics of resected periampullary cancers.

Anatomical cancer sites	Frequency	Percentage (%)
Pancreatic head	44	55
Ampulla of Vater	26	32.5
The duodenum	5	6.25
Distal CBD	5	6.25
Resected margins		
R-0 (free margin)	70	87.5
R-1 (micro residual margin)	10	12.5
R-2 (macro residual margin)	0	0
Number of lymph nodes		
Absence of involved LNs	35	43.75
1–3 involved LNs	38	47.5
>4 involved LNs	7	8.75
Grading types		
Well differentiated (grade-I)	54	67.5
Moderately differentiated (grade-II)	19	23.75
Poorly differentiated (grade-III)	7	8.75

Our study showed that PAC was more common in male patients (52.5%) than in female patients (47.5%), with a male: female ratio of 1.1:1.0. These results align with the literature, which reports a higher prevalence in male patients (62.2%) than in female patients (37.8%) (male:female ratio of 1.6:1.0) [38]. This near-equal sex distribution is observed when patients are grouped by primary site. The peak incidence of PAC occurred at 46–60 years, representing 38.75% of patients. This is consistent with the literature, which reports a mean age of 56 years [38]. Dutta et al. [7] also reported that 85% of patients with PAC were aged between 40 and 70 years, while another study showed a mean age of 58 years [40].

Our study revealed that cigarette smoking (36.25%) was the major risk factor for pancreatic cancer, followed by type 2 DM (27.5%). These results are consistent with the literature, which reports a higher prevalence of pancreatic cancer in regular cigarette smokers (21.3%) and patients with type 2 DM (25%) [2, 10, 12].

The most common clinical symptom was scleral icterus accompanied by darkly colored urine and itching, observed in 47.5% of patients. This is consistent with the literature, which reports yellowish sclera in 0%–90% of patients [6]. Such symptoms are often ignored because of the silent and aggressive nature of these malignancies. The most common sign in this study was deeply jaundiced sclera, present in 47.5% of patients. This is consistent with a study by Siddique et al. [16], who found

malignant jaundiced sclera in 56% of patients. Moreover, we discovered a palpable gallbladder in 27.5% of patients. This is consistent with the literature, which reports a palpable gallbladder in the form of Courvoisier's sign in 14.6% of patients [18]. Ascites was present in 16.25% of patients. This is in agreement with the results of Patel et al. [20], who observed ascites in 26% of patients. Additionally, we found no signs of distant metastasis in any patient. This contrasts with a report by Slaar et al. [21], who reported that 21% of patients had signs of distant metastasis. This discrepancy may be due to meticulous MDT diagnostic evaluation facilitating radical resection.

No patient had a family history of PAC. This disagrees with the literature, which reports that 10% of patients have associated genetic mutations and familial inheritance [13]. This finding requires further funded genetic studies, particularly in developing countries such as Sudan.

We found that 63.25% of patients lived in rural areas. This contrasts with a report by Zahnd et al. [15], who found a higher incidence of PAC in urban than rural areas (10.2% vs. 4.8%, respectively). This is related to the low availability of modern healthcare facilities and diagnostic centers in rural areas.

The diagnostic evaluation of the severity of biliary obstruction initiated by LFT showed increased levels of serum alkaline phosphatase (>120 IU/L) in 77.5% of

patients and direct bilirubin (>0.35 mg/dL) in 73.75%. These findings are similar to the literature, which reports that long-term abnormal LFT values provide early diagnostic clues regarding PAC [17]. Our study also showed an abnormal bleeding profile in 15% of patients. This finding is similar to the literature, which commonly reports coagulopathies in patients with PAC. Such coagulopathies are related to progressive biliary obstruction associated with vitamin K malabsorption and hepatic dysfunction, which leads to a prolonged prothrombin time [17]. Serum CA19-9 was markedly elevated in 52.5% of patients, mainly those with pancreatic adenocarcinoma. Our results are similar to a study by Duffy et al. [24], who reported that CA19-9 provided optimal detection of pancreatic adenocarcinoma with a sensitivity and specificity of 79%–81% and 80%–82%, respectively. We also found that serum CEA was elevated in 23.75% of patients. This is consistent with a study by Kim et al. [25], who reported that serum CEA was helpful in the diagnosis of distal cholangiocarcinoma (10%–99%) and pancreatic cancer (44%–88%).

In this study, TUS revealed biliary tree dilation in all patients. This is in agreement with Vardar et al. [26], who reported high diagnostic sensitivity rates of TUS for biliary dilatation (95%) and site of obstruction (86%). However, TUS had a low sensitivity rate (77%–84%) for detecting the cause of biliary obstruction. Moreover, our results disagree with those of Clarke et al. [27], who found low sensitivity (67%) and specificity (40%) of TUS in identifying PAC, particularly pancreatic cancer. Contrast-enhanced abdominopelvic CT revealed that the most common staging category of PAC was local stage, affecting 92.5% of patients. These results are consistent with international studies reporting accurate radiological information about PAC resectability with high sensitivity (90%) and specificity (72%) [23, 28]. MRCP provided detailed depictions of biliary tree dilatation and accurately showed the obstruction site in 65% of patients with PAC. This is in agreement with Chen et al. [29], who reported that MRCP had higher diagnostic accuracy (94.4%) than abdominopelvic CT (91.6%) and TUS (33.6%). Through the open classical Whipple's procedure, we achieved complete resection in 75 (93.75%) patients. This is consistent with a study by House et al. [28], who achieved a high resectability rate of 83% with this procedure. Additionally, Fang et al. [23] achieved a resectability rate of 75%.

The most common postoperative histopathological pattern was malignant lesions in 91.25% of patients. This is similar to the results in the literature showing high rates of malignant lesions (88.6%) [36].

The most common anatomical site of PAC in this study was the pancreatic head (55%), followed by the

ampulla of Vater (32.5%), duodenum (6.25%), and distal CBD (6.25%). This agrees with the literature, which reports malignant lesions in the pancreatic head (56.3%) followed by the ampulla of Vater (19.9%), duodenum (9.7%), and distal CBD (7.6%) [2]. Our findings are also consistent with those of Mekki et al. [41], who found that pancreatic cancers (53.4%) were the most common, followed by ampullary cancers (24.1%), duodenal cancers (15.5%), and distal cholangiocarcinoma (7%). Adenocarcinoma was the most common histopathological subtype of PAC, revealed in 82.5% of patients. This agrees with the literature, which shows that the most common histopathological subtypes are adenocarcinoma (93%) and neuroendocrine tumors [37, 38]. We also found that a free resection margin (R0) was the most common resection category (87.5% of patients). This agrees with some studies in the literature, showing R0 in 81.8%–95.5% of cases. Additionally, our findings agree with another study that achieved R0 in 86.04% of patients [34, 38]. Moreover, these results are consistent with Yeo et al. [42], who reported high R0 rates in ampullary cancer (97%) and pancreatic cancer (71%). Furthermore, we achieved micro-residual margins (R1) in 12.5% of patients. This contrasts with Lee et al. [39], who reported R1 in 20% of pancreatic head cancer and 12% of ampullary cancer. Early patient presentation to referral clinics with meticulous MDT meetings, surgical approaches, and histopathological assessment contributed to these results.

Lymphovascular invasion was detected in 37.5% of patients. This agrees with the literature reporting lymphovascular invasion in 38.6% of cases. Additionally, one study showed lymphovascular invasion in 37.2% of cases [34, 38]. Another study disagreed with our findings, confirming lymphovascular invasion in 100% of cases [36]. This is related to the fact that most patients in our study were staged after the MDT meeting as local stage, which is associated with a low risk of lymphovascular invasion.

We revealed cancerous (1–3) LN involvement in 47.5% of patients. Our findings agree with multiple studies in the literature reporting LN metastases in 35.3%–46.7% of patients [34, 36, 38, 43]. This is related to accurate surgical resection for early stage PAC.

We also detected perineural invasion in 55% of patients. This is similar to the literature showing perineural invasion in 53.5%–100% of patients [34, 36, 38]. This finding is related to accurate diagnosis of PAC, especially local-stage pancreatic head cancers, which are associated with a low risk of LN involvement and perineural invasion.

Well-differentiated cancer (Grade I) was the most common histopathological differentiation of PAC, reported in 67.5% of patients. Our finding agrees with the literature, which reports high rates of well- and

moderately differentiated PAC [36]. However, another study disagreed with our findings, revealing moderately differentiated cancer (66%) as the most commonly observed [37]. Additionally, our findings disagree with those of Bouvet et al. [35], who found moderately differentiated cancers in 50% of patients. This was related to meticulous diagnostic evaluation, preoperative MDT meetings, and appropriate resection of PAC with clear margins.

Finally, the overall mortality rate was 0%. This is inconsistent with the literature, which shows a high mortality rate of PAC accounting for 597,329 deaths worldwide [44]. This is related to accurate long-term regular postoperative follow-up, which reduces the occurrence of fatal morbidities.

5 | CONCLUSIONS

Updated knowledge regarding the management modalities of PAC is a prerequisite for accurate histopathological assessment and good surgical outcomes. Furthermore, histopathological analysis helps clinicians to select effective postoperative therapies for greater improvement in survival outcomes.

AUTHOR CONTRIBUTIONS

Ismail Mohammad Adam: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); supervision (supporting); validation (supporting); visualization (supporting); writing – original draft (supporting); writing – review & editing (supporting). **Elfatih Yousif Abdelrahim:** Conceptualization (equal); data curation (supporting); formal analysis (supporting); investigation (supporting); methodology (supporting); project administration (supporting); supervision (supporting); validation (supporting); visualization (supporting); writing – original draft (supporting). **Wael Mohialddin Ahmed Doush:** Conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); project administration (lead); resources (lead); software (lead); supervision (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review & editing (lead).

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Datasets are not to be made publicly available by the local Research Ethics Committee because of ethical reasons. However, the data might be available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Our research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical approval was obtained from the local Research Ethics Committee of Faculty of Medicine and Health Sciences, Omdurman Islamic University, at the committee meeting number (186) dated on Wednesday 8th September 2021 to use the Sudanese patients after they have written and signed consent to publish this original article for purpose of research and collected his medical data from the international medical websites and medical literatures. No clinical trials were conducted in this study.

INFORMED CONSENT

All patients provided written informed consent at the time of entering this study.

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