



## Research Article

# Management Modalities of Pancreatic Cancer and Surgical Outcomes of Braun's Anastomosis Addition in Whipple's Procedure: A Single-center Prospective Study

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## ABSTRACT

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**Keywords:** Braun's anastomosis, Delayed gastric emptying, Pancreatic cancer, Whipple's procedure



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**Background:** Pancreatic cancer is an aggressive malignancy with a high mortality rate. Many morbidities associated with Whipple's procedure that endanger patients' life which need updated surgical techniques to lower these morbidities. The aim of this study is to determine management modalities of pancreatic cancer and surgical outcomes of adding Braun's jejunojunostomy to Whipple's procedure for reduction of postoperative risks in Sudanese patients to reach excellent surgical practice.

**Subjects and Methods:** This is a prospective-cohort study conducted during the period between January 2022 and July 2023 at Ibn Sina specialized hospital, Khartoum, Sudan, on sixty-three patients diagnosed with resectable pancreatic cancer. Addition of Braun's jejunojunostomy to elective open Whipple's surgery was performed.

**Results:** Seventy-three percent of patients diagnosed with pancreatic cancer were males with the ratio (3:1). Patients' distribution according to age ranged between 46 and 60 years representing (41.3%). The significant reported comorbidities that associated with PC were diabetes mellitus (30.2%) and businessmen (39.7%). Most of patients were lived in rural areas (57.1%). Abdominopelvic CT-scan revealed stage (II) of pancreatic cancer in (68.2%) of patients. The predominant morbidity after addition of Braun's jejunojunostomy was wound infections noticed in (17.5%) of patients. Moreover, other complications were categorized as follows: pulmonary infections in (6.35 %) of cases, postoperative diabetes mellitus in (4.76 %) of cases, entero-cutaneous fistula in (4.76 %) of cases, delayed gastric emptying in (3.17%) of cases, biliary leak in (3.17%) of cases, (3.17%) of cases, pancreatic fistula in one case (1.58%), gastric outlet obstruction in one case (1.58%) and postoperative GIT bleeding in one case (1.58%). Postoperative hospital stay of patients ranged between 8-15 days for (66.7%) of cases. The mortality rate was zero.

**Conclusions:** To reduce the rate of lethal surgical morbidities of Whipple's procedure, we recommend addition of Braun's jejunojunostomy as useful technique. Moreover, it will potentially help in improving the quality of surgical practice and survival outcomes of patients who are diagnosed with pancreatic cancer.

## Introduction

Pancreatic cancer (PC) considered as the second common malignancy of the gastrointestinal tract after colorectal cancer and the overall incidence is 8-10/100,000 individuals. Also, it became the fourth cause of cancer-related death at the United States in both men and women, with estimated 37,390 deaths in 2012 AD. Moreover, this cancer found in men (5.5/100,000) and women (4/100,000) worldwide (1, 2). The incidence of PC markedly increases with age (average of 65 years). Sometimes ten percent of cases discovered at or before age of 50 years (3). About 61.7% of patients are living in an urban region (4). In the literature, there were several described risk factors for PC. These include African-Americans have higher rates than Caucasians. Tobacco smoking observed in 25% of cases. Some studies found PC in 20% of obese patients (BMI  $\geq$  30 kg/m<sup>2</sup>). Dietary factors such as processed meats, foods with nitrosamines and fried meals with high cholesterol contributed to PC in 48% of patients (1, 5). Chronic pancreatitis due to heavy alcohol consumption led to PC development (6). Diabetes mellitus (DM) had a strong relationship with PC in 9.7% of cases. Also, 30% of patients had PC after DM diagnosis by twenty years (7). About 5%–10% of PC cases were diagnosed specifically in the first-degree relatives and ten percent of patients had gene mutation. Helicobacter pylori bacterial infection was discovered in 4%–25% of cases (1). Pancreatic cancer is a silent disease usually detected in advanced stages due to non-specific ignored symptoms such as general malaise, flatulence, abdominal bloating, vomiting, constipation and diarrhea. Patients with painless jaundice and weight loss often had locally advanced stage and deteriorated condition. In the literature, the common clinical presentations were loss of appetite (45%), jaundice (41%), abdominal pain (33%), weight loss (32%), pale stools (26%), unusual upper Gastrointestinal tract (GIT) bloating (25%), itching (22%), altered ability to sleep (16%) and dark urine (15%), (8). When serum bilirubin exceeded 100  $\mu$ mol/l, it gave high sensitivity (71.9%) and specificity (86.9%), (9). Usually, serum biomarkers are used for monitoring of staging, recurrence and metastatic extent. Moreover, high levels of Cancer antigen 19-9 (CA19-9) were noticed in advanced stages (10). Serum Carcinoembryonic antigen (CEA) is independent predictor, elevated in 30%–60% of patients. Preoperative combined results of CEA, CA19-9 and CA125 more or equal to 1000 U/mL were accurately detected patients with poor response to Whipple's surgery (11). Recently, radiological modalities were rapidly improved PC diagnosis. The sensitivity of TUS, abdominopelvic Computerized tomography scan (CT-scan) and Magnetic resonance cholangiopancreatography (MRCP) were 67.3%, 65.8% and 57.5%, respectively (12). Moreover, Endoscopic ultrasonography accuracy of Lymph nodes (LNs) staging is account 64%–82% and showed 90% of sensitivity when compared with abdominopelvic CT-scan (55%), particularly malignant lesions below 2-3 cm in size (13). Recently, complete surgical resection is the only potential curative option and at the time of presentation, 15%–20% of patients were potentially resectable (14). The most staging system that used for pancreatic cancer is the American joint committee on cancer (AJCC) -TNM system which helps in evaluation of long-term clinical prognosis and survival rate. Furthermore, this staging system determine treatment

choices (surgical resection and oncological therapies) and divided patients into resectable, borderline resectable and unresectable categories (15, 16). In the United States, general 5-year survival rate for PC is eleven percent. According to AJCC-TNM system the estimation of 5-year survival rate of patients divided into: early local stage (42%), local advanced stage (14%) and distant metastatic stage (3%), (17). Pancreaticoduodenectomy is the first curative treatment for operable PC described first by Allen Whipple in 1940 AD. In addition, post-operative morbidities reached up to sixty percent. Pancreatic fistula and delayed gastric emptying (DGE) remain the most common lethal risks (18, 19). Other post-operative complications were categorized as follows (20-28):

(A) Post-operative bleeding (2%-18%); (B) Delayed gastric emptying (14%–30%); (C) Pancreatic fistula (3%-26%); (D) Post-operative wound infections (6%–17%); (E) Pneumonia (4.3%); (F) Afferent loop syndrome (0.3%–1.0%); (G) Postoperative diabetes mellitus (40.4%); (H) Gastric outlet obstruction (10%-15%); (I) Biliary leakage (3%-8%).

There is a long-standing interest in accurate techniques to reduce the occurrence of associated morbidities of Whipple's surgery (29). Various anastomotic methods described in the literature, like the Roux-en-Y technique, were introduced for supplementation of classical Whipple's procedure (30). Moreover, Braun's jejunojunostomy (BJJ) is a digestive reconstruction of side-to-side anastomosis between afferent and efferent jejunal loops distal to the gastrojejunostomy site. It showed beneficial surgical advantages such as stabilization of afferent and efferent limbs of the gastrojejunostomy with reduced chance of twisting and angulation. Also, it lowers the rate of DGE through the diversion of pancreatic and biliary secretions from the afferent limb. This will decrease anastomotic edema, mucosal irritation, and reflux gastritis.

Furthermore, it decreases the redo rate, Nasogastric tube (NGT) reinsertion times, length of hospital stay, and vomiting during postoperative GIT recovery. There is a low incidence of postoperative biliary leakage (4.76%) and pancreatic fistula through the reduction of pressure within the biliopancreatic limb. BJJ can also decrease surgical morbidities such as intra-abdominal abscesses, wound infections, and postoperative bleeding. Few studies in the literature demonstrated BJJ's efficacy in reducing postoperative morbidities (19, 31). Hence, this study aims to determine management modalities of pancreatic cancer and surgical outcomes of adding Braun's jejunojunostomy to Whipple's procedure for the reduction of postoperative risks in Sudanese patients to reach excellent surgical practice.

## Subjects and Methods

This is a prospective-cohort study conducted during the period between January 2022 and July 2023. The study received no funding and was conducted in the gastroenterological surgical department of Ibn Sina Specialized Hospital, Khartoum, Sudan. Before the study commenced, ethical approval was obtained from the local research ethics committee of the Faculty of Medicine and Health Sciences, Omdurman Islamic University, at the committee meeting number

(202) on Sunday 19<sup>th</sup> December 2021. A written consent was taken from the participants. Data in this study including demographic characteristics, clinical presentation, provisional diagnosis, modalities of investigation, risk factors of PC, surgical indications and postoperative complications were collected by a questionnaire. Inclusion criteria are the following: Sudanese patients aged 15 to 75 years or more of either sex who were clinically diagnosed as pancreatic cancer confirmed by Trans-abdominal ultrasonography (TUS) and MRCP. Then, variable PC stages were revealed by abdominopelvic CT-scan with Intravenous route and water-soluble contrasts. These patients underwent operable elective open Whipple's procedure combined with BJJ. Exclusion criteria included: laparoscopic Whipple's surgery, non-operable cases, biliary traumatic injuries, and other hepatobiliary cancers. Also, all patients with incomplete records and any other co-morbidity which precluded GA. The clinical details of included patients were entered into a spread sheet (Excel 2016 for Windows). This data was statistically analyzed by using SPSS version 23 (IBM SPSS Statistics for Windows, Chicago, Illinois, IBM Corp, USA). For comparison between groups, Chi-Square statistical test was conducted. The statistical results were considered significant when the P-value was <0.05. Open elective Whipple's procedure in this study were proceeded with the supine positioning of patients and General anesthesia with endotracheal intubation. NGT was inserted for gastric decompression to get a better operative field exposure. Then, through bilateral subcostal incision the subcutaneous fat, fascia and muscles were cut and dissected with an electro-cautery to open the peritoneal cavity. Operable pancreaticoduodenectomy performed through division of the duodenum 2–3 cm distal to the pylorus with safe protection of right gastric artery. Hepatoduodenal ligament and para-aortic LNs were completely dissected in the standard way. Then, the neural tissues around the superior mesenteric artery were dissected (extended LNs dissection). A retrocolic reconstruction was used for end-to-side hepaticojejunostomy and end-to-side pancreaticojejunostomy. pancreaticojejunostomy (PJ) was performed in duct-to-mucosa fashion with an internal short plastic stent placed at the anastomotic site. The antecolic end-to-side gastrojejunostomy was performed approximately 45-50 cm distal to the hepaticojejunostomy (HJ). In the BJJ, antecolic side-to-side jejunojunctionostomy was added between the afferent and efferent jejunal loops 30 cm distal to gastrojejunostomy site, (Figure 1), (32). The gastrojejunostomy and BJJ were performed in two layers, using interrupted 3–0 polyglactin Lembert sutures for the outer posterior and anterior rows. The inner rows were sewn in a continuous locking fashion posteriorly and as Connell stitch anteriorly with 3–0 polyglactin suture. Intra-abdominal drains were placed posteriorly to the PJ site and anteriorly to the HJ site. Postoperative monitoring including clinical follow up, abdominal surgical drains checking, requesting of Liver function tests and pancreatic enzymes.

## Results

In this study, sixty-three patients were diagnosed with operable pancreatic cancer and underwent elective open Whipple's procedure. Pancreatic carcinoma was more common in males 46 (73%) than females 17 (27%) with ratio (3:1), (Figure 2). Distribution of patients according to age ranged between 46 and 60 years

representing 26 (41.3%) of patients, (Table 1). The most common presenting symptoms were scleral icterus with highly dark colored urine and itching in 37 (58.7%) of cases, vague epigastric pain in 12 (19.1%) of cases, weight loss with anorexia in 8 (12.7%) and symptoms of anemia in 6 (9.5%) of cases. In abdominal examination, clinical signs were discovered and arranged as follows: clinical jaundice in 37 (58.7%) patients, epigastric abdominal masses in 12 (19.1%) patients, abdominal tenderness in 6 (9.5%) patients, pale conjunctiva in 6 (9.5%) patients and wasted body in 2 (3.2%) patients. Thirty-six patients (57.1%) resided in rural areas while 27 patients (42.9%) resided in urban areas. Clinical presentation of distant metastasis was not found in all patients of this study. The significant comorbidities that increased risk of PC were diabetes mellitus in 19 patients (30.2%), cigarette smoking in 15 patients (23.8%), heavy alcoholic consumption in 12 patients (19%), chronic pancreatitis in 8 patients (12.7%), positive family history in 6 patients (9.5%) and *Helicobacter pylori* infection in 3 patients (4.8%). Furthermore, patient's occupation had strong relationship with pancreatic cancer development and categorized as follows: 25 (39.7%) businessmen, 13 (20.6%) farmers, 11 (17.5%) housewives, 9 (14.3%) retired persons and 5 (7.9%) lap-technicians. Preoperative laboratory tests and diagnostic radiological tests were done in all patients (100%) including liver function test and serum tumor markers (CA 19-9, CEA and alfa fetoprotein (AFP)). Liver function tests values were arranged as follows: the ranges of total bilirubin were (0 -1.2 mg/dl) in 15 (23.8%) of cases, (1.3-5 mg/dl) in 20 (31.7%) of cases, (6-10 mg/dl) in 11 (17.5%) of cases and (> 10 mg/dl) in 17 (27%) of cases. The ranges of direct bilirubin were (0-5 mg/dl) in 30 (47.6%) of cases, (6-10 mg/dl) in 16 (25.4%) of cases, (11-15 mg/dl) in 7 (11.1%) of cases and (> 15 mg/dl) in 10 (15.9%) of cases. The ranges of indirect bilirubin were (0-5 mg/dl) in 58 (92%) of cases, (6-15 mg/dl) in 3 (4.8%) of cases and (> 15 mg/dl) in 2 (3.2%) of cases. The ranges of serum albumin were (1-2.9 g/dl) in 10 (15.9%) of cases, (3-6 g/dl) in 48 (67.2%) of cases and (> 6 g/dl) in 5 (7.9%) of cases. The values of tumor markers in the serum categorized as follows: the range of CA19-9 (0-37 u/mL) highly seen in 49 (77.8%) of patients, (Table 2). The range of CEA (0-2.5 ng/mL) was highly detected in 34 (54%) of patients, (Table 3). Also, the range of AFP (0-40 ng/mL) was highly detected in 46 (73%) of patients, (Table 4). TUS and MRCP imaging showed intra & extrahepatic dilated biliary tree with distended gallbladder in 47 (74.6 %) of patients, dilated pancreatic duct in 3 (4.8%) of patients and combined two mentioned radiological signs in 13 (20.6%) of patients. According to staging of abdominopelvic CT-scan, operable PC was staged as follows: stage (II) in 43 patients (68.2%), stage (III) in 17 patients (27%) and stage (I) in 3 patients (4.8%), (Table 5). After preoperative multi-disciplinary team decision, all patients (100%) underwent operable elective open Whipple's procedure with clear surgical margins and BJJ was performed. Moreover, estimated amount of intraoperative bleeding arranged as follows: (0-500 ml) in 59 (93.65%) of cases, 500-1000 ml in 3 (4.76 %) of cases and 1-2 liter in one case (1.59%). Postoperative complications were observed in 28 (44.4%) of patients. While the rest of patients in this study not had these morbidities (55.6%). These complications were categorized as follows: wound infections in 11 (17.5%) of cases, pulmonary infections in 4 (6.35 %) of cases,

postoperative DM in 3 (4.76 %) of cases, entero-cutaneous fistula in 3 (4.76 %) of cases, DGE in 2 (3.17%) of cases, biliary leak in 2 (3.17%) of cases, pancreatic fistula in one case (1.58%), gastric outlet obstruction in one case (1.58%) and postoperative GIT bleeding in one case (1.58%). Postoperative hospital stay was categorized as follows: 0-7 days for 16 patients (25.4%), 8-15 days for 42 patients (66.7%) and 16-30 days for 5 patients (7.9%). All patients of this study (100%) had intra-peritoneal drains which were removed within five days of fine postoperative care. The mortality rate of our patients was zero. The results of this study were statistically significant (P-value < 0.05).

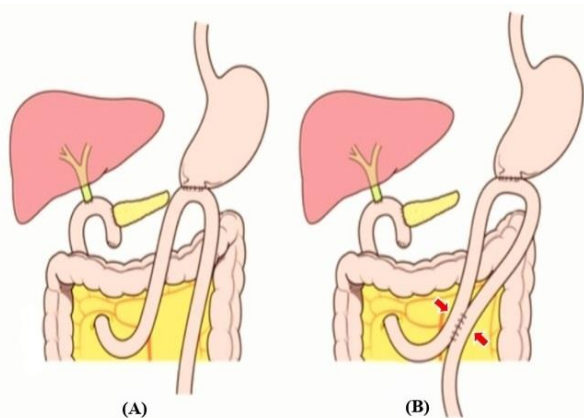


Figure 1: Intra-operative copied photo showed (A) Classical Whipple's surgery. (B) Classical Whipple's procedure had antecolic side-to-side Braun's jejunojunctionostomy between the afferent and efferent jejunal loops performed 30 cm distal to gastrojejunostomy site (32).

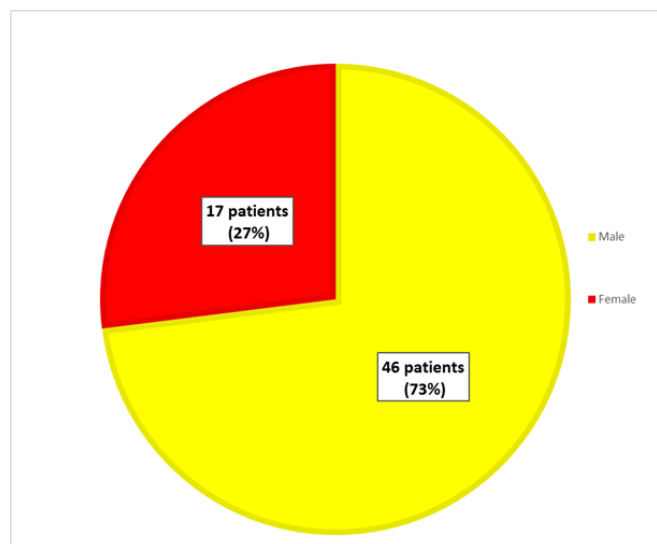


Figure 2: Gender distribution of patients diagnosed with pancreatic cancer.

### Discussion

Our study revealed that pancreatic cancer was more common in the male patients (73%). The male-to-female ratio is (3:1). This is consistent with the literature reporting that men are more to have PC than women (1, 2). The mean age of PC is between 46 and 60 years,

accounting for 41.3% of cases. This agrees with the results of the literature reported that raising the risk of PC with age up to sixty years due to progressive silent invasive nature of this malignancy (3).

Table 1: Age distribution of patients diagnosed with pancreatic cancer.

Age (Years)	Frequency	Percentage
15-30	3	4.8%
31-45	8	12.7%
46-60	26	41.3%
61-75	21	33.3%
> 75	5	7.9%
<b>Total</b>	<b>63</b>	<b>100%</b>

Table 2: Preoperative serum (CA19-9) test.

CA 19-9 (u/ml)	Frequency	Percentage
0-37	49	77.8%
38-100	3	4.8%
>100	11	17.4%
<b>Total</b>	<b>63</b>	<b>100%</b>

Table 3: Preoperative serum (CEA) test.

CEA (ng/ml)	Frequency	Percentage
0-2.5	34	54%
2.6-10	28	44.4%
>10	1	1.6%
<b>Total</b>	<b>63</b>	<b>100%</b>

Table 4: Preoperative serum (AFP) test.

AFP (ng/ml)	Frequency	Percentage
0-40	46	73%
40-200	6	9.5%
>200	11	17.5%
<b>Total</b>	<b>63</b>	<b>100%</b>

Table 5: Abdominopelvic CT-scan staging categories of pancreatic cancer.

CT-scan staging categories	Frequency	Percentage
Stage (I)-(local)-(cancer confined to the pancreas + absence of LNs involvement).	3	4.8%
Stage (II)-(local)-(cancer confined to the pancreas with involvement of up to three nearby LNs).	43	68.2%
Stage (III)-(locally advanced)-(cancer is outside the pancreas + spread to nearby organs and four or more LNs).	17	27%
<b>Total</b>	<b>63</b>	<b>100%</b>

The most common clinical presentation was jaundice sclera (58.7%) followed by epigastric pain and masses in (19.1%). Our results go with the literature which has reported the most common complaints



were loss of appetite (45%) and jaundice (41%), (8). Our study showed that most of the PC patients came from rural areas (57.1%). This disagreed with Kirkegard et al. who noticed increased incidence of PC in urban areas (61.7%), (4). This related to bad life-style of patients and deficient diagnostic health care facilities. the coexistence of diabetes mellitus (DM) was found to be a predominant comorbidity in (30.2%) of cases. This agrees with the literature showed that DM is responsible for 9.7% of cases (7). Our study reported businessmen (39.7%) had strong association with PC. An extensive revision in the literature was done. We found no relevant surgical studies that revealed the relationship between patients' jobs and PC development. We reported high direct bilirubin value (0-5 mg/dL) in (47.6%) of patients. Our results go with the literature, which shows serum bilirubin gave the optimum sensitivity and specificity for diagnosis of PC (71.9% and 86.9%), respectively (9). In this study, serum CA19-9 value (0-37 u/ml) was detected in (77.8%) of patients, and AFP value (0-40 ng/mL) noticed in (73%) of patients. Our findings agreed with the literature reported increased CA19-9 and AFP values in patients with advanced PC and considered CA19-9 as gold standard biomarker used in postoperative monitoring of PC patients (10, 33). Moreover, serum CEA value (0-2.5 ng/mL) was found in (54%) of patients. This is consistent with Meng et al. study who stated serum CEA was increased in 30%–60% of PC patients (11). These findings were related to early diagnosis of cases with suspicious presentation in referral clinics. TUS and MRCP successfully detected radiological signs of PC in (74.6%) of patients in the form of intrahepatic and extrahepatic dilated biliary tree with distended gallbladder. Moreover, preoperative abdominopelvic CT-scan is considered a necessary additional imaging modality to complete PC staging work-up and to determine PC resectability. Therefore, the most common stage of PC in this study was stage-II in (68.2%) of cases. Our results are similar to the literature showed that TUS, abdominopelvic CT-scan and MRCP had good sensitivity rates in differentiating operable cases of PC (67.3%, 65.8% and 57.5%), respectively (12). In this study, the rate of post-operative complications after addition of BJJ in elective open Whipple's surgery were detected in (44.4%) of cases. Moreover, wound infection is the most common diagnosed morbidity in (17.5%) of cases. These findings were in agreement with the literature reported wound infection is the most common septic complication in 6%–17% of cases. Furthermore, addition of BJJ to Whipple's surgery will reduce infection rate of the surgical wound (19, 23). Eventually, the overall mortality rate was zero. This result disagreed with the literature reported the mortality rate of PC was high and accounted for 37,390 deaths in the United States (1). This related to accurate surgical care with regular follow-up of our patients postoperatively. The main strength of our study are updated PC management modalities and the applicability of adding BJJ to Whipple's surgery for reduction of lethal morbidities in Sudanese patients to reach excellent surgical practice. Also, this is the first prospective study in Sudan described surgical impacts of BJJ addition to Whipple's procedure. The small number of patients is a limitation of our study that needs to be addressed. Future studies are recommended to compare the findings of this study with larger sample sizes and longer periods.

## Conclusion

To reduce the rate of lethal surgical morbidities of Whipple's procedure, we recommend addition of Braun's jejunostomy as useful technique. Moreover, it will potentially help in improving the

quality of surgical practice and survival outcomes of patients who are diagnosed with pancreatic cancer.

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## Author contributions:

Wael Mohialddin Doush was responsible for original manuscript writing, editing, supervision, and critical revision of contents. Wael Mohialddin Doush, Elfatih Yousif Abdelrahim, and Mohamed Sadig Omara were responsible for data collection, data analysis and manuscript design. Wael Mohialddin Doush was responsible for manuscript drafting and revision. All authors read and gave the final approval of the manuscript to be published.

## Statement of Ethics:

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 on the committee meeting number (202) on Sunday 19<sup>th</sup> December 2021. A written informed consent was obtained from all participants to participate in the study.

## Funding

There is no financial support or sponsorship from any institute.

## Conflict of Interest

The authors declare that they have no conflict of interest.

## Data availability

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

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