EXPERIENCE OF WHIPPLE'S PROCEDURE AT A TERTIARY CARE LEVEL HOSPITAL IN THE DEVELOPING WORLD- A PIMS EXPERIENCE

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Abstract

Objective: To assess and evaluate experience of Whipple's procedure in terms of morbidity and mortality in a tertiary care hospital of a developing country. **Materials and Methods:** A retrospective study was conducted at General Surgery department in Pakistan Institute of Medical Sciences Islamabad. Data of all adult patients (Age> 12 years) undergoing Whipple's procedure performed from January 2007 to December 2019 was collected from hospital record. A multivariate performa was used to record personal data of the patients, patient presentation, duration of hospital stay, duration of surgery, histological type, morbidities associated with the procedure and overall mortality. Data was then entered in SPSS version 20 and analyzed using chi square and T test. **Results:** A total of 227 patients were included in the study with 187 (82.4%) male patients and 40 (17.6%) female patients. Mean age of the participants was 57.3 ± 6.4. There was a mean operating time of 312 ± 34 minutes for Whipple's procedure. Mean length of hospital stay after surgery was 9.4 ± 3.2 days. A total of 37 cases (16.29%) developed wound infections where as complications like pancreatic fistula (n=5), Biliary fistula (n=1), bleeding (n=2), gangrenous Roux en Y loop (n=1) were less commonly present. Postoperative hematemesis requiring re-exploration was seen in 3 patients (1.3%) whereas 11 patients (4.84%) developed Systemic Inflammatory Response Syndrome (SIRS). There was an overall mortality of 3.96% (n=9). **Conclusion:** Outcomes of Whipple's procedure in our institute are comparable with literature from other high volume centers.

Keywords: Whipple's Procedure, Mortality, Morbidity

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INTRODUCTION

Although many surgeons addressed carcinoma pancreas and Ampulla of Vater by improvising various techniques, Allen Oldfather Whipple popularized the technique of resection of pancreas alongwith duodenum also known asPancreaticoduodenectomy (PD) followed by reconstruction. [1,2] Initially PD was performed in two stages as revealed by a seminal report published by Allen O Whipple in 1935 with findings based on three cases.[1] It progressed on to become a single stage procedure as evident from 10 year experience of Allen Whipple's published in 1946, which comprised of PD with complete excision of head of Pancreas and entire Duodenum.[1] For his remarkable contribution to the cause this procedure became a namesake of Allen Oldfather Whipple as Whipples Procedure.

It is one of the most complex, challenging and demanding operation, testing a surgeons training and practices. However such a complex operation was associated with aformidable mortality of 25%.[3] However over time with more centralization of Hepato-Pancreatico-Biliary services, better understanding and availability of intensive Care units, improvements in understanding and management of organ dysfunction and failure, decreased operative time due to availability of energy devices and robotic retractors and less bleeding and intraoperative replacement of blood has led to a significant drop in mortality to 2.5% or less. This is because of reduction in mortality to acceptable rates, recently, Whipple's Procedure is being offered liberally to old age, frail patients and today any patient who can be accepted for anesthesia, can undergo Whipple's procedure without a concern for in-hospital mortality.[3,4]

This decrease in overall mortality and morbidity meant that Whipple's procedure could be undertaken in a low resourceful developing world. In our institute aHepato-Pancreatico-Biliary unit at the Department of Surgery, Pakistan Institute of Medical Sciences, Islamabad, Pakistan, worked as a referral center for such cases from 2007to present. High number of referral cases led to the development of a set of techniques and trends within the institute which we believe helped in keeping acceptable morbidity and mortality ratesfollowing Whipple'sprocedure.

Methodology

A retrospective study was conducted inthe Department of Surgery at Pakistan Institute of Medical Sciences Islamabad and data of the

patients who underwent Whipple's procedure from January 2008 to December 2019 was evaluated. The record from hospital's HMIS system and department's own data register was obtained and assessed. A multivariate performa was used to record the obtained information. Data of the patients including age, gender, co-morbiditiesand symptoms at presentation was recorded in each performa. Researchers also recorded the histology type, site of tumour, recipient of pre-operative Endoscopy or biliary decompression and drainage, neo-adjuvant/ adjuvant chemotherapy. Operative time, intra operative blood loss,length of ICU and hospital stay, postoperative complications like blood loss, wound infection, pancreatic fistula formation and in hospital mortality were also taken into account.

All adult age (12years or more according to our hospital policy) patients who had undergone Whipple's procedure during the defined time period were included after obtaining a written informed consent but those cases with missing files or incomplete records were excluded.Data thus obtained was entered in SPSS version 20 and data analysis was done by using means and frequencies. Co-relations were obtained using tests of significance including Chi square test and T tests. Data was then presented as tables and charts.

Approval Committee

Before the study initiation, legal and ethical approvals were obtained from the Ethical Review Board of Pakistan Institute of Medical Sciences (PIMS) Islamabad, Reference numberECPIMS/15/01; dated 28 August 202 and the investigationwas performed in accordance with the ethical guidelines.

Results

A total of 227 Whipple's procedures were performed from January 2007 to December 2019 at Pakistan Institute of Medical Sciences Islamabad, a high volume hepato-pancreatico-biliary referral center with more than 25 cases of Whipple's procedure performed each year from 2012-2015 (Figure 1).

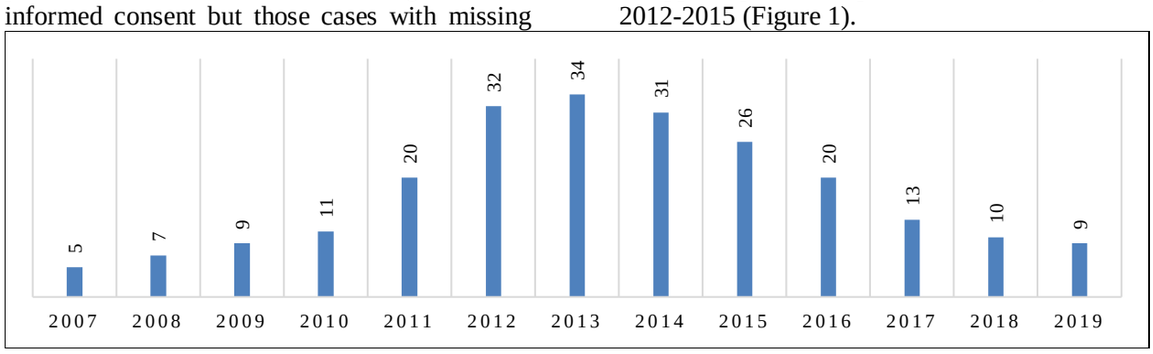

Figure 1: Number of cases of Whipple's procedure performed per year

In our practice ERCP and biliary decompression are not performed routinely however 67% (n=152) of the patients had received preoperative Endoscopic Retrograde Cholangio Pancreaticography (ERCP) and biliary decompression, all of whom were referred cases and they has received ERCP as per referral hospitals policy.One patient was referred by an oncologist after receivingNeo-adjuvant therapy believing it to be a borderline resectable pancreatic cancer. Adjuvant chemotherapy was received by 48 patients (21%).

Most common type of tumor treated with Whipple's procedure was Adenocarcinoma of the head of Pancreas (n=127) followed by Peri-ampullary carciconoma (n=91). There were 3 patients who had Neuroendocrine tumor and Primary duodenal carcinoma each, two cases of Gastrointestinal stromal tumor (GIST) and one case of Leiomyosarcoma of Duodenum. One patient who had Neuroendocrine tumor presented in Emergency department with massive hematemesis and was in shock, and underwent successful surgery in emergency settings.

Another 38 patients were planned for Whipple's procedure based on the findings of CT scan. However on commencement of surgery the tumour was found to be unresectable, indicating that CT scan tends to under-stage the disease in 1 out of 6 cases. These cases were excluded from study. There were 187 (82.4%) male patients and 40 (17.6%) female patients. Mean age of the participants was 57.3 ± 6.4. A vast majority of the patients had Diabetes (n=163), Hypertension (n=198) and other comorbidities like chronic kidney disease. Most common presentation was a triad of obstructive jaundice (n=225), anorexia (n=227) and weight loss (n=225) Table 1.

Table 1: Presenting signs and symptoms of patients who underwent Whipple's procedure

Symptom and signs at presentation	Frequency
Jaundice	225
Anorexia	227
Weight loss	227
Palpable gall bladder	222
Blunt trauma	2
Hematemesis ± shock	2

There was a mean operating time of 312 ± 34 minutes for Whipple's procedure. In our institute we performed PD by using upper abdominal transverse incision and the use of Thompson retractor replaced more conventional retraction techniques.Initially anastomosis was performed

using Roux en Y pancreaticojejunostomy however with time it was shifted to classical technique to save time and expedite surgery. Pancreaticojejunostomy was performed using duct to mucosa technique. Two drains were placed, with right drain in Morrison's pouch and left drain in lesser sac. Mean length of hospital stay after surgery was 9.4 ± 3.2 days. Patients received ICU care following surgery for an average of 2.8 ± 1.2 days. Per-operative bleeding was estimated on average to be 410ml ± 55ml. In the beginning use of prophylactic Octreotide administration was a routine practice in our set up till the time drains were in situ however this practice was discontinued by 2016 as evidence based literature suggested no role of octreotide in decreasing incidence of pancreatic fistula formation.

Out of these 227 patients, 37 cases (16.29 %%) reported developing wound infections mostly after third postoperative day. Complications like pancreatic fistula (n=5), Biliary fistula (n=1), bleeding (n=2), gangrenous Roux en Y loop (n=1), Renal failure (n=1), Deep Venous Thrombosis (n=1) were also reported but were uncommon. Major morbidity included cardiac events (n=11, 4.84%) and pneumonia (n=38; 16.7. Three patients reported having massive hematemesis post operativelywhich required re-exploration (1.3%). Eleven patients (4.84%) developed Systemic Inflammatory Response Syndrome (SIRS) and there was an overall mortality of 3.96% (n=9).

Patients developing SIRS or other systemic complications had higher incidence of mortality ($p<0.05$). Participants having Neuroendocrine tumour had higher mortality ($p<0.05$) than other tumour types. Multiple previous co-morbidities like Diabetes and Chronic renal disease resulted in higher incidence of developing systemic complications however it was not statistically significant. Different surgical techniques involving anastomosis did not contribute any significant difference in overall morbidity and mortality. There was no statisticallysignificant improvement found in mortality or morbidity amongst the patients after undergoing preoperative biliary decompression and drainage ($p=0.218$). Use of prophylactic octreotide administration had no significant effect on decreasing drain output and preventing pancreatic fistula formation.

DISCUSSION

In the current study it was observed that a vast majority of our patients were male and only a handful of female patients (17.6% of total participants) underwent Whipple's procedure. This trend was in contrast to a similar study conducted at Aga Khan Hospital Karachi where female patients were almost doublethe percentage as compared to our study population.[5]

Candidates for Whipple's procedure presented with obstructive jaundice and pruritus which common sense dictates should be decompressed before surgery to improve patient care. Howeverno preoperatively biliary drainage (PBD) maybe the best management of preoperative Jaundice in patients with resectable pancreatic cancer (RPC) before pancreaticoduodenectomy (PD) as evident from our study. Rather ERCP and preoperative biliary drainage increases the risk of biliary infection as explained by Freeman et al that ERCP may result in cholangitis, pancreatitis, intestinal perforation or bleeding and even death.[6]Hence direct surgery should be considered the best therapeutic strategy for the treatment of obstructive jaundice secondary to RPC. However PBD may be considered in patients with borderline resectable pancreatic cancer acquiring neoadjuvant therapy.[7-9]

Mean operating time and length of hospital stay in our study was comparable to studies conducted by other developing countries like Iran.[10]Complications like wound infection were commonly encountered in developing world as reported by Shukla et al from India.[11] Overall mortality in current study was 3.96% which was consistent with that seen in high volume centers in developing world where a range of 2-5% mortality was reported.[11,12] Similar mortality rate of 3.9% was observed in a study conducted in Indiana USA analyzing an experience of Whipple's procedure spanning 20 years.[13] The researcher reported that postoperative complications like pancreatic fistula, cardiopulmonary events and sepsis were noticed which the case is also in current study.[13]In a study conducted at Freeman hospital UK, it was reported that prophylactic use of octreotide had no effect in preventing pancreatic fistula formation.[14]Similar literature led us to give up our previous practice of prophylactic octreotide administration in early post-operative period. Our study finds no statistical difference in prevention of pancreatic fistula formation before and after we discontinued using prophylactic octreotide.A sharp rise in the number of Whipple's procedures was recorded in our institute from 2011-2014 with the establishment of a dedicated Hepato-Pancreatico-Biliary unit, turning our hospital into a high volume center. When compared with literature from other high volume centers there is comparable morbidity and mortality in Whipple's procedure conducted in our institute.[12]

Various techniques are described in literature for reconstruction after resection of part of stomach, common bile duct, gallbladder, duodenum, first six centimeters of jejunum and head of pancreas in Whipple's procedure. Special emphasis has been placed on the technique of anastomosis of pancreas to the gut. There was no significant difference in terms of complications like leakage and local collections, sepsis or pancreatic fistula formation after adopting various techniques of anastomosis, like duct to mucosa pancreaticojejunostomy, Dunking, Blumgart's Pancreaticojejunostomy or pancreaticogastrostomy.[15-20] Similar findings have been shown in our study that there was no impact on the overall mortality or morbidity following Whipple's procedure due to difference in anastomosis technique (Roux en y and classical pancreaticojejunostomy).

Conclusion

In high volume centers Whipple's procedure carries low mortality and fewer incidences of major morbidities. Adopting own guidelines based on the demographics and resources of a developing country can help improveoverall survival and quality of life of patients undergoing Whipple's procedure. Centralizing of referral cases to dedicated Hepato Pancreatico Biliary units or institutes can be a step forward.

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Authors contribution: Dr Mumtaz Ahmad Khan, Dr Namrah Mahmood, Dr UmbarRafique……. - Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, Drafting the work or revising it critically for important intellectual content. Final approval of the version to be published. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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