ORIGINAL ARTICLE

MANAGEMENT AND OUTCOME OF JAUNDICE SECONDARY TO MALIGNANCIES OF THE GALL BLADDER, BILIARY TREE AND PANCREAS: A SINGLE CENTRE EXPERIENCE

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Background: Obstructive jaundice due to malignancies of the biliary tree, gall bladder and pancreas account for a significant number of patients managed by tertiary centres. Management options are curative or palliative, depending on disease stage. This study was performed to see the effectiveness of treatment modalities for these patients and eventual outcome. **Methods:** This cross-sectional analytical study was conducted at the Department of Gastroenterology and Hepatology, Shaikh Zayed Hospital Lahore, from January 2015 to June 2016. All adult patients aged 18 and above of either sex presenting with obstructive jaundice secondary to malignant disease originating from the gallbladder, biliary-tree or pancreas were included in the study. The disease was staged after admission. The patients then underwent endoscopic, surgical or percutaneous drainage and were followed up for a period of one year. **Results:** Two hundred & sixty-two patients presenting with jaundice due to malignancy arising from the biliary tree, gall bladder or pancreas were enrolled between January 2015 and June 2016, 141 (53.8%) males and 121 (46.2%) females. Eighty (30.5%) had cholangiocarcinoma, 70 (26.7%), had gall bladder tumours, 61 (23.3%) pancreatic cancer and 51(19.5%) had ampullary tumours. 31 (11.8%) patients had disease qualifying curative surgical resection. One hundred & eighty-five (70.6%) patients underwent palliative therapy in the form of percutaneous in 86 (32.9%) and endoscopic drainage in 126 (48.1%). Twenty-eight (10.7%) patients refused all treatment. Eighteen (6.9%) patients died before undergoing any therapeutic intervention. Thirty-three (12.6%) died during hospital stay. Survival at 3, 6 and 12 months was 49.2% (129 patients), 28.2% (74 patients) and 8.4% (22 patients), respectively. These 22 included all patients who had undergone curative resection. We attributed the largest number of deaths, 197 (75.2%) patients, to metastatic/advanced disease and associated complications. **Conclusion:** The results showed that patients with advanced disease who were only eligible for palliative therapy, at first presentation, constituted the majority of patients. These patients require skilled endoscopy and interventional radiology teams for successful biliary drainage.

Keywords: Gall bladder tumour; Cholangiocarcinoma; Ampullary tumour; Pancreatic tumour; Obstructive jaundice; Ultrasound; CT scan; ERCP; Percutaneous biliary drainage

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INTRODUCTION

Obstructive jaundice of malignant origin constitutes a fairly large number of patients that present with jaundice to tertiary care units.[1] Treatment options for jaundice secondary to malignancies depend upon the stage of the disease and clinical condition of the patient. These malignancies include cholangiocarcinoma, gall bladder tumours, pancreatic tumours, peri-ampullary tumours, hepatic malignancies and metastatic disease.[2]

Treatment options available are either curative or palliative. Curative treatment involves surgical resection with or without chemotherapy. Liver transplantation may be a curative option in a few patients. Patients in good physical condition with early stage disease are referred directly for curative surgery. In other cases, who are not deemed good risks and require optimization, endoscopic or percutaneous interventions may be used as a bridge to surgery when treatment of cholangitis or lowering of high bilirubin is required prior to surgery.[3]

Palliative treatment options include endoscopic or percutaneous stenting or palliative surgical procedures. The treatment modalities depend on different factors which include age, functional status, co-morbidities and stage of disease. Endoscopic therapy or ERCP includes placement of a plastic or metallic stent (SEMS: Self-expandable metallic stent). The choice of stent usually depends on stage of disease and expected survival. Plastic stents are used in cases of early disease for drainage as a bridge to surgery or in cases of advanced disease with expected survival below 3 months. Percutaneous drainage may be internal (Percutaneous Transhepatic Biliary Stenting: PTBS) or external (Percutaneous Transhepatic Biliary Drainage:

PTBD) depending on ease of biliary access. Similar to ERCP, internal drainage by percutaneous route is done with SEMS.[4–6]

In our country, financial constraints also dictate the choice of stent during ERCP with plastic stents being a cheaper option (8–10 times cheaper than SEMS). However, this upfront cost may be misleading as metal stents are associated with lower long-term complications such as inadequate drainage and stent blockage and hence lower long-term expenditures. Plastic biliary stents have higher rates of stent occlusion which translates to need for repeat drainage procedures. This translates to higher costs.[7–10]

Similarly, high costs may dictate the use of external drainage (PTBD) with plastic drains instead of internal drainage with SEMS (PTBS) and therefore more patients opt for PTBD which is 4–5 times cheaper than PTBS. This is again an effect of lower upfront costs. PTBS is associated with lower long-term complications and better survival as compared to PTBD which translates to lower long-term costs.[11,12]

The aim of this study was to see the effectiveness of treatment modalities for patients presenting with obstructive jaundice due to malignancies of the biliary tree and pancreas and eventual outcome of these patients after admission to a tertiary care centre.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted at the Department of Gastroenterology and Hepatology, Shaikh Zayed Hospital Lahore, from January 2015 to June 2016. The study was initiated after approval from the institutional review board. All adult patients aged 18 and above of either sex presenting with obstructive jaundice secondary to malignant disease originating from the gallbladder, biliary-tree or pancreas, as confirmed on ultrasound and contrast enhanced CT, were included in the study.

Recruitment was done on an intention to treat basis. Patients with early stage disease, meeting criteria for surgical resection were referred for curative surgery. Patients labelled as having irresectable disease on the basis of advanced local spread, distant metastasis with or without ascites were listed for palliative therapy. The patients underwent management of disease by endoscopic biliary drainage. Patients in whom endoscopic access was not possible or unsuccessful, were referred for percutaneous biliary drainage. They were then followed up after discharge for a period of 12 months.

RESULTS

Two hundred & sixty-two patients, 141 (53.8%) males and 121 (46.2%) females, were enrolled between January 2015 and June 2016.

Cholangiocarcinoma constituted the largest number with 80 (30.5%) patients. Patients with cholangiocarcinoma included those with hilar cholangiocarcinoma, distal CBD tumours, proximal CBD tumours and intrahepatic cholangiocarcinoma. The second most common were gall bladder tumours with 70 (26.7%) patients while the remaining patients had pancreatic tumours and ampullary tumours (Table-1).

Thirty-one (11.8%) patients underwent curative treatment in the form of surgical resection of tumour. 185 (70.6%) patients underwent palliative biliary drainage. Twenty-eight (10.7%) patients refused any form of treatment. 18 (6.9%) patients died before undergoing any therapeutic intervention.

Amongst the 31 patients who were referred for curative surgical resection, 12 (39%) patients directly underwent surgery while 19 (61%) patients underwent biliary drainage procedure (ERCP or PTBD) as a bridge to surgery. Four (1.5%) patients received post-surgical anti-tumour therapy in the form of radiotherapy and/or chemotherapy. 2 patients died of post-surgical infection and resulting complications. Of the remaining 29, 22 were alive after one year while 7 were lost to follow up.

Palliative treatment was divided into patients undergoing ERCP and percutaneous trans-hepatic biliary drainage procedure (PTBD or PTBS). Palliative surgery was not performed in any patient.

ERCP was done in patients who were physically fit and with no technical hindrance (such as duodenal infiltration). Percutaneous biliary drainage procedures were performed in two patient categories: patients not fit for ERCP, patients in whom ERCP was unsuccessful (either in terms of unsuccessful cannulation or inadequate drainage of biliary channels) or technically not possible (such as tumour mass impeding passage of scope into duodenum). Thirteen (5%) patients underwent both ERCP and PTBD for drainage of right and left biliary systems simultaneously when ERCP was only able to drain one system.

Of the patients undergoing endoscopic drainage, 74 were treated with plastic biliary stent placement while self-expanding metal stents (SEMS) were placed in 56 patients. Duodenal stenting was performed in 11 patients after biliary drainage in patients with duodenal luminal obstruction from malignant infiltration. Four patients had mal-positioned plastic stents while wire cannulation of the targeted bile ducts for stent placement during ERCP was unsuccessful in 39 patients. These 43 (16.4%) patients were then referred for percutaneous drainage. ERCP was technically not possible due to luminal obstruction and tumour infiltration in 33 (12.6%) patients. A total of 112 patients were referred to the

interventional radiology teams for percutaneous biliary drainage procedures. 26 (9.9%) patients refused to undergo percutaneous drainage therapy. Of the remaining 86 (32.8%), 30 (11.5%) underwent internal drainage (PTBS) while 56 (21.4%) underwent external drainage (PTBD). These 86 patients included 13 (5%) who, as outlined above, had previously undergone ERCP and stenting of right or left ductal systems prior to being referred for percutaneous drainage.

One hundred & ninety-five (74.4%) patients were discharged from the hospital after successful curative or palliative therapy. Thirty-four (13%) were discharged on request or left against medical advice. Thirty-three (12.6%) died during hospital stay. Less than half (129 patients: 49.2%) of the patients were alive after 3 months following discharge from the hospital, 74 patients (28.2%) at 6 months and 22 (8.4%) after a year. These 22 had all undergone curative surgical resection of their tumours. 37 (14.1%) patents were lost to follow-up **(**Table-4).

We attributed 197 (75.2%) deaths to metastatic/advanced disease, 14 (5.3%) to sepsis following post-ERCP cholangitis, 9 (3.4%) due to acute kidney injury and cholangitis which was present on admission before ERCP or percutaneous drainage could be performed and 2 (0.8%) to post-surgical complications.

Table-1: Type of malignancy causing jaundice

CT growth	Frequency	Percent
Cholangiocarcinoma	80	30.5
Gall bladder	70	26.7
Pancreatic	61	23.3
Ampullary	51	19.5
Total	262	100.0

Table-2: Outcome of patients referred for ERCP

ERCP technical outcome	Frequency	Percent
Successful	126	48.1
Unsuccessful cannulation of bile duct (patient referred for percutaneous drainage)	43	16.4
Not possible due to duodenal luminal obstruction by infiltrating tumour	33	12.6
ERCP not performed (patients referred directly for surgery or percutaneous drainage or refused therapy)	60	22.9
Total	262	100.0

Table-3: Outcome of patients referred for percutaneous drainage

Percutaneous drainage	Frequency	Percent
PTBS	30	11.5
PTBD	56	21.4
Refused	26	9.9
Not referred for percutaneous drainage (patients underwent ERCP or were referred for surgery or refused therapy)	150	57.3
Total	262	100

Table-4: Frequency distribution of survival after admission

Survival after admission in tertiary care hospital	Frequency	Percent
Less than 3 months	129	49.2
6 months	74	28.2
1 year	22	8.4
Lost to follow up	37	14.1
Total	262	100.0

DISCUSSION

Malignant obstructive jaundice is a serious condition and if not detected early, carries a poor prognosis. A timely diagnosis requires an ability to recognize key points in history and examination, followed by definitive workup and referral to specialist centres. The specialist centres themselves must be well staffed and equipped with dedicated hepatobiliary teams consisting of physicians, surgeons, interventional radiologists and oncologists.

Direct curative resection or biliary drainage coupled with curative resection of the malignancy is the best treatment for such patients. We had a number of patients who required biliary drainage prior to surgery as low pre-operative bilirubin is associated with better recovery and lesser complications.[13,14]

Unfortunately, in our experience, many patients present late in whom only palliative treatment is possible. We noted in our study that a very small number of patients presented with disease at a stage which was amenable for curative intervention. Most had presented late and were only fit for palliative treatment. This thereby translated in poor survival following discharge from the hospital. This observation was echoed in similar studies from other developing countries.[15,16]

Palliative treatment included endoscopic and percutaneous biliary drainage procedures. The stents deployed to drain the biliary system included plastic and metallic stents. Increased costs lead to choosing a plastic stent in cases where a metal stent would have been more feasible, as further discussed below.

In many cases, as also noted in our study, combined endoscopic and percutaneous drainage was necessary as endoscopic stenting was unsuccessful or achieved suboptimal drainage. The latter is especially important in malignancies involving the hilum whereby bilateral stenting of both right and left ductal systems is needed.[17–19] This underlines the importance of having trained, experienced and fully equipped interventional radiology teams in cases where endoscopic therapy fails or is not possible.

In patients with malignancies causing luminal infiltration and obstruction of the duodenum, endoscopic placement of metallic stents in the duodenum was performed. Surgical bypass is also possible though no patient underwent this procedure

in our study group as most were unfit for such procedures.

We observed that more than half the patients had died within 3 months following discharge from hospital. Survival rates at 3 months, 6 months and 12 months were 49.2%, 10.3%, and 6.9%, respectively, with overall median survival of 82 days. Our median survival time is low compared to other studies, which can be explained by late referral leading to advanced disease at presentation and poor general condition of our patients.[12] We noted that over 60% of our patients had presented two months or more after developing jaundice. This meant more advanced disease stage when patients presented to us. This finding is extremely important.

There is a basic inability to recognize clues in a patient's history and examination among primary care teams. This results in such patients being placed in a long cycle of general practitioner visits and symptomatic treatment. This is further compounded by weak basic ultrasound facilities associated with such primary care teams who fail to detect key findings. Hence referral for a CT also occurs late. This results in overall late presentation to tertiary care teams. It is therefore necessary to train primary care teams, especially general practitioners to recognize danger signs in a patient with jaundice of an obstructive nature. They should be trained to refer such patients for an early CT and management by tertiary care facilities.

In the small number of patients who were lucky to have early disease meeting criteria for curative resection, we saw good survival. All the 22 patients alive at 1 year were those who had undergone curative removal of malignancies.

Another important observation was the preference for plastic stents due to much higher cost of SEMS. Plastic stents cost on average Rs 5000–7000 ($ 45–65) while metallic stents cost around Rs 50,000–70,000 ($ 450–650), thereby leading to preference for cheaper stents among financially constrained patients. International studies have noted that although the upfront cost is higher, the long-term costs associated with metal stents are lower.[20,21] This however is difficult to communicate to poor patients who struggle to purchase even plastic stents.

Lastly, there were a large number of patients in our population who were directly or indirectly referred for percutaneous drainage. Again underlining the importance of interventional radiology teams in tertiary care hospitals. Cost again is an important factor with PTBD costing around Rs 30,000 ($ 222) and PTBS Rs 125,000 ($925). This is another factor in patients simply refusing therapy on cost grounds.

CONCLUSION

Obstructive jaundice arising from the biliary tree, gall bladder and pancreas constitutes a significant management load of a tertiary care GI unit. The results show that patients with advanced disease who are only eligible for palliative therapy represent the majority of this workload. Tertiary care units where these patients are referred need to have integrated hepatology, interventional radiology and hepatobiliary surgical teams in order to provide effective curative and palliative treatment. These patients have short survival times after discharge from hospital. In order to change this situation to a more favourable clinical outcome, early diagnosis and prompt treatment is paramount. This will require training of primary care physicians and robust primary care diagnostic tools for early referral and definitive curative therapy. It is also vital to have an in-country facility for manufacturing stents and associated equipment in order to bring down procedural costs. This will lessen the burden on both self-paying and government/insurance sponsored treatment patient groups.

AUTHORS' CONTRIBUTION

AS: Literature search, conceptualization of study, data collection, data analysis, data interpretation, write-up & proof reading. SJ & FUA: Data collection, data analysis, data interpretation. KM: Write-up & proof reading

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