

An inquiry of Obstructive Jaundice

at Tribhuvan University Teaching hospital, Kathmandu, Nepal



Sabina Delin

Degree project in Medicine

Sahlgrenska Academy

An inquiry of Obstructive Jaundice

at Tribhuvan University Teaching hospital,
Kathmandu, Nepal

Degree project thesis in Medicine

Sabina Delin

Supervisors:

Göran Kurlberg, MD, Sahlgrenska Academy, University of Gothenburg, Sweden

Yogendra P. Singh, Prof. Chief Surgeon at the department of surgery at Tribhuvan University
Teaching Hospital, Kathmandu, Nepal



Programme in medicine
Sahlgrenska Academy
University of Gothenburg, Sweden, 2018

Table of Contents

1. Introduction.....	1
1.1 Country background.....	1
1.2 Health care system	1
1.3 The hospital	2
1.4 Obstructive jaundice as a disease.....	2
1.5 Obstructive jaundice research	4
2. Aim.....	4
3. Objective	4
4. Material and methods	5
4.1 Retrospective part	5
4.2 Prospective cross-sectional part.....	7
4.3 Statistical methods	8
5. Ethics	9
6. Results.....	10
6.1 Retrospective data.....	10
6.2 Prospective cross-sectional data	14
7. Discussion	17
7.1 Retrospective data.....	17
7.2 Prospective cross-sectional data	21
7.3 Methodological considerations	23
8. Conclusion.....	26
9. Populärvetenskaplig sammanfattning på svenska	27
10. Acknowledgment	28
11. References	29
12. Appendices.....	31
12.1 Attachment A: Patient form.....	31
12.2 Attachment B: Informed consent.....	32
12.3 Attachment C: Collection form for both retrospective and prospective cross-sectional part.....	33
12.4 Attachment D: Flow-chart for the retrospective and the prospective part.....	35
12.5 Attachment E: Ethical approval	36

Abstract

This degree project in medicine, “An inquiry of Obstructive Jaundice at Tribhuvan University Teaching hospital, Kathmandu, Nepal” written by Sabina Delin, medical student at the University of Gothenburg, Sweden, 2018.

Introduction: No previous studies have been made in Nepal concerning the causes and symptoms of obstructive jaundice. This study explores correlations between the disease and sex, age, underlying causes and symptoms.

Method: The study consisted of two parts. The first was a retrospective study where one-hundred-and-ten patients were included. Their medical records were used as a basis. The other was a prospective cross-sectional study where eighteen patients were included, of the one-hundred-and-ten patients from the retrospective part. A patient form and their medical records were used to collect data.

Results: Retrospective data: 110 patients were included. There were 61 (55.5 %) females and 49 (44.5 %) males. About half of the patients had a malignant cause to the disease and half had a benign cause. The mean age of the patients with malign cause was 61 years compared to the mean age of 47 years for those with benign cause. There was a difference of 14 - years in mean difference. The most common cause was distal cholangiocarcinoma (15.5%) followed by pancreatitis (13.6%). The most common presentation of obstructive jaundice (presented as percentage of how many patients had each symptom) was jaundice (79.1%), other symptoms (58.2%), RUQ - pain (40.9%), itching (38.2%), anorexia/loss of appetite/loss of weight (38.2%) and epigastric pain (37.3%). **Prospective cross-sectional data:** 18 patients were included, of these were 11 (61.1%) women and 7 (38.9%) men. There were 10 (55.6%) malign cases, 6 (33.3%) benign cases and 2 (11.1%) patients with unknown cause. The mean age of the patients with malign cause was 62 years compared to the mean age of 34 years for those with benign

cause. There was a difference of 28 years in mean difference. Hilar cholangiocarcinoma was the most common cause of all followed by bile duct injury. The presenting symptoms noted in the medical journals were jaundice 58.8 %, itching 41.2%, anorexia/weight loss/loss of appetite 35.3%, RUQ - pain 35.3%, fever without chills 35.3%, clay-coloured stool 29.4%, other symptoms 29.4%, dark urine 17.6%, epigastric pain 17.6 % and fever with chills 5.9%. The symptoms found in the patient forms were jaundice 83.3%, itching 77.8%, RUQ - pain 55.6%, fever with chills and rigor 33.3%, clay-coloured stool 38.9% and dark urine 61.1%.

Conclusions: It is more common for older people to have a malignant cause of obstructive jaundice. This study indicates other proportions of the malign spectrum, compared to comparative studies, with distal cholangiocarcinoma as the leading cause. It seems like cholangiocarcinoma is more common in Nepal compared to what studies have shown in neighbouring countries. This indicates a different pattern of care-seeking due to i.e. economic factors or that cholangiocarcinoma as a cause to obstructive jaundice is more common in Nepal and possibly has a higher incidence in the Nepalese population.

Keywords: Obstructive Jaundice, Aetiology, Symptoms

1. Introduction

This Degree Project, initiated by Prof. Singh, Chief surgeon at the Department of Surgery at T.U.T.H. is an attempt to elucidate this area of medicine from a Nepali perspective.

1.1 Country background

Nepal is situated in south Asia bordering to China in the north and to India in all other directions. Nepal has a diverse landscape with lowlands with its forests and forested watersheds to the Himalayas with mountains, alpine pastures and temperate forests and the inner Himalayan valley with cold deserts and rivers. The population is around 26 million people and comprises about 101 ethnic groups that speak more than 92 languages. The official language is Nepali (The Official Tourism Website for Nepal, 2017). The BNP per person is 732 US dollars in 2015 (compared to 50 273 US dollars per person in Sweden). Thus, Nepal is a low-income country with a life expectancy at birth of 68 years (WHO, 2012). The literacy rate between the ages of 15-24 years was 79.4 % in 2006 (Central bureau of statistics, 2007).

However, during the last decades there has been a considerable improvement in economic status, demographic parameters and the health status of the population. As one of many examples the improvements made over the past 20 years in maternal and neonatal health has led to a decrease in mortality for children under five years from 142 to 40/1000 children. (WHO, 2012).

1.2 Health care system

The access to health care for the entire population can be difficult, especially concerning the rural areas with difficult terrain where there are not as many hospitals or health posts.

Still, most of the people have a health post within 30 minutes of travelling, but only a third have a public hospital within the same range (Roshan Khadka, Student at Mahidol University Follow, 2016). The total expenditure on health per capita is 137 dollars (WHO, 2014) compared to 5. 219

dollars per capita in Sweden (WHO, 2014). At present, most of the expenditure regarding health care is financed by on-use basis. However, the government intends to make it more publicly funded in the future, especially for people with a low income as a first step (WHO: Country office for Nepal, 2007).

Today, parts of the health care are free of charge i.e. immunization of children, deliveries at institutions, family planning services, treatment of heart, liver and kidney diseases and cancer at governmental hospitals. 70 kinds of essential drugs are provided free of charge as well as screening and treatment of TB and leprosy (Roshan Khadka, Student at Mahidol University Follow, 2016). The government plans to provide health insurance within three years to all Nepali citizen (Ghimire, 2017).

1.3 The hospital

Tribhuvan University Teaching Hospital (T.U.T.H.) is a non-profit hospital situated in Kathmandu. It was built in 1983 and provides medical care for the most needed. T.U.T.H. is an integrated part of the institute of medicine of Tribhuvan University and conducts medical research. It is a tertiary care hospital which with its 22 departments has the greatest number of specialities of any hospital in Nepal. It provided medical services to around 400 000 patients during the last year (Institute of Medicine, 2012).

1.4 Obstructive jaundice as a disease

Obstructive jaundice is a common surgical problem in the world and poses a challenge to surgeons, anaesthesiologists and intensive care teams. These patients need invasive techniques to relieve the obstruction in the bile tree and sometimes surgery that is associated with an elevated risk of complications and mortality. Obstructive jaundice patients are more pre-disposed to developing nutritional deficits, infectious complications, acute renal failure and impairment of cardiovascular function. They can suffer from coagulopathy, hypovolemia and endotoxemia, which can lead to significantly increased mortality and morbidity.

Cholestasis is a condition where there is an interruption in the excretion of bile. It can be divided into intrahepatic cholestasis, obstruction within the liver, and extrahepatic cholestasis, obstruction of the bile ducts outside the liver (K. Modha. 2015). There are two major functions of hepatic bile, it works as an emulsifier of dietary fat in the lumen of the gut through the detergent action of bile salts and helps to eliminate bilirubin, excess cholesterol and other waste products that are not enough water-soluble to be excreted through urine. (Robbins et al., 2010).

When there is an obstruction it causes the bile salts, lipids and bilirubin to accumulate in the blood stream. Intrahepatic cholestasis can be caused by intrinsic parenchymal disorders such as Primary Biliary Cholangitis, hepatitis due to drugs and cystic fibrosis (K. Modha. 2015).

Extrahepatic cholestasis is caused by a mechanical blockage. This could be due to gallstones, tumours in the bile ducts, pancreatic cancer or other conditions that cause increased pressure of the bile duct, such as scar tissue (from previous infection or surgery) or a cyst. (Robbins et al., 2010). This obstruction of the bile ducts, named obstructive jaundice or previously surgical jaundice, can in rare cases be caused by the nematode *Ascaris Lumbricoides* (Khuroo, Rather, Khuroo, & Khuroo, 2016). The clinical manifestations of altered bile formation and flow are jaundice, a condition where conjugated bilirubin circulating in the blood stream dissolves in the subcutaneous fat which leads to a yellowish discoloration of the skin, sclera and mucous membranes. The benign cause is more common in young people opposed to the malignant cause that is more common in older people (K. Siddique. 2011). Extrahepatic obstruction of the bile channel, a mechanical blockage, is often possible to alleviate through surgery. Therefore, a correct and fast diagnosis is important. This contrasts with intrahepatic obstruction, caused by secretory failure of the hepatocytes which leads to disturbances in the bile formation. This condition is normally not benefited by surgery and it could even worsen the patient's condition. (Robbins et al., 2010).

1.5 Obstructive jaundice research

The incidence of obstructive jaundice in the population is not fully known today, due to lack of research in significant areas. The problem is especially large in developing countries, like Nepal, where quite often no studies have been made concerning the causes and symptoms of obstructive jaundice. Although, lessons can be learnt from similar studies on this topic from neighbouring countries such as India (Gupta, Singh, Goel & Tank, 2017) and Pakistan (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008).

2. Aim

The postoperative morbidity can be as high as 20-30% (Wang, Yu, 2013). The aetiology of the obstruction predicts and explains the differences in morbidity and mortality (Gupta, Singh, Goel & Tank, 2017). What could help us improve the management and treatment of patients with obstructive jaundice, if not a better understanding of the presenting symptoms and causes of obstructive jaundice? Quite often no studies have been made concerning the causes and symptoms of obstructive jaundice. This Degree Project is an attempt to elucidate this area from a Nepali perspective.

3. Objective

The objective was to describe the patients with obstructive jaundice at T.U.T.H. and initiating more research.

The main question of this study regards “What are the proportions of different aetiologies of obstructive jaundice at T.U.T.H.?”

To address this, other sub-questions were addressed as follows:

- What are the demographic parameters like age, sex, urban – rural, ethnic background.

- Are there any correlations between age and sex?
- What symptoms do the patients present with? Which was the first presenting symptom?
- How are the patients diagnosed? Are ultrasound, CT and MRI used?
- What are the methods of treatment? What are the purpose? Are there any complications?
- How many days do the patients spend in the hospital?

4. Material and methods

The research study has taken place at the Department of surgery, T.U.T.H. Kathmandu, Nepal.

4.1 Retrospective part

The first part of the study was a retrospective part using two methods to include patients. The first method was to go through the admittance books of the three surgical wards, the Female Surgical Ward (FSW), the Male Surgical Ward (MSW) and the Annex-1 Ward, starting from the Nepali date of 2074-1-1 until 2074-7-15 which corresponds to the English calendar of 14th April until the 1st October 2017. The admitted patients with any preliminary diagnosis that was connected to the bile duct system or any connected organ such as the liver, gall bladder or pancreas were searched. The diagnoses and words connected to the bile duct system, that can cause obstructive jaundice found in the admittance books were the following : symptomatic cholelithiasis, biliary colic, hilar and distal cholangiocarcinoma, gall bladder cancer, gall bladder polyp, ampulla of water cancer (pen ampullary and periampullary carcinoma), pancreatic carcinoma (head of pancreas cancer), biliary stricture, acute mild and severe cholangitis, acute cholecystitis, congenital structural defects, choledochal cysts, abdominal lymph node enlargement due to for example TB, acute and chronic pancreatitis, acute necrotising biliary pancreatitis, pancreatic pseudocysts, parasitic infection, blunt abdominal trauma and trauma including surgical complications such as bile duct injury, dislodged Percutaneous transhepatic

biliary drainage (PTBD), status post Whipple's procedure, hepatocellular carcinoma, liver abscess, cystadenoma of the head of the pancreas and metastases in the connected area. The in-patient number, name and preliminary diagnosis were written down. This list of patients was used to search firstly in the computerised medical records system after the discharge papers. Most of the patients that were found through this method could either easily be excluded or included depending on the information in the discharge papers. The patients were included based on clinical signs such as jaundice, biochemical parameters as an elevation of total and direct bilirubin, preferably with an ALP increase and radiological signs of dilated bile ducts where searched for. If the picture in general was that of an obstruction in the bile ducts, the patient was diagnosed with obstructive jaundice. When there was no information about jaundice, elevated bilirubin, elevated ALP or radiological signs of obstruction the patient was assumed not to have obstructive jaundice and was excluded. If there was something pointing to an obstruction and the case was unclear, attempts were made to find the medical record in the archive. After this process was completed the patients complete medical records were searched for, for those cases that could not be found in the computerised system or those that had incomplete records, in the medical records archives. Many medical records were lost and could not be found. All the medical records that could not be found in the archive were asked for at least two times. The medical records that were found were subject to the same inclusion and exclusion criteria's. Data collection were performed using the collection form (Attachment C). This second form was produced solely for the collection of data, this form was designed by the author after researching the medical records.

Furthermore, an expanded cross search was done in the computerized journal system for patients admitted, from the Nepali calendar date of 2074-1-1 until 2074-6-14 corresponding to the 14th April until the 1st October in the English calendar, at the surgical ward with the diagnosis of either obstructive jaundice, bile duct, bile duct injury, gallbladder, PTBD or

cholangiocarcinoma which led to that one more patient was included out of 54 patients that was found, 32 was already included and the rest could be excluded.

In total there were 1855 patients in the admittance books between these dates. Out of these there were 503 patients that had a preliminary diagnosis that were determined to be of relevance. 32 of these patients could not be found, either due to that the numbers in the admittance books were faulty or because the records could not be found in the medical archive. 342 patients were excluded since their medical records showed no signs of obstructive jaundice. 129 patients were found to have obstructive jaundice. Out of these obstructive jaundice cases, 10 were duplicates of the same patients and the same hospitalizations. Of the 119 remaining patients, 3 were in some essential aspect missing data and 18 was in-hospitalizations of the same patient at another time but with the same disease and were therefore excluded. 98 individual patient cases remained and were included in the study.

The second method was to include patients from those found at the ward, taking part in the prospective part of the study (described below in section 5.2). This meant that additionally 12 patients, which were not already included in the retrospective series, out of the 18 patients, could be included. This made a total of 110 patients in the retrospective part (Attachment D).

4.2 Prospective cross-sectional part

The second part of the study was a prospective cross-sectional part. A patient form was produced (Attachment A), focusing on symptoms and lifestyle factors. The form was translated into Nepali by the help of Google translate and further by corrections made by Dr Bikal Ghimire. The form was then corrected into its final form and printed by the office secretary. A Nepali consent form (Attachment B) was created after the adaptation of a model consent form with the addition of the study name, department and the name of the author. Patients were recruited using the same kind of criteria in accordance with the same principles as in the retrospective part of the study, using the same search words to find patients that could have

obstructive jaundice. The admittance books of the three surgical wards: MSW, FSW and the Annex-1 Ward were searched each morning that the author was present at the hospital. This was done starting from the 1st October until the 1st November. The room number of these patients were written down and their medical records were collected and searched after signs of obstructive jaundice. The same inclusion criteria were used as in the retrospective part. The patients that had obstructive jaundice were asked to be part of the study and fill out the patient form (Attachment A). The patients were asked to participate in the research study by asking them to read the consent form and the patient form and if needed they were given the opportunity to ask questions. They had the possibility to ask questions in Nepali by talking to a nurse working at the ward. Furthermore, the medical records of these patients were used to fill out the collection form (Attachment C) and these patients were also included in the retrospective part. This form was completed by reading the medical records of the patients at the ward. When these were incomplete the author searched the online medical records and asked for the complete medical records in the medical records archive. 19 patients were at the ward when the author was present and 18 of these were included in the study and completed the patient form. One patient was discharged before the author had found a relative of the patient or a nurse that could translate and ask the patient to participate (Attachment D).

When calculating the statistical significant correlations between smoking, alcohol habits and malignant disease, the patients were grouped in two different groups based on if they were smoking or not and if they consumed alcohol or not. This was due to the small number of patients in the study.

4.3 Statistical methods

The data were transcribed into computerized versions of the collection forms. The data that would be used for creating graphs and be presented in the scientific report were transcribed into

Statistical Package for Social Sciences (SPSS). Age groups were made using “transform and recode” into groups of < 40, 41 to 65 and > 65 years. Groups of different aetiology were made dividing them into 12 categories: hilar cholangiocarcinoma, distal cholangiocarcinoma, carcinoma gallbladder, carcinoma head of pancreas, carcinoma pancreas, ampullary and periampullary carcinoma, cholangitis, choledocholithiasis, cholecystitis, pancreatitis and bile duct injury. The functions “analyse – descriptive statistics - descriptives and frequencies” were used in SPSS. Bar graphs, cross tables and the function to custom tables were used. Excel were used for calculations using the functions “mean” and “antal.om”. Tables were made in Excel. For the prospective data the patients were divided into categories of either currently smoking or not currently smoking as well as alcohol consumption or no alcohol consumption, which were created using excel. MATLAB were used to calculate statistical significance by two sample t-test and correlations. Regression analysis was conducted using MATLAB. Statistical significant p-value was considered when $p < 0.05$.

5. Ethics

The study adhered to the principles of the Helsinki Declaration. The author gained approval of the institutional review board (IRB) at the institute of medicine (Attachment E). The author influenced in no way the medical care of the patients. The patients informed consent was gained by explaining to the patients about the study, asking them to give consent and complete the patient form for all patients taking part in the prospective part of the study. There were very general questions in the form and no intrusive questions.

6. Results

6.1 Retrospective data

The total number of patients with obstructive jaundice was 110. There were 61 (55.5%) females and 49 (44.5%) males. The mean age of the study population was 55 years. Most patients were over 40 years old, 83 (75.45 %) patients. Most patients were in the age group of 40-65 years old, 59 (53.6%) patients. The mean age of the malignant cases was 61 years (± 3.5 , 95% confidence interval) compared to the mean age of benign cases that was 47 years (± 4.4). There were on average a 14-year age difference between the groups which is statistically significant $p = 3.13 \times 10^{-6}$. About half of the patients had a malignant cause 56 (50.9%) to the disease and half had a benign cause 52 (47.3%). The patients under 40 years of age with a malignant cause to the disease consisted of 4 (3.6 %) patients in total. The group of patients below 65 years with a benign cause were 47 (42.7%) in total. (Table 1 and Figure 1)

Table 1: Table over sex, age group and malignant or benign cause of obstructive jaundice of the retrospective part of the study with 110 patients in number and percentage.

		Total number (%)	Malignant cases (%)	Benign cases (%)	Unknown cases (%)
Sex	<u>Women</u>	61 (55.5%)	28 (45.9%)	32 (52.5%)	1 (1.6%)
	<u>Men</u>	49 (44.5%)	27 (55.1%)	20 (40.8%)	1 (2.0%)
Age group Distribution (Years)	<u>Under 40</u>	27 (24.5%)	4 (14.8%)	22 (81.5%)	1 (3.7%)
	<u>41 to 65</u>	59 (53.6%)	33 (55.9%)	25 (42.4%)	1 (1.7%)
	<u>66 and over</u>	24 (21.8%)	19 (79.2%)	5 (20.8%)	0 (0%)
	<u>Mean age</u>	55	61	47	49
Causes of obstructive jaundice		110 (100%)	56 (50.9%)	52 (47.3%)	2 (1.8%)

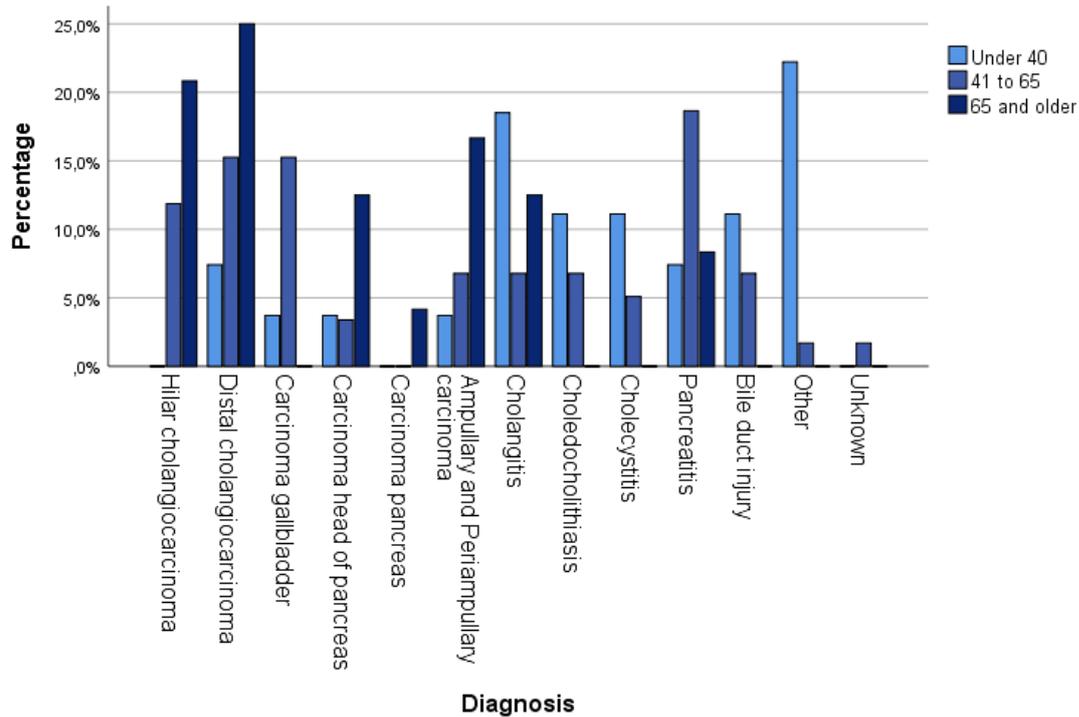


Figure 1: Bar graph of age group distribution over different causes of obstructive jaundice, malign causes to the left side and benign causes to the right side, for the retrospective part of the study with 110 patients.

The most common cause of obstructive jaundice was distal cholangiocarcinoma, affecting 15.5% ($\pm 6.8\%$, 95% confidence interval) of the patients. The second most common cause was pancreatitis, with 13.6% ($\pm 6.4\%$). This order is however not statistically significant. Among the malignant causes distal cholangiocarcinoma 17 (15.5%), hilar cholangiocarcinoma 12 (10.9%) and carcinoma of the gallbladder 10 (9.1%) were common causes. Of the benign causes pancreatitis 15 (13.6%), cholangitis 12 (10.1%), choledocholithiasis 7 (6.4%) and bile duct injury 7 (6.4%) were the most common causes (Table 2).

Table 2: Table with different aetiology in number and percentage, retrospective study

Causes of obstructive jaundice		Number (percentage)
Malignant cause (n=56)	Hilar cholangiocarcinoma	12 (10.9%)
	Distal cholangiocarcinoma	17 (15.5%)
	Carcinoma gallbladder	10 (9.1%)
	Carcinoma head of pancreas	6 (5.5%)
	Carcinoma pancreas	1 (0.9%)
	Ampullary and Periampullary Carcinomas	9 (8.2%)
Benign cause (n= 52)	Cholangitis	12 (10.1%)
	Choledocholithiasis	7 (6.4%)
	Cholecystitis	6 (5.5%)
	Pancreatitis	15 (13.6%)
	Bile duct injury	7 (6.4%)
	Others	6 (5.5%)
Unknown cause (n=2)	Unknown	2 (1.8%)

The share of patients having Carcinoma of the Pancreas as a cause was 6.4% ($\pm 4.6\%$, 95% confidence interval), while as cholangiocarcinoma was 26.4 % ($\pm 8.3\%$), this difference is statistically significant ($p=1.69e-04$).

Carcinoma of the gallbladder as a cause to obstructive jaundice was more common among females and ampullary and periampullary cancer was only found among males (Figure 2).

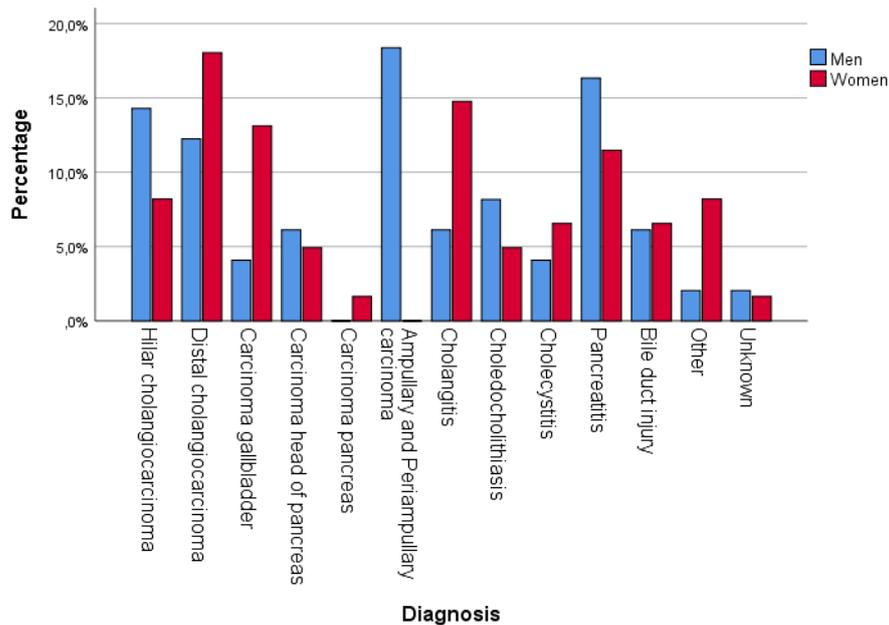


Figure 2: Bar graph of proportions of women and men related to diagnosis, retrospective part of the study

The presenting symptoms of obstructive jaundice were (percentage of patients having each symptom): jaundice (79%), other symptoms (58%), RUQ - pain (41%), itching (38%) and anorexia/loss of appetite/loss of weight (38%) and epigastric pain (37%) (Table 3).

Symptoms	Total (%)
Jaundice	87 (79.1%)
Right Upper Quadrant pain	45 (40.9%)
Epigastric pain	41 (37.3%)
Itching	42 (38.2%)
Fever with chills and rigor	13 (11.8%)
Fever without chills and rigor	37 (33.6%)
Clay coloured stool	30 (27.3%)
Anorexia/loss of appetite/loss of weight	42 (38.2%)
Dark urine	29 (26.4%)
Other	64 (58.2%)

Table 3: with symptoms of obstructive jaundice in percentage of patients for each symptom, of the retrospective part of the study.

Some symptoms are significantly positively related to malign disease, namely; itching ($p= 1.04 \times 10^{-5}$), clay-coloured stool ($p=0.0022$), anorexia/loss of appetite/loss of weight ($p=0.00016$), and dark urine ($p=0.016$). There is a significantly negative correlation between fever with chills and rigor and malignant disease, ($p=0.027$). There are no significant differences between different sex and symptoms or difference between sex contra malign and benign cause. There is a positively significant correlation between age and itching, $c=8.7$ and $p=0.0057$. There is a significant positive correlation between age and anorexia, $c=8.3$ and $p=0.0094$.

6.2 Prospective cross-sectional data

The total number of patients that were included were 18. There were 11 (61.1%) women and 7 (38.9%) men. The mean age was 51.5 years, this is not significantly different from the retrospective study. The youngest patient was 21 years old and the oldest was 73 years old. 50% of the patients were between 45 and 65 years. There were 10 (55.6%) malignant cases, 7 (38.9%) benign cases and 2 (11.1%) patients with unknown cause of obstructive jaundice (Table 4).

		Total number (%)	Malignant cases (%)	Benign cases (%)	Unknown cases (%)
Sex	Women	11 (61.1%)	4 (22.2%)	6 (33.3%)	1 (5.6%)
	Men	7(38.9%)	6 (33.3%)	0 (0%)	1 (5.6%)
Age group Distribution (years)	Under 40	6 (33.3%)	0 (0%)	5 (27.8%)	1 (5.6%)
	41 to 65	9 (50.0%)	7 (38.9%)	1 (5.6%)	1 (5.6%)
	66 and over	3 (16.7%)	3 (16.7%)	0 (0%)	0 (0%)
	Mean age	51.5	62.4	34.3	48.5
Causes of obstructive jaundice		18 (100%)	9 (50.0%)	7 (38.9%)	2 (11.1%)

Table 4: Table over sex, age group and malignant or benign cause of obstructive jaundice of the retrospective part of the study, with number and percentage.

The mean age of the patients with malignant cause were 62.4 years (± 5.3 , 95% confidence interval, not significantly different from the overall mean above) and 34.3 years (± 6.1 , borderline significantly different from the overall mean above, $p=0.069$) for those with benign cause, a difference of 28 years in mean difference. The difference is statistically significant ($p=7.9e-06$). The mean age, for those with unknown cause, was 48.5 years. There were no malignant cases below 40 years of age. Out of 6 benign cases, 5 were below 40 years of age. All the patients over 65 years of age had a malignant cause to the disease.

	Causes of obstructive jaundice	Number (%)
Malignant cause (n=9)	Hilar cholangiocarcinoma	5 (27.8%)
	Distal cholangiocarcinoma	1 (5.6%)
	Carcinoma gallbladder	1 (5.6%)
	Carcinoma head of pancreas	0 (0%)
	Carcinoma pancreas	0 (0%)
	Ampullary and Perampullary Carcinoma	2 (11.1%)
Benign cause (n=7)	Cholangitis	1 (5.6%)
	Choledocholithiasis	0 (0%)
	Cholecystitis	0 (0%)
	Pancreatitis	2 (11.1%)
	Bile duct injury	3 (16.7%)
	Others	1 (5.6%)
Unknown cause (n=2)	Unknown	2 (11.1%)

Table 5: Table with different aetiology in number and percentage, prospective cross-sectional study

There were only females that had bile duct injury and pancreatitis as a cause. Only men had periampullary and ampullary carcinoma and carcinoma gallbladder as a cause. Hilar cholangiocarcinoma is the most common reason for obstructive jaundice followed by bile duct injury as the second most common (Table 5).

The presenting symptoms noted in the medical journals were jaundice 66.7 %, itching 61.1%, fever without chills and rigor 38.9%, anorexia/weight loss/loss of appetite 38.9%, other symptoms 38.9%, RUQ - pain 33.3%, clay-coloured stool 33.3%, dark urine 22.2%, epigastric pain 16.7% and fever with chills 5.6%.

The symptoms from the patient forms were jaundice 83.3%, itching 77.8%, dark urine 61.1%, RUQ - pain 55.6%, anorexia/weight loss/loss of appetite 44.4%, clay-coloured stool 38.9%, and fever with chills and rigor 33.3% (Table 6).

Symptoms	Medical records, n (%)	Patient forms, n (%)
Jaundice	12 (66.7%)	15 (83.3%)
Right Upper Quadrant pain	6 (33.3%)	10 (55.6%)
Itching	11 (61.1%)	14 (77.8%)
Fever with chills and rigor	1 (5.6%)	6 (33.3%)
Clay coloured stool	6 (33.3%)	7 (38.9%)
Anorexia/loss of appetite/loss of weight	7 (38.9%)	8 (44.4%)
Dark urine	4 (22.2%)	11 (61.1%)

Table 6: Table with symptoms of obstructive jaundice, for the prospective part of the study, from both the medical records and from the patient forms.

More patients themselves noted itching in the patient form compared to what was written in the medical records, 77.8 % compared to 61.1 %, $p= 0.0093$. The patients noticed having dark urine in 61.1% of the cases compared to 22.2 % which was noted in the medical records, $p=0.0041$. It was near significant, $p=0.10$, that 83.3 % says they have had jaundice compared to 66.7% in the medical records. There are no significant differences in presenting symptoms between sexes.

However, there are a near significant difference in that fewer women report itching in the patient forms compared to men, $p=0.078$ and near significant that fewer women report dark urine than men, $p=0.098$. All men with known cause ($n=6$) in the prospective study have a malignant cause, compared to that 40% of the women have a malignant cause, the difference is statistically significant, $p=0.014$.

There are near significant positive correlations between RUQ - pain and dark urine, $p=0.0725$ and RUQ - pain and fever, $p=0.1045$. A positive significant correlation between itching and jaundice exists, $c=0.43$ and $p=0.0448$. Itching and anorexia has a positive correlation, $c=0.4$ and $p=0.0448$. There are near significant positive correlations between itching and clay-coloured stool, $p=0.078$ and between itching and dark urine, $p=0.1038$. Fever and anorexia are positively correlated, $c=0.525$ and $p=0.0172$. There is a near significant positive correlation between fever

and clay-coloured stool, $p=0.0974$. Dark urine and anorexia are positively correlated $c=0.475$ and $p=0.0417$.

Usage of alcohol and smoking are positively correlated with malign cause. Usage of alcohol with malign cause, $c=0.67$ and $p=0.0035$. Smoking with malign cause, $c=0.6$ and $p=0.014$. There is a strong correlation between usage of alcohol and smoking $c=0.68$ and $p=0.0027$. There is a positive correlation between smoking and RUQ - pain, $c=0.475$ and $p=0.0417$. Alcohol and RUQ – pain is positively correlated $c=0.575$ and $p=0.0125$. It is near significant that smoking is positively correlated to dark urine, $p=0.0976$. It is near significant that alcohol is positively correlated with jaundice, $p=0.1$.

7. Discussion

7.1 Retrospective data

Due to lack of research and published articles, there was only three articles published which could be accessed and therefore those three articles are the foundation of the following discussion.

This study found that there was a mean age of 61 years for the malignant cases compared to the mean age of the benign cases that were 47 years. There was on average a 14-year age difference. The correlation between malignant cause and older age is described in comparative studies as well. Gupta found the mean age of malignant cases to be 68.5 years and the mean age of benign cases to be 42.7 years (Gupta, Singh, Goel & Tank, 2017). Siddique found the mean age of malignant cause to be 56.4 years and the mean age of benign cause to be 42 years (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008). Chalya found the mean age of malignant cases to be 58.6 years and that of benign cases to be 42.6 years (Chalya, Kanumba and Mchembe, 2018). The result of this study is supported by previous studies that it is more common for older people to have a malignant cause whereas younger people more often have a benign cause.

About half of the patients had a malignant cause to the disease and half had a benign cause indicating that both causes could be equally common and the benign cause being more common than indicated in previous studies. Other studies have found that the malignant cause was prevalent in 56.6% of cases (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) and another study found it in 63.9% of cases (Gupta, Singh, Goel & Tank, 2017). These two studies had a lesser number of patients 36 (Gupta, Singh, Goel & Tank, 2017) and 60 (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) compared to this study with 110 patients, possibly explaining the differences. In a third study, 58.6 % of the patients had a malignant cause to the disease (Chalya, Kanumba and Mchembe, 2018). This study had included 116 patients over the course of 4 years in a hospital with over 950 beds, indicating that there should have been more patients with obstructive jaundice. There is a possibility that patients with a malignant cause are more easily diagnosed with obstructive jaundice, due to them having a usually longer hospital stay, more chronic symptoms and usually need invasive methods of treatment as compared to patients with a benign obstruction which could even resolve on its own or heal with conservative treatment. Therefore, making them easier to include in the studies. The study made in India is a retrospective study where they have included all patients positively diagnosed with extrahepatic obstructive jaundice, over the course of one year (Gupta, Singh, Goel & Tank, 2017). What is striking is that they only include patients that have received a diagnosis, possibly losing many patients that are not diagnosed, as is usually the case with these patients. The study made in Tanzania also include patients with a clinical diagnosis of obstructive jaundice (Chalya, Kanumba and Mchembe, 2018). In this study made in Nepal, with 110 patients, there was a minority that had “obstructive jaundice” written in their medical records. Indicating that not all patients with obstructive jaundice are given the diagnosis, possibly explaining the difference between this study and previous studies.

The most common cause was cholangiocarcinoma in this study compared to other studies were carcinoma head of pancreas was the most common malignant cause, described to be between

30-65% of malignant causes compared to only 10.7% in this study. This could be due to different cancers having different prevalence in different populations. However, the patterns of care-seeking at the tertiary care hospital might vary depending on i.e. economic situation. The patients having cholangiocarcinoma and seeking care at T.U.T.H. might be a group of patients with a good economy, quite wealthy, coming as a last resort after already seeking care at private hospitals making this group amounting to a larger number of patients than what would be expected. Probably there are many patients with more common cancers like carcinoma of the pancreas that are seeking care only at the local hospitals in different parts of the country and due to their economic situation never seek T.U.T.H. for advanced care. Thus explaining the large number of patients with cholangiocarcinoma compared to carcinoma of the pancreas at T.U.T.H.

The mean age of the study population were 55 years which are supported by two other studies that found the mean age to be 49.5 years (Gupta, Singh, Goel & Tank, 2017) and 56.4 years (Chalya, Kanumba and Mchembe, 2018) respectively. Most patients were over 40 years old (75.5 %). Most patients were in the age group of 40-65 years (53.6%) which indicates that the patients are younger compared to in the study made by Gupta that described more than 50% of cases to be between 55 and 75 years old (Gupta, Singh, Goel & Tank, 2017).

There were 55.5 % females and 44.5 % males strengthening previous results that obstructive jaundice is more common in females than in males. This have been found in previous studies which have found 66.7% females and 33.33% males respectively (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) and 56.9% females and 43.1 % males (Chalya, Kanumba and Mchembe, 2018). In opposition another study has found the proportions to be 44.4% females and 55.6% males (Gupta, Singh, Goel & Tank, 2017). That a majority of patients are female seems reasonable due to that it is more common for females to suffer from gallstones, predisposing to both malignant and benign causes of obstructive jaundice.

The most common presentation of obstructive jaundice was jaundice (79.1%), other symptoms (58.2%), RUQ - pain (40.9%), itching (38.2%) and anorexia/loss of weight/loss of appetite (38.2%) and epigastric pain (37.3%). According to Gupta the most common symptoms were jaundice (91.7%), loss of appetite (77.8%) and pain abdomen (75%) (Gupta, Singh, Goel & Tank, 2017). The results are strikingly different in prevalence. The high percentage of patients with loss of appetite (77.8%), in the study by Gupta, can be understood when put in relation to the large proportion of patients with malignant disease, 63.9 % in their study. There is a difference in how many patients suffer from itching, in this Nepalese study 38.2% compared to in the other studies there are 66.7% (Gupta) and 55% (Siddique). Itching should be correlated to jaundice and bilirubin levels. Total bilirubin and itching is positively correlated, $C=112,2$, with $p=0.0021$. It could be that it differs how regularly the patients are specifically asked about itching, this might have been overlooked. In comparison between the prospective cross-sectional study where 77.8 % of the patients describe itching (when asked specifically about itching), 38.2% in the retrospective seems low.

Clay-coloured stool ($p= 0.0035$) and anorexia/loss of weight/loss of appetite ($p=0,0012$) were significantly more common in malignant disease in this study and was also found in the study made by Siddique (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008). In opposition to that study, this study also found that itching ($p= 3.069 \times 10^{-5}$), and dark urine ($p=0.0083$) was more common in malignant disease.

In this study there were not any correlations regarding pain and malignant or benign disease. However, Siddique found that RUQ - pain was more commonly seen in benign disease (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008).

7.2 Prospective cross-sectional data

The proportions of 61.1% women and 38.9% men in this study were similar to the proportions of 66.7% females and 33.33% males described in a study made in Pakistan (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008). This stands in opposition to 44.4% females and 55.6% males described in a study made in Uttar Pradesh, a state in India bordering to Nepal (Gupta, Singh, Goel & Tank, 2017). However, there were a majority of females in the larger retrospective study as well, supporting that females are more often suffering from obstructive jaundice.

Half of the patients were between 45 and 65 years old, which corresponds with the results of the retrospective study. Another study found that more than 50% of the patients were in the age group of 55-75 years (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) also indicating that most patients are middle-age or above.

There were 55.6% malign cases, 38.9% benign cases and 11.1% of cases with unknown cause to the disease, this proportion corresponds well to other studies which have found that the malignant cause was prevalent in 56.6% of cases (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) and another study found it in 63.9% of cases (Gupta, Singh, Goel & Tank, 2017).

The mean age of the patients with malign cause were 62.4 years and 34.3 years for those with benign cause. A difference of 28 years in mean age difference. This comes close to 25.8 years as mean difference which Gupta found, the mean age of malignant cases to be 68.5 years and the mean age of benign cases to be 42.7 years (Gupta, Singh, Goel & Tank, 2017). Siddique found the mean age of malignant cases to be 56.4 years and the mean age of benign cases to be 42 years (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) which is also in the same area, supporting that it exists a real difference between the two different patient groups and that the older patients more often have a malignant cause to the disease.

Hilar cholangiocarcinoma is the most common cause which corresponds with the retrospective part of the study and stands in opposition to previous studies by Siddique and Gupta. In both

other studies carcinoma head of pancreas was much more common, it was the most common cause with 53.8% (Gupta, Singh, Goel & Tank, 2017) and the second most common cause with 30.0% (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) as opposed to 0% in this prospective study. This could be due to the small size of the study, there were 5.5% of patients in the retrospective study with a larger study size. Still there is a large difference which could indicate that carcinoma head of pancreas is less common in Nepal or that it is due to the relatively small size of the studies 36 patients in the study by Gupta and 60 patients in the study by Siddique. This indicates that carcinoma head of pancreas is less common in Nepal compared to in India and Pakistan. Cholangiocarcinoma was the cause in 11.7% (Siddique, Ali, Mirza, Jamil, Ehsan, Latif & Malik, 2008) and 11.1% of the cases (Gupta, Singh, Goel & Tank, 2017) in the other studies compared to 26.4 % in this study. This difference could be attributed to the possibility that cholangiocarcinoma is more common in Nepal or due to the different care-seeking patterns of the patients.

The patients report having the symptoms themselves more frequent than what is written in the medical records and this is true for all of the symptoms. It is possible that this is solely because they might be measuring different things. In the patient form the patients are asked to indicate which symptom/symptoms they have had or has while the medical journals quite often only describe the chief complaint at the present time and the complete history of the disease with symptoms can be overlooked, especially if the patient already have received a diagnosis and are given palliative treatment. Then it appears that it is not interesting enough to describe for example if the patient have/have had jaundice, itching or dark urine or to order lab works to prove the high bilirubin levels, if this is already known and the patient is hospitalized for a reinsertion of a PTBD for example. One other interpretation is that the patients are not always asked if they have or have had those symptoms, asked about the course of the disease, listened to or the information is simply not written down in the medical journals.

7.3 Methodological considerations

The study was designed by the author, an outsider, not familiar with the setting, how things worked at the hospital and who could not speak the local language. This was a disadvantage and it had a negative effect on the study design and the possibility to interact with patients and staff. Overall the study design was good enough to access the data required to answer the basic questions of aetiology, sex and age as well as symptoms. All this information was accessible in the medical journals. It was more complicated to access other data such as data concerning symptoms, treatment and diagnostic methods. The patient form was made in a simple enough manner and most patients managed to complete the form, a few did however struggle and needed guidance. This could be since several of the patients themselves was illiterate and their family completed the form, or they managed by the help of a nurse. Most of the patients did not complete the form themselves but their family did that for them. Since the families are close, the family stays with the patient every day, buys the needed medications and other health expenditures themselves, they are trustworthy to complete the forms since they know everything about the patient's history. However, since the patients did not complete the forms themselves there is a risk that some data are lost on the way. Most patients stayed in rooms with several other patients and this meant that everything could be overheard and there was no privacy. Another downside to the prospective study was the fact that the author could only stay for a couple of weeks, this meant that only 18 patients could be included. Preferably, to do this kind of study, the person caring for the patients and working at the hospital should be the one doing the study. This would mean that the person could include patients during a longer period, using a more elaborate patient form or gathering information themselves by examination and interviewing the patients about symptoms. Since the author had limited time, there was no time to evaluate the form and change it according to the needs and questions arising. The author was limited to the medical journals which varied in quality. The limitations were less when doing the retrospective part of the study since that part was based solely on the medical records and the

information that was there were used. The limitation here was to find as many patient medical records as possible, to make certain that the included patients were representative patients, as medical records were lost, and the online records were not complete. The medical records varied in quality.

The admittance books posed a challenge since they were hand written and often there were miswritings of the patient numbers making it impossible to find the right patient medical records in the archive, since they were organised after patient number.

The biggest challenge was to decide upon which patients to include or exclude. Quite often there were information lacking in the medical journals concerning at least one of the three criteria's that determined the diagnosis. The author could not find any discussion in the previous studies where it was described how they dealt with questionable cases and where exactly they determined where the border was of what was and what was not an obstruction. Most patients, determined to have obstructive jaundice, never received a diagnosis of obstructive jaundice in their medical records but going through their records the author could understand that that was the case and include them in the study. To do this kind of study it was necessary to decide upon the diagnosis based on lab works, clinical data and radiological data. The study would have a completely different population if only those patients that had obstructive jaundice written in their records were included.

Some questions remain, those that were aimed at investigating how the patients were diagnosed, methods of treatment and purpose of the treatment could not be answered in this study. There were not enough data in the medical records to answer these questions. There were data missing concerning radiological method as well as methods of treatment and purpose. There were not a great enough quantity of information regarding ERCP and complications in the medical records. If the author would have tried to answer these questions as well, the study would have needed to be reshaped and have grown immensely. To be able to collect data about treatment methods of

stenting with ERCP or PTBD and its complications it would have been necessary to go through the radiology lab, using their records or preferably by doing a prospective study in combination with the two departments. The next step would have been to perform a comparison of both techniques and looking at patient quality of life or patient satisfaction and survival. This would be very interesting and the hospital, the hospital staff and patients would have benefited of having these two methods evaluated. Since a great part of the world has already abandoned PTBD in preference of ERCP stenting, for the benefit of the patients with increased survival rates (Sugiyama et al., 2014). This will probably be the next step in Nepal as well over the course of the years.

Regarding the first presenting symptom, this data could not be properly obtained since the first presenting symptom was not generally written down in the records especially not for the patients with malign cause. The patients usually already had the diagnosis of cancer and obstructive jaundice when they were admitted at the ward which meant that the history of the present illness, of this hospitalization was written down but more rarely the symptoms of the start of the disease itself. This meant that data concerning the first presenting symptom was not accessible by this method. Data concerning length of hospitalisation could not be retrieved in all cases and was often missing which meant that the author could not answer that question.

Discussing the symptoms, it would be interesting to describe the course the symptoms took. This was something the author had wished to do but it turned out to be impossible since this was not written in the patient records frequent enough. The ideal would be, for the surgeon working at the ward to perform a prospective study over the course of a year. Including all the patients going through the ward with the help of a member of every surgical team at the wards and composing a more detailed questionnaire or going through the medical records, talking to the patients and examining the patients themselves. This would suffice to collect better data of symptoms and time course.

Since cholangiocarcinoma seemed to be more common, compared to in neighbouring countries, this could be an interesting topic to explore further. It is important to remember that T.U.T.H is a referral hospital in Nepal, thus explaining some part of the high number of patients with cholangiocarcinoma at the surgical ward but it is probably not the only factor. It would be interesting to investigate if this relatively large number of patients, with cholangiocarcinoma, could be explained by considering the pattern of which the patients were seeking care. If the patterns of seeking care does not explain this difference other explanations must be considered. If there are any specific risk factors or genetics that are unique for Nepal. Further studies, describing the course of the disease, survival time and complications would be essential in the continuing research field since there are no register of cancer patients in Nepal.

8. Conclusion

As previous studies have shown; this study confirms that older people more often have a malignant cause to obstructive jaundice opposed to younger patients. As opposed to other studies in neighbouring countries, this study indicates other proportions of the malignant spectrum, with distal cholangiocarcinoma as the leading cause. It could be due to different patterns of care-seeking due to i.e. economic reasons. However, it could indicate that the malignant causes of obstructive jaundice vary in different countries and that cholangiocarcinoma might be more common in Nepal compared to in neighbouring countries.

This study serves as an important first step in the continuing exploration of the research field.

9. Populärvetenskaplig sammanfattning på svenska

Obstruktiv gulsot – orsaker och symptombild Nepal

Obstruktiv gulsot är ett tillstånd då det föreligger en obstruktion i gallvägarna som kan ge gulsot, klåda och vitfärgad avföring som symtom. Det kan bero på många olika orsaker, både maligna och benigna. Det är en relativt outforskad gren inom medicinvetenskapen, särskilt i utvecklingsländer som Nepal. Förhoppningen var att den här studien skulle bidra till att utveckla sjukvården och bidra till mer forskning i Nepal. Syftet med projektet var att kartlägga och beskriva de olika orsakerna till sjukdomen och symtom samt relatera detta till olika faktorer som ålder och kön. Studien baseras på patienter från en kirurgavdelning på ett sjukhus i Kathmandu. Studien bestod utav två delar. 110 patienter deltog i den tillbakablickade delen som baserades på deras medicinska journaler. Utav dessa svarade 18 patienter även på ett patientformulär. Med stigande ålder var det vanligare att patienterna hade en malign orsak till sjukdomen, skillnaden bestod i medel på 28 år. I den här studien var den vanligaste orsaken kolangiokarcinom (en cancer som utgår ifrån gallvägarna) som orsak till obstruktiv gulsot vilket skiljer sig från andra jämförbara studier i grannländer. Det tyder på att patienternas sökmönster är annorlunda eller att kolangiokarcinom som orsak till obstruktiv gulsot kan vara betydligt vanligare i Nepal jämfört med i grannländerna.

10. Acknowledgment

I would like to thank my supervisors Göran Kurlberg, Dr Bikal Ghimire, Prof.Y.P. Singh for your guidance in this degree project. Warmest thanks to Sten A foundation scholarship for sponsoring me and for making this project possible. Many thanks to all the wonderful staff at the Female Surgical Ward, Male Surgical Ward and Annex-1 for answering questions, always helpful and helping with translations and explaining to the patients about the study. Thanks to Miss Jyoti for correcting and transcribing the patient form and consent form in Nepali. My deepest thanks to Prof. Yogendra Shakya with family and wonderful staff at Hotel Metropolitan Kantipur for hospitality, friendliness and for introducing me to the wonderfully interesting Nepali culture. I also want to thank Victor Bergh Alvergren for helping me with the calculations when I wanted to succumb to defeat and almost gave up trying.

11. References

- Central Bureau of Statistics, (2007). Population Profile of Nepal. Kathmandu: Central Bureau of Statistics.
- Chalya, P., Kanumba, E. and Mchembe, M. (2018). Etiological spectrum and treatment outcome of Obstructive jaundice at a University teaching Hospital in northwestern Tanzania: A diagnostic and therapeutic challenges.
- Ghimire, S. (2017). My Republica - Govt to provide health insurance to all Nepali within 3 years. Admin.myrepublica.com.
- Retrieved 21 March 2017, from <http://admin.myrepublica.com/feature-article/story/43213/govt-to-provide-health-insurance-to-all-nepali-within-3-years.html>
- Gupta, A. K., Singh, A., Goel, S., & Tank, R. (2017). Profile and pattern of obstructive jaundice cases from a tertiary care teaching hospital of Uttar Pradesh. *International Surgery Journal*, 4(2), 743. doi:10.18203/2349-2902.isj20170225
- Institute of Medicine. (2012) T.U. Teaching Hospital. Re-trieved 2017-03-18, from http://www.iom.edu.np/?page_id=182
- Khuroo, M. S., Rather, A. A., Khuroo, N. S., & Khu-roo, M. S. (2016). Hepatobiliary and pancreatic ascariasis. *World Journal of Gastroenterology*, 22(33), 7507. doi:10.3748/wjg.v22.i33.7507
- Modha, K. (2015). Clinical Approach to Patients With Obstructive Jaundice. *Techniques in Vascular and Interventional Radiology*, 18(4), 197-200. doi:10.1053/j.tvir.2015.07.002
- Nepal Tourism Board. The official Tourism Website for Nepal, (2017). Retrieved 18 March, 2017, from [http:// www.welcomenepal.com/plan-your-trip/people.html](http://www.welcomenepal.com/plan-your-trip/people.html)
- Robbins, S. L., Kumar, V., & Cotran, R. S. (2010). Robbins and Cotran pathologic basis of disease. Philadelphia, PA: Saunders/Elsevier.
- Roshan khadka, Student at Mahidol University Follow. (2016, October 24). Health care system of nepal. Retrieved March 22, 2017, from <https://www.slideshare.net/roshankhadka8/health-care-system-of-nepal>
- Siddique K, Ali Q, Mirza S, Jamil A, Ehsan A, Latiif S, Malik AZ. (2008). Evaluation of the aetiological spectrum of obstructive jaundice. *J Ayub Med Coll*. 20(4):62-6.
- Sugiyama, G et al. (2014). Evaluation of endoscopic biliary stenting for obstructive jaundice caused by hepatocellular carcinoma. *World Journal of Gastroenterology*, 20(22), 6968. doi:10.3748/wjg.v20.i22.6968
- Wang, L., & Yu, W. (2014). Obstructive jaundice and perioperative management. *Acta Anaesthesiologica Taiwanica*, 52(1), 22-29. doi:10.1016/j.aat.2014.03.002
- WHO. (2007). Health System in Nepal: Challenges and Strategic Options. November 2007.

WHO. (2012). Nepal: WHO statistical profile. Retrieved 18 March, 2017, from <http://www.who.int/gho/countries/npl.pdf?ua=1>

WHO. (2017). Countries: Nepal. Retrieved 18 March 2017, from <http://www.who.int/countries/npl/en/>

WHO (2017). Countries: Sweden. Retrieved 19 March, 2017, from <http://www.who.int/countries/swe/en/>

12. Appendices

12.1 Attachment A: Patient form

**Patient form for the study – Causes of Obstructive Jaundice, presentation and management
– a clinical study at Tribhuvan University Teaching hospital**

In patient number :

Name :

Contact number:

Admission date:

Age years

Male Female Other

Urban/City Rural/Countryside Other

Religion : Hindu Buddhist Christian Muslim Other

Ethnic group/ caste :

Which one/ones of these symptoms have you had ? (choose one or more)

- Jaundice/Ikterus
- Abdominal pain in the upper right side of the abdomen
- Itching
- Fever with chills Fever without chills
- Pale or clay-colored stool
- Anorexia/loss of appetite and/or loss of weight
- Dark urine
- Other

Which one of these symptoms did you notice **FIRST** when you fell ill ? (choose one or more)

- Jaundice/Ikterus
- Abdominal pain in the upper right side of the abdomen
- Itching
- Fever with chills Fever without chills
- Pale or clay-colored stool
- Anorexia/loss of appetite and/or loss of weight
- Dark urine
- Other

Smoking/chew tobacco

- Never smoked Stopped smoking less than 6 months ago
- Stopped smoking more than 6 months ago
- Smokes but not daily Smokes ½ - 1 pack/day Smokes 1½ - 2 packs/day or more

Alcohol consumption:

- Never less than 1 time / week
- 1-2 times / week More than 2 times / week

Diet

- Vegetarian Non – vegetarian Other

12.2 Attachment B: Informed consent

MODEL INFORMED CONSENT FORM IN ENGLISH

Department of GI and General surgery,

Tribhuvan University Institute of Medicine, Kathmandu, Nepal,

Study Title: Causes of obstructive jaundice, presentation and management – a clinical study at Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Study Number: Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

Please do initial in box (Subject)

- (i) I confirm that I have read and understood the information sheet and consent form dated ____ []
for the above study and have had the opportunity to ask questions.
- (ii) I understand that my participation in the study is voluntary and that I am free to withdraw at
any time, without giving any reason, without my medical care or legal rights being affected.
- (iii) I understand that the researchers and the IRB and other regulatory authorities will not need []
my permission to look at my health records both in respect of the current study and any
further research that may be conducted in relation to it, even if I withdraw from the trial. I
agree to this access. However, I understand that my identity will not be revealed in any
information released to third parties or published.
- I agree not to restrict the use of any data or results that arise from this study provided such a []
use is only for scientific purpose(s)
- (v) I agree to take part in the above study. []

Signature (or Thumb impression) of the Subject/Legal Guardian:

Date: ____/____/____

Signatory's Name: ____/____/____

Signature of the Investigator: _____ Date: ____/____/____

Study Investigator's Name: _____

Signature of the Witness _____ Date: ____/____/____

Name of the Witness: _____

12.3 Attachment C: Collection form for both retrospective and prospective cross-sectional part

Obstructive jaundice patient information chart

In patient number :

Name :

Contact number :

Ward :

Admission date :

Discharge date :

Patient factors

Age years

Male Female

Urban Rural

Religion : Hindu Buddhist Christian Muslim Other

Ethnic Group :

Work : .

Tobacco: yes no

Never smoked Stopped smoking less than 6 months ago

Stopped smoking more than 6 months ago

Smokes but not daily Smokes ½ - 1 pack/day Smokes 1½ - 2 packs/day or more

Alcohol consumption :

Never less than 1 time / week Alcoholic

1-2 times / week More than 2 times / week

Vegetarian : **Non-vegetarian :**

Family history general :

Previous diseases :

Co-morbidities :

HTN DM CVD ASA -treatment Others :

PTB COPD

Discharge diagnosis :

Malignant Benign

When did the symptoms first present :

Symptoms:

- Jaundice
- Abdominal pain (right hypochondrium)
- Itching
- Fever without chills Fever with chills
- clay colored stool
- Anorexia/loss of appetite and/or loss of weight
- Dark urine
- Other:

First presenting symptom/symptoms

- Jaundice
- Abdominal pain (right hypochondrium)
- Itching
- Fever without chills Fever with chills
- clay colored stool
- Anorexia/loss of appetite and/or loss of weight
- Dark urine
- Other:

Diagnostic method - Clinical

Lab work: TC(WBC): TBilirubin: DB:

GPT/GOT/ALP: protein/albumin : PT/INR:

Urea/creatinin: HgB : RBS(glu):

Plt: Temperature: Amylase:

Lipase: CEA: LDH: GGT:

Diagnostic method: USG CT MRCP ERCP

Treatment

Stent : PTBD ERCP (Other) :

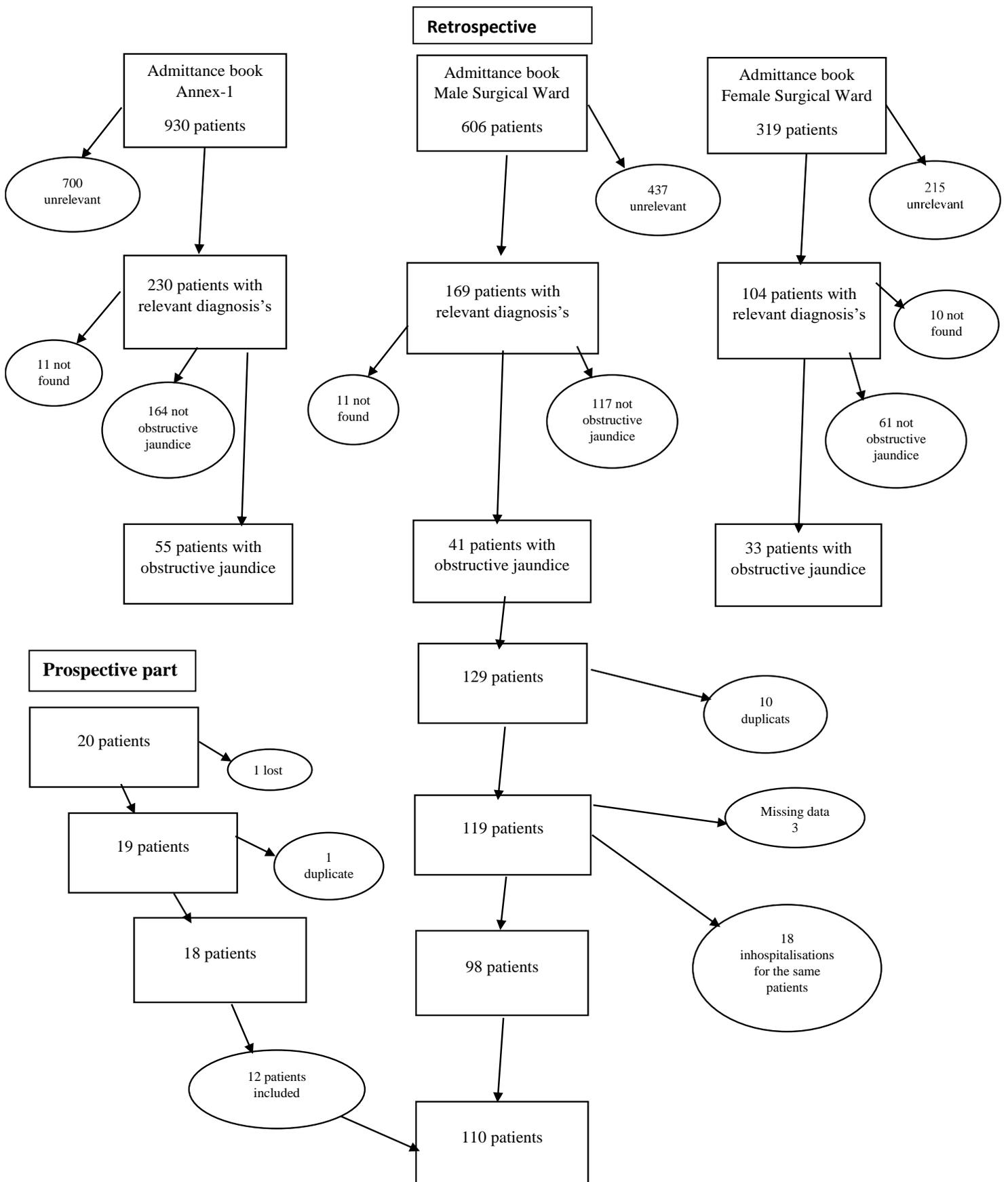
Purpose/ Aim :

ERCP - complications : Pankreatitis Intestinal perforation Bleeding

Infection(cholangitis) Other :

Re-do

12.4 Attachment D: Flow-chart for the retrospective and the prospective part



12.5 Attachment E: Ethical approval

त्रिभुवन विश्वविद्यालय
चिकित्सा शास्त्र अध्ययन संस्थान
डीनको कार्यालय, महाराजगंज
पो.ब.नं.: १५२४, काठमाडौं, नेपाल।
फोन नं. ४४१०९११, ४४१२०४०, ४४१३७२९, ४४१८१८७



Tribhuvan University
Institute of Medicine
Office of the Dean
Maharajgunj, P.O. Box: 1524
Kathmandu, Nepal
Ph.# 4410911, 4412040, 4413729, 4418187

पत्र संख्या / Ref.: - ११९(८-११-६)५८५/६७५

मिति / Date:- 9 Oct., 2017

Research Department

Ms. Sabina Delin
Medical Student
University of Gothenburg
Sweden.

Ref: Approval of Research Proposal: Causes of obstructive jaundice, presentation and management- A clinical study at Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Dear Ms. Delin,

Thank you for the submission of under graduate research proposal entitled “**Causes of obstructive jaundice, presentation and management- A clinical study at Tribhuvan University Teaching Hospital, Kathmandu, Nepal**” to the Institutional Review Board (IRB), Institute of Medicine (IOM) Tribhuvan University on 8 October, 2017.

I am pleased to inform you that the above mentioned proposal has been approved by Institutional Review Board (IRB), Institute of Medicine on 9 Oct., 2017.

As per IRB rules and regulations the investigator has to strictly follow the protocol stipulated in the proposal. Any change in objective, problem statement, research questions or hypothesis, methodology, implementation procedure, data management and budget may be made so and implemented after prior approval from this Research Department and IRB. Thus, it is compulsory to submit the detail of such changes intended or desired with justifications prior to actual change in the protocol.

You are also requested to follow the ethical guideline of IRB, Institute of Medicine.

After completion of your study you must submit a copy of research report to the Research Department.

If you have any further queries, please do not hesitate to contact us.

Prof. Dr. Yogendra P. Singh
Member Secretary
Institutional Review Board



Cc
HOD
Department of GI & General Surgery
Maharajgunj Medical Campus
IOM, Maharajgunj

2074/06/24