ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

DEPARTMENT OF SURGERY

DIVISION OF GI SURGERY, HEPATOPANCREATOBILIARY(HPB) UNIT

PERIOPERATIVE OUTCOMES AND ASSOCIATED FACTORS OF PATIENTS WITH HEPATIC RESECTION, IN CENTRAL ETHIOPIA: A MULTICENTER PROSPECTIVE COHORT STUDY

BY: ANDUALEM DAGNE (GENERAL SURGEON, HPB FELLOW)

A THESIS SUBMITTED TO THE DEPARTMENT OF SURGERY, SCHOOL OF MEDICINE, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SUB SPECIALITY CERTIFICATE IN HPB SURGERY

JULY,2023

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INVESTIGATOR: ANDUALEM DAGNE (GENERAL SURGEON AND HPB FELLOW)

ADVISOR: ZEKI ABDURAHMAN (CONSULTANT GENERAL AND HPB SURGEON)

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ADDIS ABABA

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Name of advisor/s	1. Zeki Abdurahman (Consultant General and HPB surgeon, Associate professor of Surgery) Phone: +251918350100 E-mail: zaksurgery@gmail.com
The full title of the research project	Perioperative outcomes and associated factors of patients with hepatic resection, in Central Ethiopia: a multicenter prospective cohort study.
Study period	From July 1, 2022 – June 30, 2023.
Study area	Tertiary hospitals in Addis Ababa ➢ Tikur Anbessa Specialized Hospital(TASH) ➢ Yekatit 12 Comprehensive Specialized Hospital (Y12 CSH) ➢ Addis Hiwot General Hospital (AdHGH) ➢ Amin General Hospital (AmGH) ➢ Lancet General Hospital (LGH)
Budget	94,534.00 birr

Declaration

This is to certify that the thesis paper entitled "Multicenter prospective cohort study on perioperative outcomes and associated factors among patients treated with hepatic resection at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023", is submitted in partial fulfillment of the requirements for the subspecialty certificate in Hepatopancreatobiliary surgery in Department of Surgery, Addis Ababa University. It is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificate. The assistance and help I received during the course of this thesis development is duly acknowledged.

Dr. Andualem Dagne	_____	_____
Name of the candidate	Signature	Date

Approval of the advisors

I hereby certify that I have supervised, read, and evaluated this thesis paper titled "Multicenter prospective cohort study on perioperative outcomes and associated factors among patients treated with hepatic resection at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023" by Dr. Andualem Dagne prepared under my guidance. I approve this thesis to be submitted for oral defense.

1. Dr. Zeki A (consultant General and HPB surgeon) _____ _____

   Advisor's name Signature Date

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Table of Contents page

List of figure

List of table

Abbreviations and Acronym

AdHGH	Addis Hiwot Specialized Hospital
AmGH	Amin General Hospital
ASA	American Society of Anesthesiology
ECOG	Eastern Cooperative Oncology Group
HPB	Hepatopancreatobiliary
ISGLS	International Study Group for Liver Surgery
LGH	Lancet General Hospital
LOS	Length of hospital stay
PHH	Post Hepatectomy Hemorrhage
PHLF	Post Hepatectomy Liver Failure
SPSS	Statistical Product and Service Solutions
TASH	Tikur Anbessa Specialized Hospital
Y12CSH	Yekatit 12 Comprehensive Specialized hospital

Abstract

Introduction: As a relatively recent experience practiced only in a few tertiary centers across Ethiopia, the perioperative outcome of patients with hepatic resection is barely known. The main objective of this study is to assess perioperative outcomes and associated factors among patients treated with hepatic resections from July 1, 2022 – June 30, 2023, at tertiary hospitals in Addis Ababa, Ethiopia.

Methods: It is multi-center prospective cohort study. Data were collected regarding demographics, comorbidities, the extent of resection, intraoperative findings, perioperative morbidity, and mortality. Data was entered into epidata version 3.1 and exported to SPSS version 26 for descriptive analysis and statistical analyses using binary logistic regression.

Result: A total of 76 patients underwent hepatic resection, there were 44 females and 32 males. One-third (32.9%) of these patients had underlying liver disease. The main indication was primary hepatic cancer in 65.8% with HCC in 55.3%. The majority (82.9%) of patients had anatomic-based hepatic resections. Major hepatectomy was performed in 34.2% of patients. The mean duration of surgery was 3.2±1.23 hr., the length of hospital stay was 6.04 ± 3.35 days while the median blood loss was 800ml (IQR 500-1000 ml), and 40.8% of the patients required transfusions. Overall 30-day mortality and morbidity were 3.9% and 32.9% respectively. Morbidity was higher in patients requiring blood transfusion (p=0.008) and malignant disease indications (p= 0.071) although not statistically significant.

Conclusion: The perioperative morbidity and mortality of hepatic resection are consistent with the other published literatures. The requirement for blood transfusion and malignant disease indications were associated with higher morbidity.

Keywords: Hepatic resection, Perioperative outcome, Multivariable analysis

1. Introduction

1.1 Background

Liver surgery has evolved from being almost nonexistent to comprising a range of operations that can safely remove nearly any amount of liver tissue. The first surgeons who performed hepatic resection did it without understanding the segmental anatomy of the liver. With a description and a better understanding of this segmental anatomy of the liver, anatomic liver resection was made possible through time in the course of history by the work of courageous surgeons[1].

Worldwide hepatic resection is performed routinely for several indications for both benign and malignant disease conditions such as malignant tumors, benign tumors, calculi in the intrahepatic ducts, hydatid disease, and abscesses [2]. As time goes by, the indications for liver resection have changed with an increasing proportion of patients with hepatobiliary malignancy, including patients with cirrhosis, who may currently undergo liver resection associated with complex reconstruction of vascular structure[3]. Although hepatic resection is performed through open surgery, laparoscopic and robotic access surgeries are safe and feasible alternatives in a well-selected patient with experienced hands[4]

As the volume of liver surgery increase and advances in technical expertise, perioperative mortality is declining steeply while morbidity improvement is modest[5]. This is because of remarkable advances in techniques of liver resection, improved patient selection requiring operation, and advancement in the field of anesthesiology and blood transfusion in the last 60 years[6]. Because of this advancement, the basic risk of elective liver resections when performed in high-volume centers is low, comparable with, or lower than the risk of other elective abdominal procedures[5]. However, in low-resource settings, these advances are not readily available to surgeons resulting in increased morbidity[7].

Hepatic resection is a relatively recent experience and it is performed only in a few tertiary centers across our country. Furthermore, there is limited published data in our country assessing perioperative outcomes of hepatic resection[8].

1.2 Statement of the problem

Despite technical advances and high experience of liver resection in specialized centers, management of hepatic resection is challenging and it is still burdened by relatively high rates of postoperative morbidity and mortality[9]. In high-volume centers, the rate of postoperative mortality and morbidity, in most recent reviews, are less than 5%[10–12] and in the range of 14-45%[13–16] respectively. Whereas the respective estimates for low-volume centers were 10.1% and 57%[17].

In low-resource centers like ours, hepatic resection has higher morbidity and mortality. Common post-hepatectomy complications include fever, hemorrhage, bile leakage, liver failure, pleural effusion, ascites, and subphrenic infection[18]. This high morbidity is associated with prolonged hospital stays, increased health-related costs, and decreased patient satisfaction. The liver-specific complications posing real challenges are post-hepatectomy hemorrhage, liver failure, and bile leak.

Bleeding is a fatal complication that can occur intraoperatively or postoperatively. It was responsible for up to 20 % of death after resection[19]. The incidence of intraperitoneal hemorrhage ranges from 4.2% to 10%[18]. Different studies had identified the number of hepatic segments resected and operative blood loss as factors predictive of overall morbidity and mortality[2]. Moreover, blood loss, transfusion, and extent of resection have been correlated specifically with increased rates of postoperative liver failure and bile leaks[20]. Different techniques are being utilized to minimize intraoperative bleeding like parenchymal sparing segment-based resection, low CVP anesthesia, and hemostatic and energy devices during parenchymal transection[21,22].

Posthepatectomy liver failure (PHLF) is one of the most severe complications following hepatectomy and is a major cause of perioperative mortality with its incidence varying widely in the literature, between 1.2% to 32%[23]. With careful patient selection and the introduction of anatomic and functional assessment of the liver, its prevalence is on the decline and ranges from 1% to 6%[14,17,20]. The other liver-specific complication is bile leakage, its incidence ranges from 4.0% to 17%[18].

The common disease conditions for which hepatectomy is indicated and its perioperative morbidity and mortality in Ethiopia in general and the tertiary hospitals in Addis Ababa, in particular, are not well studied. This prospective multicenter cohort study assessed the

perioperative outcomes and associated factors of hepatic resection patients in tertiary hospitals in Addis Ababa

1.3 Significance of the Study

This study has identified sociodemographic patient characteristics, common indications of hepatic resection, and the perioperative morbidity and mortality of patients operated in the study period as well as the factors affecting this outcome. Identifying the burden of perioperative morbidity and mortality and factors affecting outcomes of hepatic resection has paramount importance. Knowing this will aid in better preoperative patient selection and optimization of the associated factors before surgery and provide essential input for both the physician and patient during decision-making.

The finding of this study will be an input in developing evidence-based treatment guidelines in resource-poor settings like our country. It will also influence policymakers and program implementers at national as well as regional levels to set up policy guidelines aiming to improve treatment outcomes of hepatic resection. Moreover, it can also be used as input for further research and contribute to the expansion of knowledge in the field of HPB surgery.

2. Literature review

2.1 Indications for Hepatic Resection

Early descriptions of operations on the liver usually concerned with complete or partial avulsion of some portion that was protruding externally as a result of abdominal trauma mainly following battle. Following the first planned hepatic resection in Germany by Langenbuch in 1888 and a true anatomic liver resection with preliminary vascular control in 1952 by Lortat-Jacob and Robert, different surgeons across the globe started to do hepatic resection for both benign and malignant diseases of the liver[24] [25]. The most common indication for partial hepatectomy involves the removal of metastatic lesions mainly colorectal cancer and NET liver metastasis[2,5]. With due time, indications for liver resection have changed with an increasing proportion of patients with hepatobiliary malignancy, including HCC, cholangiocarcinoma, and bile duct cancer[7,26].

2.2 Perioperative outcome of hepatic resection

In the landmark report by Foster and Berman in 1977, which involved a multicenter analysis of 621 hepatic resections for a variety of indications mortality was 13% and over 20% for major resections. The study showed that 20% of the deaths resulted from hemorrhage[19]. In subsequent large series, the mortality rate associated with liver resections has decreased from 5% to 20% in patients operated on before 1980 to usually less than 5% in patients operated on thereafter despite surgical intervention becoming more aggressive. Better perioperative results, with operative mortality rates typically less than 5% are noted mainly in high-volume centers [10–12].

This improvement is explained by better patient selection and anesthetic monitoring, refined understanding of liver anatomy and use of vascular clamping, expanded use of parenchymal-sparing approaches, and probably by the emergence in the mid-1980s of hepatobiliary surgery as a distinct specialty[27]. Liver resections are being increasingly performed in high-volume units, by specialized surgeons have also played a role in reducing perioperative death[21].

Regardless of the improvement in mortality, morbidity rates remain elevated with overall rates of 14% to 45% reported in large volume centres[13] and major morbidity figures (Clavien–Dindo classification ≥3) listed in the vicinity of 30%[14–16]. In a recent multi-institutional study of 2056 patients undergoing hepatic resection between 1990 and 2011 by Hyder and colleagues;90-day mortality was 1.6%, overall morbidity was 19.3%, and liver-specific complications included postoperative ascites (2.5%), biliary leak (3.2%), bleeding (0.9%), abscess (0.7%), and liver

insufficiency/failure (0.5%)[22]. Of note, whereas bleeding accounts for a minor percentage of overall morbidity in the current series, 30 years ago it was the primary cause of overall mortality following hepatectomy[19].

Another study in China by Huang and his associates retrospectively analyzed a total of 2008 patients who underwent consecutive hepatectomies and showed consistent findings. The overall postoperative complication rate was 14.44%, of which 12.54% of resections were performed for primary liver cancer, 16.40% for secondary liver cancer, and 16.32% for hepatholithiasis. The overall hospital mortality was 0.55%, and that for malignant liver disease was 0.51%. High mortality (2.53%) was associated with extensive liver resections for hilar Cholangiocarcinoma[14].

In a multi-institutional Japanese study by Beppu and his colleagues, postoperative complication rates were 14.1% and the level of morbidity was comparable with the other studies. Postoperative complications following hepatic resection were incisional SSI (3.5%), bile leakage (2.9%), ascites and pleural effusion (1.2%), and intra-abdominal hemorrhage (0.6%). The mortality rate was less than 1%[28].

The major cause of morbidity following hepatectomy can be systemic, local, or liver-specific complications. Of systemic complication pulmonary complications like pleural effusion, atelectasis occurs from 2% to 9% in multiple large series[2,15,22]. Liver-specific complications include post-hepatectomy liver failure, bile leak/biloma, postoperative hemorrhage, and sterile perihepatic collection or ascites. The rate of these complications in most studies is less than 10% and even lower in high-volume centers[2,15,22].

In a retrospective review of 100 patients who have undergone hepatic resection between 2008 and 2016 in Pakistan, morbidity and mortality in this review were comparable to the rates reported in other the literature. The overall morbidity rate was 41% and the 90-day mortality rate was 6%. In 56 % of the cases, the indication was primary liver cancers[17].

In Africa, there is limited data assessing the indication and perioperative outcome of hepatic resection. In a single-center retrospective analysis in Northwest Nigeria, over a period of 18 years (2000-2018), there were 29 hepatic resections mostly for liver trauma (22/29) and it is nonanatomic liver resection (25/29). Bile leak (10%) and sub hepatic abscess (3%) were the two most common complications in this review. No death was reported in this study[29]. In a review of five (5) years

of experience (Sept. 2004-Aug. 2009) with hepatic resections at Gondar University Hospital (GUH), only nine tumor resections (major, minor, and enucleations) were done. There were two deaths; one from sepsis and the other from an acute cardiopulmonary event[9].

2.3 Factors affecting the perioperative outcome of hepatic resection

No single factor is responsible for the adverse or improved perioperative outcome. General improvement in operative and anesthetic techniques, better patient selection, and the emergence of hepatobiliary surgery as a distinct area of specialization have all been cited, and probably all play a role in improving perioperative outcome[5,27]. A better understanding of hepatic anatomy and increasing application of anatomically based resections are perhaps the most important factors in this regard[2].

With refined knowledge of hepatic segmental anatomy and the introduction of parenchymal-sparing segmental resections; this offers the same benefit as classic lobar resections with less risk than is associated with the removal of a large volume of functional liver tissue[12,30]. The number of hepatic segments resected is the predictor of both perioperative morbidity and mortality[2]. In addition, segmental resections are superior to wedge resections concerning blood loss and tumor clearance[31]. Anatomic segmental resection is also a safe procedure and is superior to wedge resection as an oncologic operation for colorectal liver metastasis because it results in better tumor clearance and improved survival[31].

Liver resections can be performed with low mortality and morbidity and with acceptable LOS by an experienced liver surgeon; however, the outcome-based is most influenced by patient comorbidities entering into surgery. The strongest predictors of outcome were creatinine and ASA score. Preoperative albumin also influenced LOS but to a lesser degree[26]. Age is also an important risk factor in hepatectomy because elderly patients may harbor occult heart disease, and reduced respiratory and liver function reserves[32,33]. However, in properly selected and optimized major patients liver resections can be performed safely in patients 70 years of age or older, with early results and survival similar to those in the younger than 70 age group[34].

Liver resections are being increasingly performed in high-volume units, by specialized surgeons have also played a role in reducing perioperative death[21]. Choti et al in their review demonstrated

a 7.9% mortality rate at centers that performed less than 15 liver resections per year compared with 1.5% for centers that performed more than 15 resections per year[21]. This finding is also consistently verified in other large series studies[35,36]. But other studies showed that annual case volume did not influence LOS and had no impact on patient safety[26].

The underlying liver disease condition (cirrhosis, steatosis, obstructive jaundice) affects the operative mortality in patients undergoing elective resections. The outcome of hepatic resection in cirrhotic patients has improved remarkably in recent years with improved surgical techniques and perioperative care[37]. The mortality rate was significantly higher in patients with underlying liver disease (9.5%) than in patients without underlying liver disease (1%)[5]. Post-op morbidity is also higher in cirrhotic patients with postoperative liver insufficiency, ascites, and renal complications. But in early cirrhosis, the perioperative outcome is almost similar to in non-cirrhotic patients.

In summary, preoperative risk assessment involves the evaluation of hepatic function reserve, remnant liver volume, liver status, age, and the medical condition of the patient [32]. The application of ERAS protocols in liver surgery appeared to be safe and effective. Studies showed, it reduces the postoperative length of hospital stay and is also associated with significantly lower complication rate[s38,39].

2.4 Conceptual framework

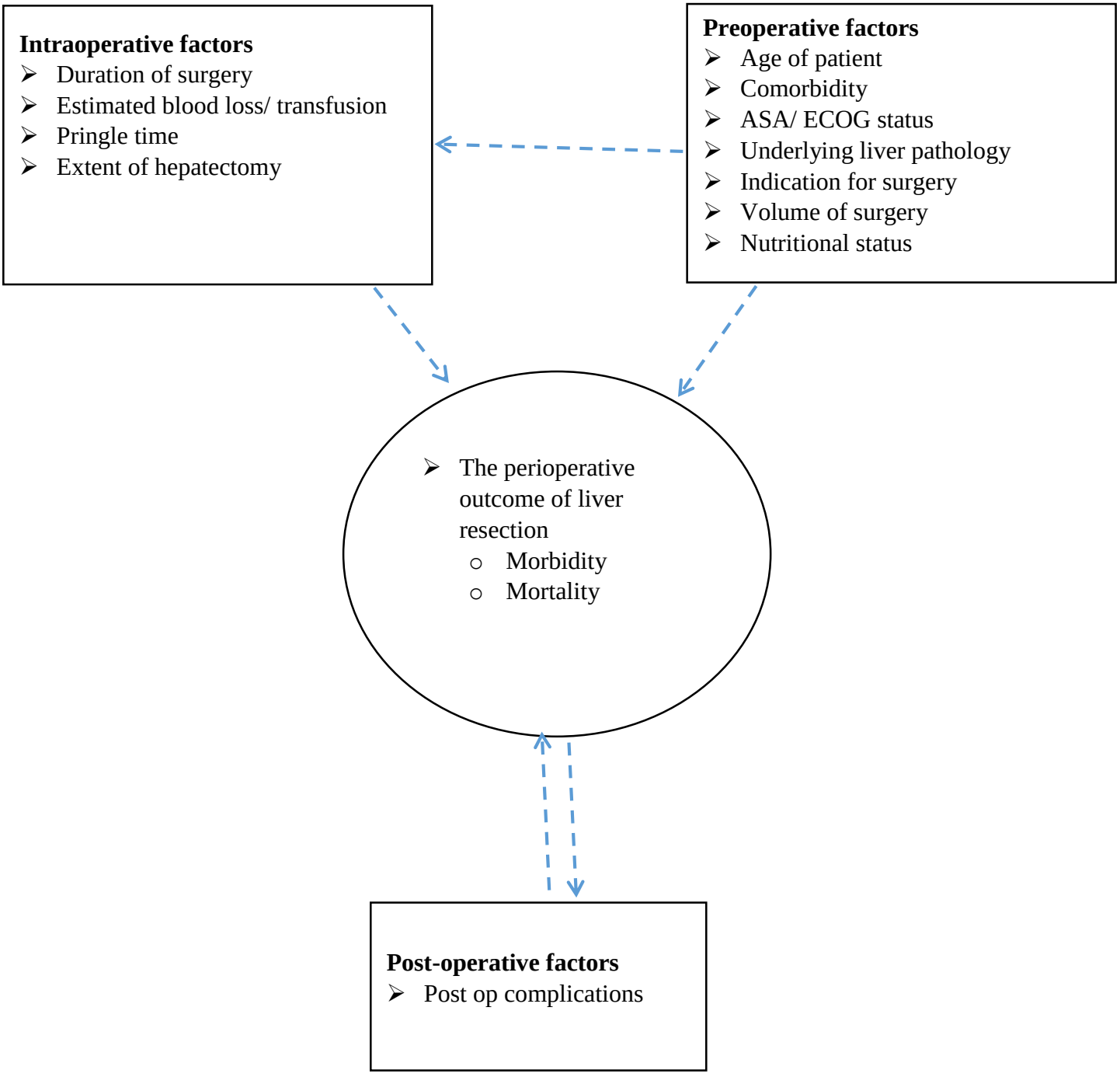

Figure 1:- Conceptual framework for the multi-center prospective cohort study on perioperative outcomes and associated factors among patients treated with hepatic resection at tertiary hospitals in Addis Ababa, Ethiopia from June 1, 2022 – June 30, 2023.

3. Objective

3.1 General Objective

- To assess perioperative outcomes and associated factors of hepatic resection patients operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023.

3.2 Specific Objectives

- ✓ To describe the perioperative morbidity and mortality of hepatic resection patients operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023.
- ✓ To identify factors affecting the unfavorable perioperative outcomes of hepatic resection patients operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023.
- ✓ To assess the practice of hepatic resection in tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023.

4. Methods and materials

4.1 Study Area and Period

The study was conducted from July 1, 2022 – June 30, 2023, at 5 tertiary hospitals located in Addis Ababa City, central Ethiopia. The specific hospitals are AdHGH, AmGH, LGH, TASH, and Y12CSH. The former three hospitals are privately owned hospitals whereas the latter two are public ones. Addis Ababa is a capital city of Ethiopia with a projected population size of more than 5.2 million in the Ethiopian Demographic and health survey 2016.

4.2 Study Design

An institution-based multi-center prospective cohort study was conducted.

4.3 Population

4.3.1 Source population

All patients who have undergone hepatic resection in the selected tertiary hospitals in Addis Ababa during the study period.

4.3.2 Study population

Among the six tertiary hospitals found in the capital city, five of them were selected to be included in the study for convenience reasons. All patients who have undergone hepatic resection in the selected tertiary hospitals during the study period were included.

4.4 Sample size determination and sampling procedure

All patients who have undergone hepatic resection during the study period in selected tertiary hospitals were included. Consecutive sampling (total enumerative sampling) was used.

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion criteria

All patients who have undergone hepatic resection in the selected tertiary hospitals in Addis Ababa during the study period were included in the study.

4.5.2 Exclusion criteria

Patients with subsegmental resection, enucleation, and simple biopsy procedures were excluded from this study.

4.6 Variables of the Study

4.6.1 Dependent variables

- Postoperative outcomes
  - Mortality
  - Morbidity
    - Postoperative hemorrhage
    - Posthepatectomy liver failer
    - Postoperative bile leak

4.6.2 Independent variables

- Socio-demographic characteristics
  - ✓ Sex
  - ✓ Age
- Clinical related characteristics
  - Preoperative comorbidity
  - Liver pathology/underlying liver disease condition
  - ASA/ ECOG status
  - Indication of hepatectomy
  - Preoperative albumin/bilirubin/creatinine
  - Duration of surgery
  - Estimated blood loss
  - Requirement for transfusion
  - Type /extent of hepatectomy
  - Porta hepatis clamp time
  - Facility/ experience/ volume of surgery

4.7 Operational Definition and term definitions

Hepatic resection: removal of the segment and above of liver tissue for managing hepatic pathology

Major hepatectomy: Surgical removal of four or more segments of the liver[40]. Major complication: Clavien-Dindo complication grade three or four[13].

Perioperative outcome: outcome of hepatic resection patients from the time of surgery till day-30[41].

Posthepatectomy Liver failure: defined according to ISGLS as postoperatively-acquired deterioration in the ability of the liver (in patients with normal and abnormal liver function) to maintain its synthetic, excretory, and detoxifying function was characterized by an increased INR (or need of clotting factors to maintain normal INR) and hyperbilirubinemia (according to the normal cutoff levels defined by the local laboratory) on or after postoperative day 5

Post hepatectomy hemorrhage(PHH): Defined by the ISGLS as any of the following in the setting of confirmed bleeding noted in drains or on imaging: (1) drop in hemoglobin level of greater than 3 g/dL, (2) any postoperative transfusion of packed red blood cells (PRBCs) for falling hemoglobin, or (3) the need for invasive intervention (e.g., embolization or relaparotomy)[23]

Bile leak: ISGLS defined a bile leak as the drainage of intraabdominal fluid with an increased bilirubin concentration (at least 3X the serum Bilirubin) on or after postoperative day 3[23]

4.8 Data collection tools and Methods

Data were collected prospectively from patients' investigations, intraoperative notes, anesthesia documentation, and patients' charts using a structured pre-tested checklist prepared in the English language. The checklist contains; socio-demographic and clinical characteristics. The data were collected by trained Nurses and residents and supervised by the principal investigator. Data collection was done on the day of surgery, the 5-7th post-operative day, the day of discharge, and finally on the 30th post-operative date.

4.9 Data quality control

Before the actual data collection, data collectors were trained for two days on the general purpose of the study and the procedures to be followed during data collection. The checklist was pre-tested in TASH and was modified and edited based on the findings. During data collection, the principal investigator checked the data for its completeness and missing information at each point. Furthermore, data were checked during entry and compilation before analysis.

4.10 Data Processing and Analysis

Data was entered into epidata version 3.1 with the necessary precautions and exported to SPSS version 26 for descriptive and statistical analyses. In bivariable analysis, a p-value of < 0.2 was used for the initial selection of independent variables that are included in the final logistic regression. Categorical variables were described with frequency, graphs, and tables whereas, continuous variables were described using mean and standard deviation for normally distributed variables while, median, and interquartile ranges if normality was not met.

4.11 Ethical Consideration

Ethical clearance was obtained from the Institutional Review Board (IRB) of the College of health sciences, Addis Ababa University. The official letters were sought and obtained from the office of the Department of Surgery. Confidentiality was secured by avoiding writing the patient's name and making sure that data remained anonymous during analysis and final reporting.

5. Result and Discussion

5.1 Result

5.1.1 Demographic Profile of Patients and Comorbidities

From July 1, 2022, to June 30, 2023, a total of 76 patients have undergone partial hepatectomy in five different hospitals in Addis Ababa. Twenty-six (34.2%) patients were operated at TASH, 16(21.1%) at AdGH, 15(19.7%) at LGH 10(13.2%) at AmGH, and 9(11.8%) were operated at Y12CSH (Fig 1). About 44 (57.9%) of patients were females and 32 (42.1%) were males with female to male ratio of 1.4: 1. The mean age was 53.7 ± 14.6 years with a range of 16-80 years. Fourteen (18.4%) of the patients were seventy years and older. Twenty-two (28.9%) of patients have at least one comorbidity. Hypertension and diabetes mellitus were the two most common comorbidities identified in 17.1% and 7.9% of patients respectively (Table 1).

Table 1: - Demographic characteristics of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia.

Item			Frequency (%)
Study population			76
	Mean age		53.7 yr.
	Range		16-80 yr.
	Age distribution	<70 yrs.	62(81.6)
		≥70 yrs.	14(18.4)
Sex	Female		44(57.9)
	Male		32(42.1)
	F: M ratio		1.4:1
Patient comorbidity	Single		16(21.1)
	Multiple		6(7.9)
	Total		22(28.9)
	Hypertension		13(17.1)
	DM		6(7.9)
	COPD/Asthma		4(5.3)
	HIV/AIDS		3(3.9)
	Cardiac disease		1(1.3)
	Old PTE		1(1.3)

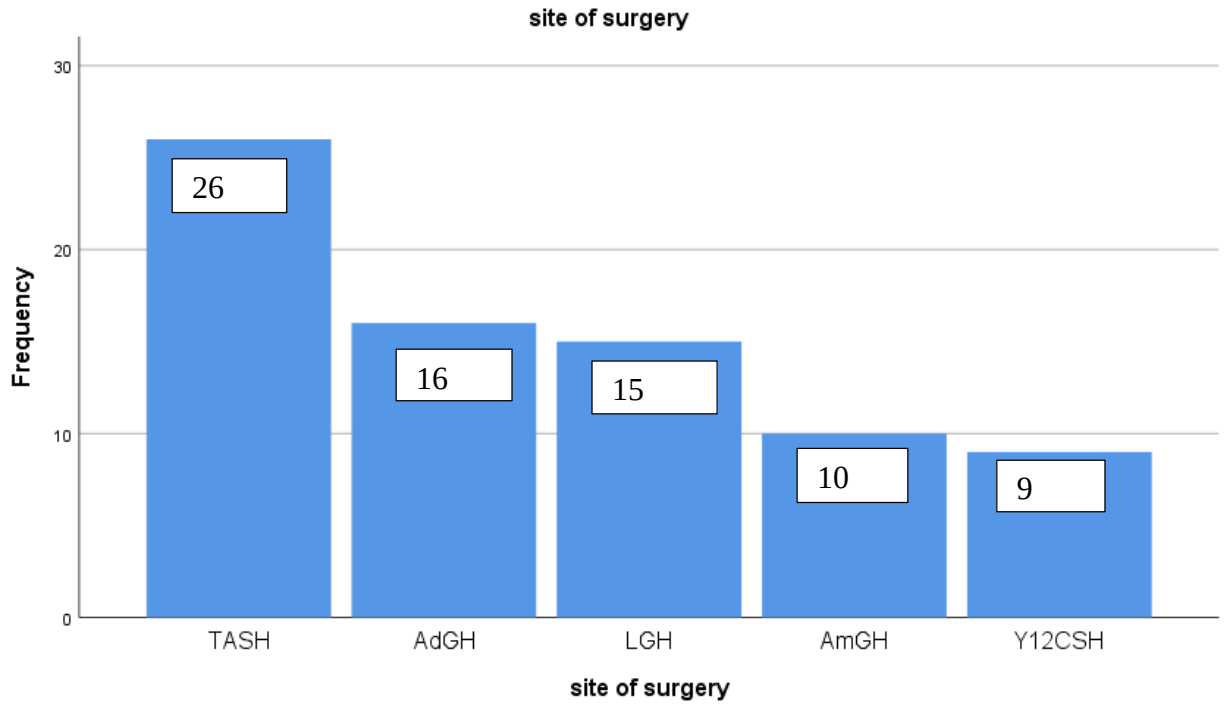

Figure 2: - Site of hepatic resection among tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76)

5.1.2 Clinical Profile of Patients

In the preoperative clinical evaluation of these patients, almost all patients in this study were having good performance status (ECOG 0) and 75% of patients were having ASA1, and 23.7% had ASA2. In the majority of the cases (72.4%), there was no preoperative or intraoperative evidence of cirrhosis. The reset, 14 patients (18.4%) were having Child A cirrhosis and 7 patients (9.2%) were having evidence of fibrosis. Underlying liver diseases were present in about one-third of the patients (32.9%), with chronic HBV infection in 22.4%, chronic HCV infection in 7.9%, fatty liver in 3.9%, and post-preoperative chemotherapy in 2.6% of patients (Table 2).

As depicted in the table below (Table 2), preoperative laboratory investigations revealed elevated bilirubin (>1.0 mg/dl) in 13.2% of the cases, hypoalbuminemia (<3.5g/dl) in 14.5%, elevated creatinine (>1.0 mg/dl) in 10.5%, Anemia (hg < 11 g/dl) in 9.2%, thrombocytopenia (< 150000) in 9.2%, elevated AST (>40 IU/l) in 18.4%, elevated ALT (> 40 IU/l) in 22.4% and elevated ALP > 270 IU/l in 13.2% of patients.

Table 2: - Clinical profile of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Clinical parameter		Frequency	Percent
ASA class	ASA1	57	75.0
	ASA2	18	23.7
	ASA5	1	1.3
ECOG	ECOG 0	76	100.0
Liver cirrhosis status	No cirrhosis	55	72.4
	No cirrhosis but intraop fibrosis	7	9.2
	Child A cirrhosis	14	18.4
Hepatic steatosis	Yes	3	3.9
Underlying liver disease	Chronic HBV infection	17	22.4
	Chronic HCV infection	6	7.9
	Post chemotherapy	2	2.6
	Total	25	32.9
Abnormal laboratory preoperative tests	Bilirubin > 1mg/dl	10	13.2
	Albumin < 3.5g/dl	11	14.5
	Creatinine > 1.0 mg/dl	8	10.5
	Hemoglobin < 11g/dl	7	9.2
	Platelets < 150000	7	9.2
	AST > 40	14	18.4
	ALT > 40	17	22.4
	ALP > 270	10	13.2

5.1.3 Patient diagnosis

The majority of patients (85.5%) were having malignant disease diagnosis. The most common diagnosis overall was hepatocellular carcinoma in 42 patients (55.3%) followed by gallbladder carcinoma in 8 patients (10.5%), intrahepatic cholangiocarcinoma in 7 patients (9.2%), and metastatic tumors (3 cases of CRCLM, 1 case of choriocarcinoma and 1 case of papillary thyroid cancer) in 5 patients (6.6%) of the cases. The remaining 14.5% were having benign disease diagnoses which includes hemangioma in 6 patients (7.9%), biliary cystadenoma in 3 patients (3.9%) 1 case of hepatholithiasis, and inflammatory mass. In the postoperative histopathology study, 3 patients were having positive margins and 16 patients were having lymphovascular invasion (Table 3).

Table 3:- Patients diagnosis/ indications of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Indication for hepatic resection	Hepatocellular carcinoma		42	55.3
	Intrahepatic Cholangiocarcinoma		7	9.2
	Gallbladder carcinoma		8	10.5
	Hemangioma		6	7.9
	Biliary cystadenoma/adenocarcinoma		4	5.3
	Colorectal cancer liver metastasis		3	3.9
	Neuroendocrine tumor		2	2.6
	Hepatholithiasis		1	1.3
	Inflammatory mass? Fasciola		1	1.3
	Metastatic bleeding choriocarcinoma		1	1.3
	Metastatic papillary thyroid ca		1	1.3
Histopathology of malignant lesions	Positive margin		3/64	4.7
	Multiple lesion		5/62	8.1
	Lymphovascular invasion		16/44	36.4
	Grade of Differentiation	Well	19/59	32.2
		Moderate	34/59	57.6
		Poor	6/59	10.2

5.1.4 Type Hepatic Resections and other procedures

As described in the table below (Table 4), anatomic-based hepatic resections were performed in the majority (82.9%) of patients. The most common types of hepatic resections were right hepatectomy in 13 patients (17.1%), right posterior sectionectomy in 11 patients (14.5%), left lateral sectionectomy in 11 patients (14.5%) and left hepatectomy in 9 patients (11.8%). Nonanatomic hepatic resections involving a variable segment of the liver were performed in 13 patients (17.1%). Although most of the patients have undergone only hepatic resection, in 4 patients (5.3%) additional nonhepatic major procedures were performed. These include roux en Y hepaticojejunostomy in 1 patient, segmental colonic resection in 1 patient, sigmoidectomy in 1 patient, and nephrectomy in 1 patient. Major hepatectomy was performed in 34.2% of patients.

Table 4: - Type of hepatic resections and histology of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Type of hepatic resection	Hepatic resection only		72(94.7%)
	Hepatic resection with additional other procedures	Total	4(5.3%)
		Hepaticojejunostomy	1
		Segmental colonic resection	1
		Sigmoidectomy	1
		Nephrectomy	1
	Right Hepatectomy		13(17.1%)
	Left Hepatectomy		9(11.8)
	Extended right hepatectomy		1(1.3%)
	Right posterior sectionectomy		11(14.5%)
	Lt lateral sectionectomy		11(14.5%)
	Central hepatectomy		3(3.9%)
	Nonanatomic resection		13(17.1%)
	Segmentectomy		6(7.9%)
	Bisegmentectomy		9(11.8%)

5.1.3 Perioperative results

Overall, the average operative time of surgery was 3.2±1.23 hr. (median operative time 3 hr.). In half of the operation (51.3%) intermittent portahepatis clamp (pringle) was utilized, and the average portahepatis clamp time was 29.6 ± 0.5 minutes (range 10- 60 minutes). In the remaining 48.7% of the case, selective vascular control was used. The average estimated blood loss was 898.6 ± 618.2ml (median 800 ml IQR 1000 ml), and blood transfusion was required in 40.8% of patients either intraoperatively or postoperatively with whole blood or components. Six patients (7.9%) required direct ICU transfer or later transfer because of clinical deterioration. The average length of hospital stay was 6.04 ± 3.35 days (median LOS was 5 days) with a range of 2 to 20 days (Table 5).

Table 5: - Perioperative results of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Variables		
Duration of surgery	Mean	3.2±1.23 hours
Portahepatis clamp time	Yes	39(51.3%)
	Mean	29.6 ± 0.5 minutes
	Range	10- 60 minutes
Estimated blood loss	Median	800ml IQR 500- 1000ml
	Range	100-4000ml
Need for transfusion	Yes	31 (40.8%)
	PRBC	10 (13.2%)
	Whole blood	23 (30.3%)
	FFP	5(6.6%)
	Platelets	3(3.9%)
Need for ICU admission		6(7.9%)
Length of hospital stay	Mean	6.04 ± 3.35 days
	Range	2-20 days

5.1.5 Perioperative outcomes

The perioperative morbidity was 32.9% (25 patients), with 21 patients (27.6%) experiencing Clavien-Dindo complication grade 1 or 2 complication and major complications occurred only in 4 patients (5.3%). Liver-specific complications occurred in 12 patients (15.8%), with postoperative ascites in 6 patients (7.9%), PHLF in 6 patients (7.9%), PVT in 2 patients, and perihepatic abscess in 1 patient. Whereas general complications occurred in 22 patients (28.9%) with pneumonia, AKI, and symptomatic pleural infections were the most common complications occurring in 7.9%, 7.9%, and 5.3% respectively. In subsequent follow up 4 patients required readmission, for percutaneous drainage of perihepatic abscess, for transfusion of severe anemia, for resuscitation and diuretics of postoperative ascites, and for poor intake and for wound closure for complete wound dehiscence (Table 6).

The postoperative mortality was 3.9% (3 patients). MOF secondary to sepsis of chest focus and PHLF were the incriminated cause of death. The 1st case was a 74 yr. old male patient with BCLC B HCC (segment 7 & 8) with Child A HBV cirrhosis who had underwent nonanatomic resection,

died on the 17th postoperative day. The remaining two patients were 65 and 50-year-old who had underwent right hepatectomy for HCC, one of this were having HBV induced liver fibrosis.

Table 6: - Morbidity and mortality of patients with hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – J30, 20232023, Addis Ababa, Ethiopia (N=76).

			Frequency	Percent
Post-operative complications	Total		25	32.9
	Major complications		4	5.3
Grade of complications	CD Grade 1		6	7.9
	CD Grade 2		15	19.7
	CD Grade 3		2	2.6
	CD Grade 4		2	2.6
Post-operative Mortality			3	3.9
	MOF secondary to sepsis of Chest focus		1	
	Type I respiratory failure of sepsis of chest focus and PHLF		2	
Liver-specific complications	Total		12	15.8
	Postoperative ascites		6	7.9
	PHLF	Total	6	7.9
		Grade A	3	3.9
		Grade B	2	2.6
		Grade C	1	1.3
	Portal vein thrombosis		2	2.6
	Perihepatic abscess		1	1.3
General complications	Total		22	28.9
	AKI		6	7.9
	Pneumonia		6	7.9
	Pleural effusion		4	5.3
	Anemia		3	3.9
	DVT/PTE		2	2.6
	Wound infection/ dehiscence		2	2.6
	Respiratory failure		2	2.6
	Pulmonary edema		1	1.3
	UTI		1	1.3

	Anastomotic leak	1	1.3
	Ileus	1	1.3
	Gastroenteritis	1	1.3
	Multiple electrolyte imbalance	1	1.3
	Hepatic encephalopathy	1	1.3
	Delirium	2	2.6
Need for readmission		4	5.3
	Post-operative ascites and Poor intake	1	
	Complete wound dehiscence for closure	1	
	Perihepatic abscess for drainage	1	
	Severe anemia for transfusion	1	

5.1.6 Factors affecting perioperative outcome

On bivariable analysis, several perioperative factors associated with increased morbidity and mortality were checked (Table 7). On multivariable analysis, morbidity was higher in patients requiring blood transfusion (p=0.008; CI (0.59-9.78) and malignant disease indications (p= 0.071; CI (0.01-1.20) though not statistically significant. (Table 8)

Table 7: - Bivariable analysis of factors associated with perioperative morbidity and mortality of hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Variables		Complication	%	P- value	Mortality	%	P- value
Age	<70 yr.	25	25/62	0.196	2	2/62	0.508
	≥70 yr.	3	3/14		1	1/14	
Indications	Benign	1	1/11	0.069	0	0/11	0.999
	Malignant	27	27/65		3	3/65	
Underlying liver disease	No	15	15/48	0.188	1	1/48	0.303
	Yes	13	13/28		2	2/28	
Liver cirrhosis status	No	17	17/55	0.087	1	1/55	0.166
	Yes	11	11/21		2	2/21	
Prop bilirubin	≤1mg/dl	27	27/66	0.091	2	2/66	0.328
	>1mg/dl	1	1/10		1	1/10	
Preop platelet	≥150000	24	24/69	0.255	2	2/69	0.185
	<150000	4	4/7		1	1/7	
Blood loss	<1000ml	16	16/52	0.110	1	1/52	0.220

	≥1000ml	12	12/24		2	2/24	
Blood transfusion	No	11	11/45	0.008	0	0/45	0.997
	Yes	17	17/31		3	3/31	
Patient comorbidity	No	20	20/54	0.956	1	1/54	0.183
	Yes	8	8/22		2	2/22	
ASA status	ASA1	20	20/57	0.584	1	1/57	0.133
	≥ ASA2	8	8/19		2	2/19	
Extent of resection	Minor	17	17/50	0.477	1	1/50	0.260
	Major	11	11/26		2	2/26	
Preop Albumin	≥3.5g/dl	23	23/65	0.524	1	1/65	0.037
	<3.5g/dl	5	5/11		2	2/11	
Preop ALT	≤40	20	20/59	0.325	1	1/59	0.104
	>40	8	8/17		2	2/17	

Table 8: -Multivariate analysis of factors associated with perioperative morbidity and mortality of hepatic resection operated at tertiary hospitals in Addis Ababa, Ethiopia from July 1, 2022 – June 30, 2023, Addis Ababa, Ethiopia (N=76).

Variable		Odds Ratio	95% Confidence Interval	P- Value
Morbidity	Age	3.53	0.63-19.77	0.151
	Underlying liver disease(yes/no)	1.24	0.28-5.40	0.771
	Liver cirrhosis	0.55	0.11-2.90	0.486
	Preop bilirubin	7.36	0.69-77.84	0.097
	Preop Platelets	0.30	0.04-2.31	0.250
	Indications(benign/malignant)	0.11	0.01-1.20	0.071
	Estimated blood loss	0.89	0.21-3.75	0.871
	Need for Transfusion	2.40	0.59-9.78	0.222

5.2 Discussion

Hepatectomy is one of the surgical management modalities with curative intent in well-selected benign and malignant hepatic tumors. It is increasingly being performed safely for several indications with associated improvement in the postoperative morbidity and mortality of the patients, especially in high-volume centers in developed countries[2,5,42]. The common disease conditions for which hepatectomy is indicated and its perioperative morbidity and mortality in Ethiopia are not well studied. This prospective multicenter cohort study has assessed the perioperative outcomes and associated factors of hepatic resection patients in tertiary hospitals in Addis Ababa.

In the demographic review, in this study, the mean age was 53.7 ± 14.6 years ranging from 16 to 80 years and a significant number of patients (18.4%) were above 70 years. This is consistent with large published series[2,15,33]. In most reviews, about 30 – 40% of the patients have at least one comorbidity, with hypertension, cardiac disease, and DM being the commonest comorbidities[2,15]. This is also true in this particular study that about 28.9% of patients were having at least one comorbidity, with hypertension and diabetes mellitus were commonest comorbidities identified in 17.1% and 7.9% of patients respectively.

With a better understanding of the segmental anatomy of the liver, functional assessment of future liver remnant, and overall advancement in the field of HBP surgery, increasing proportions of patients with underlying liver disease and liver cirrhosis are undertaking hepatic resection. One-third to half of the patients in large series have underlying liver pathology, of this 10-33% being liver cirrhosis[2,5]. In this particular study, underlying liver diseases were present in about one-third of the patients (32.9%), with chronic HBV infection in 22.4%, chronic HCV infection in 7.9%, fatty liver in 3.9%, and post-preoperative chemotherapy in 2.6% of patients. Moreover, 18.4% of patients were having Child A cirrhosis, and 9.2% of patients were having evidence of fibrosis, which is comparable with the studies stated so far. The preoperative laboratory abnormalities identified were also consistent with the previous studies[2,5].

Worldwide hepatic resection is performed routinely for both benign and malignant disease conditions of the liver with the majority (80-90%) being malignant. With due time, indications for liver resection have changed with an increasing proportion of patients with hepatobiliary malignancy, including HCC, cholangiocarcinoma, and bile duct cancer[2,7,26]. In the West, the most

common indication for partial hepatectomy involves the removal of metastatic lesions mainly colorectal cancer liver metastasis[2,5,22,43]. In contrast, in Asian countries like Japan and China, the predominant indication is primary hepatic malignancies mainly HCC[14,44]. The data in our study is comparable with the Asian data, the majority of patients (85.5%) were having malignant disease diagnosis with hepatocellular carcinoma in 55.3% followed by gallbladder carcinoma in 10.5% and intrahepatic cholangiocarcinoma in 9.2%. There were only three cases with metastatic indications.

Consistent with other large published series, anatomic-based hepatic resections were performed in the majority (82.9%) of patients. Whereas the proportions of patients with major hepatectomy (removal of 3 or more hepatic segments) (34.2%) and concomitant other major nonhepatic procedures (5.3%) is low when compared to large published series in high volume centers but comparable with low volume studies. The major hepatectomy rate was 62% in the Jarnagin et al, 2002 study and 45% in Belghiti et al 2000, with respective additional major procedure rates of 37% and 13% respectively[2,5,15,43].

In this study, the average operative time of surgery (3.2±1.23 hr.), portahepatis clamp time (29.6 ± 0.5 minutes), and the requirement for ICU admission perioperatively is comparable with other studies. However, the average estimated blood loss was 898.6 ± 618.2 ml (median 800 ml), and the requirement for blood transfusion (40.8%) of patients either intraoperatively or postoperatively is higher than what is stated in most other literature. The average length of hospital stay was 6.04 ± 3.35 days (median LOS was 5 days) which is low compared to other studies. This may be due to the low rate of major hepatectomy and concomitant major procedures.[2,5,28,45].

As evidenced in money literature, morbidity, and mortality are decreasing especially in high-volume HPB centers[2,5]. In most reviews, the mortality rate ranges between 1 to 5%, and the morbidity rate ranges between 25% to 40%[2,13,14,22,43–45]. This data is consistent with the result of our study, with the overall perioperative morbidity and mortality being 32.9% and 3.9% respectively. The majority of (27.6%) patients were having minor complications (Clavien-Dindo complication grade 1 or 2) and major complications (Clavien-Dindo complication grade 3 or 4) occurred only in 5.3% of patients. Another study from Pakistan showed comparable morbidity and mortality with this data[17].

Liver-specific complications occurred in 15.8%, with postoperative ascites in 7.9%, PHLF in 7.9%, 2 cases of PVT, and 1 case of perihepatic abscess. The rate of these complications in most

studies is less than 10% and even lower in high-volume centers[2,15,22]. Whereas, in this review, general complications occurred in 28.9% with pneumonia, AKI, and symptomatic pleural infections were the most common complications occurring in 7.9%, 7.9%, and 5.3% respectively. Of systemic complication pulmonary complications like pleural effusion, atelectasis occurred from 2% to 9% in multiple large series[2,15,22].

In the literature, several factors affecting the outcome (morbidity and mortality) of hepatic resection were identified. This includes Age >70 years, comorbidity, underlying liver disease, estimated blood loss, the volume of surgery, the extent of hepatectomy, and combined additional procedures (complex hepatectomy)[2,5,33,37,43]. In the retrospective analysis of 1803 hepatectomies (Jarnagin et al, 2002), the number of hepatic segments resected and operative blood loss were the only predictors of both perioperative morbidity and mortality[2]. In another study (Belghiti et al 2000), a concomitant extrahepatic procedure was the only independent predictor of operative death in patients with no underlying liver disease[5].

Similarly, in another analysis of 1500 consecutive hepatectomies published in 2009 (Cescon et al 2009), blood transfusions and additional procedures were associated with an increased risk of postoperative complications, whereas blood transfusions and extended hepatectomy were associated with an increased risk of postoperative mortality[45]. In this study, several perioperative factors (age, comorbidity, underlying disease, duration of surgery, preop values, EBL, pringle time, and extent of hepatic resection) were checked for association with morbidity and mortality. However, on multivariable analysis, morbidity was higher in patients requiring blood transfusion (p=0.008; CI (0.59-9.78) and malignant disease indications (p= 0.071; CI (0.01-1.20).
Recent studies have reported that advanced age is associated with increased perioperative morbidity and mortality. Age > 80 years was associated with increased 30 and 90-day mortality and morbidity in an article published in 2020 (Mueller et al 2020)[33,45]. In this study, the proportion of patients with age ≥ 70 is 18.4% and of this, 3/14 patients develop complications and 1/14 develop mortality, however, it is not statistically significant in multivariable analysis.

Limitations of the study

This study was an institutionally based prospective cohort study. It has included all patients in five tertiary centers with HBP service. The number of cases is small and doing a subgroup analytical study for mortality was difficult because of the small size.

6. Conclusion and Recommendation

6.1 Conclusion

The overall morbidity and mortality of hepatic resection is declining. The basic risk of elective liver resections when performed in high-volume centers is low and is comparable with the risk of other elective abdominal procedures. In this study, 30-day mortality and morbidity were 3.9% and 32.9% respectively, with major complications, occurring in 5.3%. This result is comparable with most literature findings. However, in this study the EBL and transfusion requirements were high. On multivariable analysis, morbidity was higher in patients requiring blood transfusion (p=0.008; CI (0.59-9.78) and malignant disease indications though not statistically significant (p= 0.071; CI (0.01-1.20).

6.2 Recommendation

It is essential to emphasize on surgical technique, utilization of energy devices and low central venous pressure anesthesia is important to reduce blood loss and associated transfusion requirements. As it is clearly stated in different articles on the importance of high-volume centers, the establishment and strengthening of these centers will have a paramount role. Although this is a prospective study, the sample size is small. We recommend further studies with large sample sizes for better clarification of the factors affecting surgical outcomes of hepatectomy in resource-limited settings like this.

7. Reference

1. Fortner, Joseph G mda; Blumgart, Leslie H mda,* A Historic Perspective of Liver Surgery for Tumors at The End of The Millennium, Journal of the American College of Surgeons: August 2001 - Volume 193 - Issue 2 - p 210-222 doi: 10.1016/S1072-7515(01)00910-3.

2. Jarnagin, W. R., Gonen, M., Fong, Y., DeMatteo, R. P., Ben-Porat, L., Little, S., ... & Blumgart, L. H. (2002). Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. Annals of surgery, 236(4), 397.

3. Kubota, K., Makuuchi, M., Sugawara, Y., Midorikawa, Y., Sakamoto, Y., Takayama, T., & Harihara, Y. (1998). Reconstruction of the hepatic and portal veins using a patch graft from the right ovarian vein. The American journal of surgery, 176(3), 295-297.

4. Gigot, J.-F., Glineur, D., Santiago Azagra, J., Goergen, M., Ceuterick, M., Morino, M., … Schockmel, R. (2002). Laparoscopic Liver Resection for Malignant Liver Tumors. Annals of Surgery, 236(1), 90–97. doi:10.1097/00000658-200207000-00014 10.1097/00000658-200207000-00014.

5. Belghiti, J., Hiramatsu, K., Benoist, S., Massault, P. P., Sauvanet, A., & Farges, O. (2000). Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. Journal of the American College of Surgeons, 191(1), 38-46.

6. Felekouras ES, Kaparelos DC, Papalambros E. The history of liver surgery, hepatectomy and haemostasis. *Hell J Surg*. 2010;82(5):280-296. doi:10.1007/s13126-010-0046-2

7. Garzali IU, Ibrahim E, Abdulrahman S. *HEPATIC RESECTION IN LOW RESOURCE SETTING: A SINGLE CENTRE EXPERIENCE IN NORTHWEST NIGERIA*.; 2020.

8. • A review of a five (5) years' experience (Sept. 2004- Aug. 2009) with hepatic resections at Gondar University Hospital (GUH). Worku et al Ethiop Med J. 2013 Jan;51(1):59-65.

9. Worku, M., Andreson, B., Abdurahman, Z., Yirdaw, S., & Wondimu, S. (2013). A review of a five (5) years experience (Sept. 2004-Aug. 2009) with hepatic resections at Gondar University Hospital (GUH). Ethiopian Medical Journal, 51(1), 59-65.

10. Bozzetti, F., Gennari, L., Regalia, E., Bignami, P., Montalto, F., Mazzaferro, V., & Doci, R. (1992). Morbidity and mortality after surgical resection of liver tumors. Analysis of 229 cases. Hepato-gastroenterology, 39(3), 237-241.

11. Tsao, J. I., Loftus, J. P., Nagorney, D. M., Adson, M. A., & Ilstrup, D. M. (1994). Trends in morbidity and mortality of hepatic resection for malignancy. A matched comparative analysis. Annals of surgery, 220(2), 199.

12. Fan, S. T., Lo, C. M., Liu, C. L., Lam, C. M., Yuen, W. K., Yeung, C., & Wong, J. (1999). Hepatectomy for hepatocellular carcinoma: toward zero hospital deaths. Annals of surgery, 229(3), 322.

13. Dokmak, S., Ftériche, F. S., Borscheid, R., Cauchy, F., Farges, O., & Belghiti, J. (2013). 2012 Liver resections in the 21st century: we are far from zero mortality. HPB, 15(11), 908-915.

14. Huang, Z. Q., Xu, L. N., Yang, T., Zhang, W. Z., Huang, X. Q., Cai, S. W., ... & Dong, J. H. (2009). Hepatic resection: an analysis of the impact of operative and perioperative factors on morbidity and mortality rates in 2008 consecutive hepatectomy cases. Chinese medical journal, 122(19), 2268-2277.

15. Cescon, M., Vetrone, G., Grazi, G. L., Ramacciato, G., Ercolani, G., Ravaioli, M., ... & Pinna, A. D. (2009). Trends in perioperative outcome after hepatic resection: analysis of 1500 consecutive unselected cases over 20 years. Annals of surgery, 249(6), 995-1002.

16. Palavecino, M., Kishi, Y., Chun, Y. S., Brown, D. L., Gottumukkala, V. N., Lichtiger, B., ... & Vauthey, J. N. (2010). Two-surgeon technique of parenchymal transection contributes to reduced transfusion rate in patients undergoing major hepatectomy: analysis of 1,557 consecutive liver resections. Surgery, 147(1), 40-48.

17. Begum, S., & Khan, M. R. (2019). First 100 hepatic resections: short-term outcomes from a low volume centre in a developing country. HPB, 21, S588-S589.

18. Jin, S., Fu, Q., Wuyun, G., & Wuyun, T. (2013). Management of post-hepatectomy complications. World journal of gastroenterology: WJG, 19(44), 7983.

19. Foster, J. H., Berman, M. M., & Ebert, P. (1977). Major problems in clinical surgery. Solid Liver Tumors, 22, 111-128.

20. Kauffmann, R., & Fong, Y. (2014). Post-hepatectomy liver failure. Hepatobiliary surgery and nutrition, 3(5), 238.

21. Choti, M. A., Bowman, H. M., Pitt, H. A., Sosa, J. A., Sitzmann, J. V., Cameron, J. L., & Gordon, T. A. (1998). Should hepatic resections be performed at high-volume referral centers?. Journal of Gastrointestinal Surgery, 2(1), 11-20.

22. Hyder, O., Pulitano, C., Firoozmand, A., Dodson, R., Wolfgang, C. L., Choti, M. A., ... & Pawlik, T. M. (2013). A risk model to predict 90-day mortality among patients undergoing hepatic resection. Journal of the American College of Surgeons, 216(6), 1049-1056.

23. Rahbari, N. N., Garden, O. J., Padbury, R., Brooke-Smith, M., Crawford, M., Adam, R., ... & Weitz, J. (2011). Posthepatectomy liver failure: a definition and grading by the International Study Group of Liver Surgery (ISGLS). Surgery, 149(5), 713-724.

24. Chen, T. S., & Chen, P. S. (1984). Understanding the liver: a history (No. 14). Praeger.

25. Douard, R., Bonnichon, P., & Lebert, R. (2008). Histoire des interventions abdominales à domicile: le cas de l'urgence. J Chir, 145(4).

26. Lorenzo, C. S., Whitney, M. L., Lurie, F., & Wong, L. L. (2005). Factors affecting outcome in liver resection. HPB, 7(3), 226-230.

27. Strong, R. W., Lynch, S. V., Wall, D. R., & Ong, T. H. (1994). The safety of elective liver resection in a special unit. Australian and New Zealand Journal of Surgery, 64(8), 530-534.

28. Beppu, T., Wakabayashi, G., Hasegawa, K., Gotohda, N., Mizuguchi, T., Takahashi, Y., ... & Takada, T. (2015). Long-term and perioperative outcomes of laparoscopic versus open liver resection for colorectal liver metastases with propensity score matching: a multi-institutional Japanese study. Journal of Hepato-Biliary-Pancreatic Sciences, 22(10), 711-720.

29. Garzali, I. U., Elyakub, A. I., & Sheshe, A. A. (2021). Hepatic Resection in Low Resource Setting: A Single Centre Experience in Northwest Nigeria. HPB, 23, S152.

30. Billingsley, K. G., Jarnagin, W. R., Fong, Y., & Blumgart, L. H. (1998). Segment-oriented hepatic resection in the management of malignant neoplasms of the liver. Journal of the American College of Surgeons, 187(5), 471-481.

31. DeMatteo, R. P., Palese, C., Janmgin, W. R., Sim, R. L., Blumgart, L. H., & Fong, Y. (2000). Anatomie segmental hepatic resection is superior to wedge resection as an oncologic operation for colorectal liver metastases. Journal of Gastrointestinal Surgery, 4(2), 178-184.

32. Fan ST. Methods and related drawbacks in the estimation of surgical risks in cirrhotic patients undergoing hepatectomy. Hepatogastroenterology. 2002 Jan-Feb;49(43):17-20. PMID: 11941945.

33. Mueller, J. L., Molina, G., Ferrone, C. R., Chang, D. C., Vagefi, P., Tanabe, K. K., ... & Qadan, M. (2021). Open hepatic resection in the elderly at two tertiary referral centers. The American Journal of Surgery, 222(3), 594-598.

34. Menon, K. V., Al-Mukhtar, A., Aldouri, A., Prasad, R. K., Lodge, P. A., & Toogood, G. J. (2006). Outcomes after major hepatectomy in elderly patients. Journal of the American college of Surgeons, 203(5), 677-683.

35. Glasgow, R. E., Showstack, J. A., Katz, P. P., Corvera, C. U., Warren, R. S., & Mulvihill, S. J. (1999). The relationship between hospital volume and outcomes of hepatic resection for hepatocellular carcinoma. Archives of surgery, 134(1), 30-35.

36. Dimick, J. B., Cowan, J. A., Knol, J. A., & Upchurch, G. R. (2003). Hepatic resection in the United States: indications, outcomes, and hospital procedural volumes from a nationally representative database. Archives of Surgery, 138(2), 185-191.

37. Cucchetti, A., Ercolani, G., Vivarelli, M., Cescon, M., Ravaioli, M., Ramacciato, G., ... & Pinna, A. D. (2009). Is portal hypertension a contraindication to hepatic resection?. Annals of surgery, 250(6), 922-928.

38. Rouxel, P., & Beloeil, H. (2019). Enhanced recovery after hepatectomy: a systematic review. Anaesthesia Critical Care & Pain Medicine, 38(1), 29-34.

39. Ni, T. G., Yang, H. T., Zhang, H., Meng, H. P., & Li, B. (2015). Enhanced recovery after surgery programs in patients undergoing hepatectomy: a meta-analysis. World Journal of Gastroenterology: WJG, 21(30), 9209.

40. Reddy, S. K., Barbas, A. S., Turley, R. S., Steel, J. L., Tsung, A., Marsh, J. W., ... & Clary, B. M. (2011). A standard definition of major hepatectomy: resection of four or more liver segments. Hpb, 13(7), 494-502.

41. Jammer, I. B., Wickboldt, N., Sander, M., Smith, A., Schultz, M. J., Pelosi, P., ... & Pearse, R. M. (2015). Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. European Journal of Anaesthesiology| EJA, 32(2), 88-105.

42. Liu, J., Zhang, Y., Zhu, H., Qiu, L., & Guo, C. (2019). Prediction of perioperative outcome after hepatic resection for pediatric patients. BMC gastroenterology, 19, 1-7.

43. Melendez, J. A., Arslan, V., Fischer, M. E., Wuest, D., Jarnagin, W. R., Fong, Y., & Blumgart, L. H. (1998). Perioperative outcomes of major hepatic resections under low central venous pressure anesthesia: blood loss, blood transfusion, and the risk of postoperative renal dysfunction. Journal of the American College of Surgeons, 187(6), 620-625.

44. Miyagawa, S., Makuuchi, M., Kawasaki, S., & Kakazu, T. (1995). Criteria for safe hepatic resection. The American journal of surgery, 169(6), 589-594.

45. Cescon, M., Vetrone, G., Grazi, G. L., Ramacciato, G., Ercolani, G., Ravaioli, M., ... & Pinna, A. D. (2009). Trends in perioperative outcome after hepatic resection: analysis of 1500 consecutive unselected cases over 20 years. Annals of surgery, 249(6), 995-1002.

Annex I: English Version Checklist

S/N	Items	Response	Remark
PREOPERATIVE PATIENT STATUS			
	Sex	1. Male 2. Female	
	Age(in years)	_____ years	
	Preoperative comorbidity	A. No B. Yes 1. Hypertension 2. Cardiac disease a. Ischemic heart disease/cardiomyopathy b. Dysrhythmia c. Valve disease 3. Diabetes mellitus	

			4. COPD/asthma 5. Peripheral vascular disease 6. Preoperative chemotherapy 7. Other	
	ASA/ ECOG status		1. 0 2. 1 3. >/=2	
	Liver pathology	Liver cirrhosis status	1. No cirrhosis 2. No cirrhosis but Intraop fibrosis 3. Child A 4. Child B 5. Child C	
		Hepatic steatosis	1. Yes 2. No	
		Noncirrhotic non steatotic	1. Chronic viral hepatitis 2. Alcoholic liver disease 3. Others(specify)	
	Indication for hepatectomy		1. Primary Malignant disease a. Hepatocellular carcinoma b. Bile duct cancer c. Cholangiocarcinoma d. Hepatoblastomas e. Gall bladder Cancer 2. Secondary to liver a. Colorectal liver metastasis b. Noncolorectal liver metastasis 3. Benign disease a. Focal nodular hyperplasia b. Adenoma c. Hydatid cyst d. Hemangioma e. Biliary cyst f. Others	
	Preoperative tests		Bilirubin___ Albumin _____ Creatinine _____ Platelet _____ Hemoglobin ……. Liver enzymes……..	NB it binomial data
	Facility/experience/ volume of surgery		1. TASH 2. Y12 GH 3. AdGH 4. LGH 5. AGH	

INTRAOPERATIVE PATIENT DATA			
	Duration of surgery (hrs)	_____	
	Porta hepatis clamp time (minutes)	……..	
	Estimated blood loss(ml)	…….. in ml	
	Does the patient transfuse blood? if yes specify(Unit)	1. Yes a. PRBC…… b. FFP……. c. Platelet……. d. Whole blood …… 2. No	
	Patients requiring ICU admission	1. Yes 2. No	
	Type of hepatectomy(specify No of segments removed)	1. Extended right hepatectomy 2. Extended left hepatectomy 3. Right hepatectomy 4. Left hepatectomy 5. Right posterior sectionectomy 6. Left lateral sectionectomy 7. Central hepatectomy 8. Bisegmentectomy 9. Segmentectomy 10. Nonanatomic resection 11. Caudate resection	
POSTOPERATIVE PATIENT DATA			
	Post OP complications	A. No B. Yes 1. Liver/Biliary a. Hepatic insufficiency/failure • Grade A/B/C b. Bile leak/biloma • Grade A/B/C c. Post hepatectomy hemorrhage • Grade A/B/C d. Perihepatic abscess e. Portal vein thrombosis f. Cholangitis 2. Pulmonary a. Pleural effusion (symptomatic) b. Pneumonia c. Atelectasis d. Respiratory insufficiency/failure e. Pneumothorax	NB. ISGLS Standard definition and grading are attached below

		f. Pulmonary embolus 3. Cardiovascular a. Arrhythmia b. DVT c. CHF d. Angina pectoris/MI e. Cardiac arrest f. Stroke/TIA g. Pericarditis/pericardial effusion 4. Genitourinary a. Urinary tract infection b. Renal insufficiency/failure c. Urinary retention 5. Gastrointestinal a. Ileus b. Bowel obstruction c. Gastrointestinal hemorrhage d. Ascites 6. Miscellaneous a. Wound infection b. Wound dehiscence c. Sepsis/bacteremia d. Unexplained fever e. Delirium 2. Other(Specify)_____	
	Length of hospital stay (days)	_____	
	Postoperative lab tests	1. Bilirubin 2. INR 3. Hemoglobin	NB. INR and Bilirubin should be determined after 5-7th POD
	Pathology of the lesion	1. Histologic subtype……. 2. Grade of differentiation……. 3. No of the lesion……. 4. Margin status…….. 5. Lymphovascular invasion……..	
	Postoperative mortality	1. If Yes a. Date of death…… b. Cause of death……	
	Readmission	1. Yes (specify the reason for readmission) 2. No	
ISGLS definition and Grading			

1. PHH= is defined by the ISGLS as any of the following in the setting of confirmed bleeding noted in drains or on imaging: (1) a drop in hemoglobin level of greater than 3 g/dL, (2) any postoperative transfusion of packed red blood cells (PRBCs) for falling hemoglobin, or (3) the need for invasive intervention (e.g., embolization or Relaparatomy)

   PHH is graded from A to C such that grade A hemorrhage may require transfusion of up to 2 U of PRBCs, grade B requires more than 2 U of PRBCs, and grade C necessitates invasive intervention

2. The ISGLS defined a bile leak as the drainage of intraabdominal fluid with an increased bilirubin concentration (at least three times the serum bilirubin concentration) on or after post-day 3

   Grade A bile leaks are transient with little to no clinical impact, grade B leaks require additional diagnostics and potentially percutaneous drainage, and grade C leaks require Relaparatomy for bile peritonitis

3. The International Study Group of Liver Surgery (ISGLS) defined it as postoperatively acquired deterioration in the ability of the liver to maintain its synthetic, excretory, and detoxifying functions, which are characterized by an increased international normalized ratio (INR) and concomitant hyperbilirubinemia on or after postoperative day 5

   This may range from a transient decline in liver function requiring no specific intervention (grade A), grade B PHLF if there is a deviation from the regular, postoperative clinical path-way, but they can be managed without invasive treatment, progress to the fulminant liver and multisystem organ failure requiring invasive treatment(grade C)