# ASSESSMENT OF YIELD AND PROCEDURAL COMPLICATION RATE IN PATIENTS UNDERGOING TRANSJUGULAR LIVER BIOPSY (TJLB): A PROSPECTIVE STUDY

**A dissertation submitted in the partial fulfilment of MD Radiodiagnosis (Branch VIII) examination of the Tamil Nadu Dr. M.G.R. Medical University, Chennai to be held in April 2017**

# CERTIFICATE

This is to certify that the dissertation entitled "Assessment of yield and procedural complication rate in patients undergoing Transjugular liver biopsy (TJLB): A prospective study" is a bonafide original work of Dr. David Narayan Rameswarapu submitted in the partial fulfilment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R. Medical University, Chennai to be held in April 2017.

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# DECLARATION

I Dr. David Narayan Rameswarapu, hereby declare that this dissertation entitled "Assessment of yield and procedural complication rate in patients undergoing Transjugular liver biopsy (TJLB): A prospective study" is an original work done in partial fulfilment of the requirement for MD Radiodiagnosis (Branch- VIII) Degree Examination of the Tamil Nadu Dr. M.G.R. Medical University, Chennai to be conducted in April, 2017.

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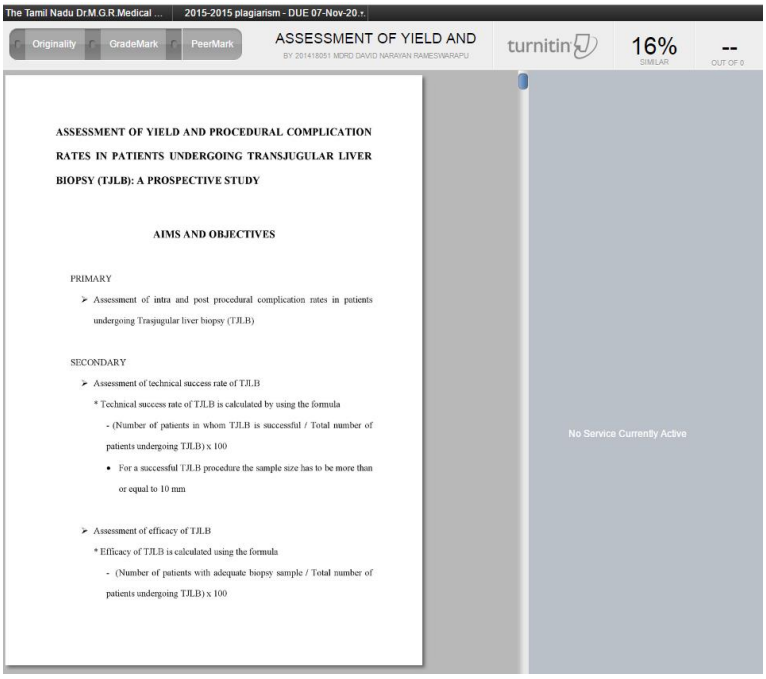
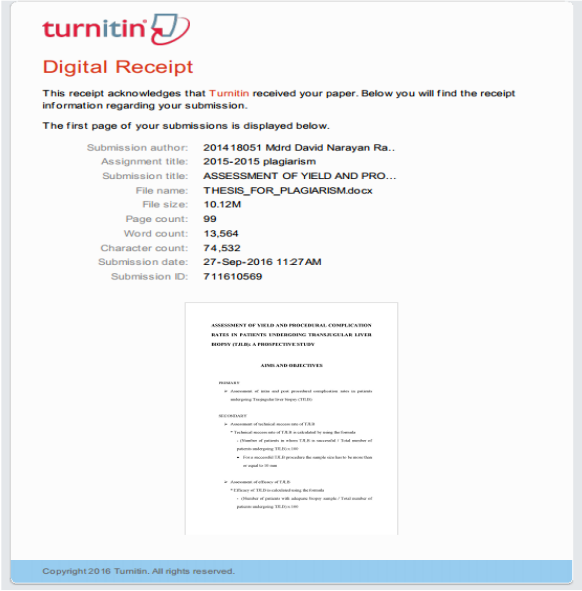
# PLAGIARISM CERTIFICATE



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# ABBREVIATIONS:

1. EASL – European association for the study of liver
2. BSG – British Society of Gastroenterology
3. PLB – Percutaneous liver biopsy
4. DLB – Direct liver biopsy
5. TJLB - Transjugular liver biopsy
6. TGLB – Transgastric liver biopsy
7. NOTES - Natural orifice transluminal endoscopic surgery
8. LFT – Liver function tests
9. HBV – Hepatitis B virus
10. HCV – Hepatitis C virus
11. PUO – Pyrexia of unknown origin
12. E2-AMA – E2 anti-mitochondrial antibody
13. ERCP – Endoscopic retrograde cholangio-pancreatogram
14. MRCP – Magnetic resonance cholangio-pancreatogram
15. AIH – Autoimmune haemolytic anaemia
16. NAFLD – Non-alcoholic fatty liver disease
17. NASH – Non-alcoholic steatohepatitis
18. NCIPH – Non cirrhotic intra-hepatic portal hypertension
19. CEA – Carcinoembryonic antigen
20. CMV – Cytomegalovirus
21. BT – Bleeding Time
22. PT – Prothrombin time

23. INR – International normalised ratio
24. aPTT – Activated partial thromboplastin time
25. HCC – Hepatocellular carcinoma
26. AV fistula – Arteriovenous fistula
27. IVC – Inferior Venacava
28. SIR - Society of Interventional Radiology
29. IRB – Institutional Review Board
30. PACS - Picture Archival and Communication System
31. RHV, MHV, LHV – Right, Middle and Left hepatic veins
32. ECG – Electrocardiogram
33. CMC, Vellore – Christian Medical college, Vellore

# CONTENTS

# ABSTRACT

**TITLE:** "Assessment of yield and procedural complication rate in patients undergoing Transjugular liver biopsy (TJLB): A prospective study"

**AIMS AND OBJECTIVES**:

Primary aim was to assess the intra and post procedural complication rate in patients undergoing trasjugular liver biopsy.

To determine the technical success and efficacy rate of TJLB.

**METHODS:**

This is a hospital based prospective, observational study approved by the Institutional Research Board (IRB). A total of 70 patients who underwent TJLB during the study period between May 2015 to July 2016 were assessed for intra and post procedural complications. Screening techniques included clinical, radiological and lab parameters. The complications were categorised into minor and major complications according to Society of Interventional Radiology criteria (SIR). Technical success and adequacy of the biopsy sample were also determined based on clinico-pathological correlation.

**RESULTS:**

Seventy patients who underwent TJLB were studied. Study population included patients between 11 to 75 years of age. Of the 70 patients who underwent TJLB, 39 were male and 31 were female.

Common indications for TJLB were thrombocytopenia (33 patients) followed by deranged bleeding parameters (25 patients), ascites (21 patients) and renal failure (18 patients). Some of the patients had multiple indications. 65 patients had right internal jugular venous access and 5 patients had left internal jugular venous access. There was increased risk of complications in patients with multiple indications (Chi square – 3.88, p value – 0.049). Female gender was found as a protective factor from complications. There is no significant statistical correlation between complication rates and age, side of IJV access, transfusions and individual indication for the procedure.

Total complication rate in patients undergoing TJLB was found to be ~ 25.7 % (18 patients). 17 patients (24.3 %) had minor complications as per Society of Interventional Radiology criteria (1). 1 patient had major complication (1.4%) in the form of intra-abdominal bleed with significant drop in haemoglobin levels, post TJLB requiring blood transfusion. Minor complications seen were moderate neck pain (3 patients, 4.3%), moderate abdominal pain (1 patient, 1.4%), elevated temperature, 100-102 deg F (2 patients, 2.9%), intra-abdominal bleed (low suspicion – 5 patients, 7.1% & high suspicion – 9 patients, 12.9%), hypertension (5 patients, 7.1%) and transient ventricular arrhythmia (1 patient, 1.4%) which was self-limiting. There was no mortality attributable to TJLB during this study.

TJLB was possible in all the patients who were posted for the procedure. Technical success which was defined as sample length more than or equal to 10 mm was achieved

in 84.3 % of patients (59 patients). The median length of sample size was 16 mm. Adequacy of the sample which was defined as 5 or more complete portal tracts or whenever histopathological analysis was contributory to the diagnosis was achieved in 87% of the patients.

**CONCLUSION:**

Transjugular liver biopsy (TJLB) is an innovative way of performing liver biopsy when percutaneous route is considered unsafe. It has a very high technical success and efficacy rate. The complication rate seen in this prospective study was 25.7% (18 patients) which was comparable with other prospective studies. Patients with multiple indications for TJLB had higher complication rates as compared to patients with single indication. TJLB is superior to other methods of liver biopsy in view of assessment of hepatic wedge pressure for evaluating portal hypertension and its pharmacological response. There was no mortality attributable to TJLB during this study.

## KEYWORDS

Transjugular liver biopsy (TJLB), Complication rate, Prospective study, Technical success rate, Efficacy rate, Society of Interventional Radiology (SIR)

# TITLE

# ASSESSMENT OF YIELD AND PROCEDURAL COMPLICATION RATE IN PATIENTS UNDERGOING TRANSJUGULAR LIVER BIOPSY (TJLB): A PROSPECTIVE STUDY

# AIMS AND OBJECTIVES

PRIMARY

- Assessment of intra and post procedural complication rate in patients undergoing Trasjugular liver biopsy (TJLB)

SECONDARY

- Assessment of technical success rate of TJLB

  * Technical success rate of TJLB is calculated by using the formula

    - (Number of patients in whom TJLB is successful / Total number of patients undergoing TJLB) x 100

      - For a successful TJLB procedure the sample size has to be more than or equal to 10 mm

- Assessment of efficacy rate of TJLB

  * Efficacy of TJLB is calculated using the formula

    - (Number of patients with adequate biopsy sample / Total number of patients undergoing TJLB) x 100

      - Adequate liver biopsy is defined as biopsy sample with at least 5 complete portal tracts (non – cirrhotic cases) or if histopathological analysis is contributory to diagnosis or management of the patient

# JUSTIFICATION

- In the past the specimens obtained by TJLB were considered suboptimal as compared to percutaneous liver biopsy (2). However with recent advances the quality of the TJLB specimens has improved and is comparable with those obtained with percutaneous technique.
- TJLB has low complication rates ranging from 0.5 to 1 % reaching as high as 15% (3–5). The complication rates are significantly low despite being performed in patients in whom percutaneous liver biopsy is contraindicated due to various reasons like coagulopathy, ascites, renal dysfunction, thrombocytopenia, shrunken liver etc. in whom there are increased risk of complications.
- Though many studies have mentioned the complication rate, technical success rate and histopathological adequacy, most of them are retrospective studies from which the exact complication rate is difficult to determine as many of the minor complications are overlooked. There is limited availability of prospective Indian data regarding complication rates in patients undergoing Transjugular liver biopsy.
- Through this hospital based observational study we are trying to determine the exact complication rates in patients undergoing TJLB in a tertiary care centre in India. Due to limited availability of prospective data in India the exact complication rates which includes both major and minor are unknown. With the knowledge of the precise complication rates, we will not only determine the role of TJLB for liver biopsies but also know what complications are most frequently

seen so that necessary precautions can be taken. We are also trying to find out the technical success and efficacy rate of TJLB to see if they are comparable with that of percutaneous liver biopsy.

# LITERATURE REVIEW

## LIVER BIOPSY

Liver biopsy is considered the gold standard in evaluating various conditions associated with liver disorders. It was first described by Paul Ehrlich in 1883 (6). There has been a great deal of modification in the biopsy technique since then and it has now become the central investigation in diagnosis and management of hepatic disease (7). Liver biopsies are performed extensively with a primary intent to diagnose specific disease conditions. Various disease conditions that can be detected are acute and chronic hepatitis, hepatic steatosis, disorders of cholestasis, infiltrative and storage disorders, infective and granulomatous disease etc. In fact it is the gold standard for diagnosis of hepatic pathology. It also has a significant role in predicting the prognosis in certain disease conditions like hepatitis, non-alcoholic fatty liver disease, cirrhosis, primary biliary cirrhosis etc. The degree of fibrosis can be graded by the pathologists which aids in determining the overall prognosis of the condition. It also helps in evaluation of conditions associated with deranged LFT, rejection following orthotopic liver transplant and in implementing treatment plans regarding certain diseases like Wilson's disease, primary biliary cirrhosis, acute alcoholic hepatitis and haemochromatosis. It also helps in assessment of treatment response and relapse in autoimmune hepatitis (6,8,9).

## **INDICATIONS** (3,4,7,9–18)

1. Acute hepatitis

   Acute hepatitis of unknown etiology has for long been an indication for liver biopsy; however in typical acute condition it may not be necessary. With advent of novel antiviral drugs, histology is indispensable for initiating appropriate treatment and monitoring the response to the same.

2. Hepatitis C

   Biopsy in a patient with hepatitis C is necessary to determine the degree of fibrosis and to exclude other causes of liver damage. EASL consensus statement (1999) suggest that ‘it is appropriate and important to obtain a percutaneous biopsy before beginning therapy in order to provide a base-line, to provide an opportunity to grade the severity of necro-inflammation and to stage progression of cirrhosis’(19).

3. Hepatitis B

   Management of the patient with chronic HBV infection is dependent on the degree of viral replication and the clinical state. According to EASL guidelines, histopathological interpretation plays an integral part in the management of patients with HCV infection.

   Liver biopsy also gives information about the degree of fibrosis, inflammation and helps in identifying other causes of liver disease, hence plays a vital role in monitoring progression of the disease and prognostication.

4. Genetic Haemochromatosis

   Liver biopsy helps to evaluate if there are any features of cirrhosis, to see if there is significant iron overload when other markers are equivocal and to rule out other causes of liver disease. It is particularly useful in suspected cases of haemochromatosis when the degree of iron overload and stage of fibrosis play a role in reaching diagnosis and management. EASL 2000 also states that though liver biopsy is the gold standard, emergence of biochemical and genetic testing would provide adequate information which would obviate the need for liver biopsy. Therefore it is recommended that liver biopsy may be indicated to determine the presence of cirrhosis and degree of fibrosis when biochemical and genetic testing do not give clear information and also to exclude other causes of liver disease.

5. Wilsons's disease

   Diagnosis of Wilson's disease is based on clinical history, examination findings like Kayser-Fleischer ring, estimation of serum copper, serum ceruloplasmin and urine copper levels before and after a d-Penicillamine challenge test. Liver biopsy helps in evaluation of cirrhosis and estimation of copper levels in hepatic tissue which may contribute to the diagnosis.

6. Pyrexia of unknown disease and infections

Histopathology and culture of hepatic tissue plays an important role in evaluation of infectious etiology involving the liver. Some of the haematological causes of PUO like lymphoma can also be detected by liver biopsy.

7. Primary Biliary Cirrhosis and Primary sclerosing cholangitis

   Elevated E2-AMA (anti-mitochondrial antibody) is a strong indicator of primary biliary cirrhosis. Thus in a classic case there is no role for liver biopsy. Primary sclerosing cholangitis is usually diagnosed by ERCP or MRCP where multiple segmental strictures, biliary dilatation, multiple diverticulae can be seen. Liver biopsy is of limited value in primary biliary cirrhosis. However liver biopsy plays a role in diagnosis of small duct primary sclerosing cholangitis.

8. Alcoholic liver disease

   Liver biopsy helps in determining fatty liver, degree of fibrosis and cirrhosis which otherwise cannot not be accurately determined. In patients with liver damage due to intake of excess alcohol, biopsy helps in determining the degree of liver damage, reversibility and other contributory factors. Histology is essential to confirm alcoholic hepatitis since in 20% of the cases clinical diagnosis is incorrect.

9. Autoimmune Hepatitis (AIH)

   Liver biopsy is indicated in diagnosis, management and follow up of patients with autoimmune hepatitis. Liver biopsy is necessary prior to cessation of immunosuppressive treatment, especially in those who are in clinical and serological

remission as in half of the cases they might have interface hepatitis and may relapse after cessation of immunosuppression.

10. Non-alcoholic fatty liver disease (NAFLD)

    Liver histology can differentiate NAFLD from non-alcoholic steatohepatitis (NASH). As NASH can progress to Cirrhosis they need to be followed up and treated.

11. Abnormal liver tests of unknown cause

    Liver histology in patients with persistently abnormal liver function tests in the absence of contributory serology or diagnostic imaging, can help in identification of the cause for liver function abnormalities.

12. Focal liver lesions

    Percutaneous biopsy of focal liver lesions help in identifying the nature of the hepatic lesion. It should however be correlated with various lab parameters like blood counts, liver function tests, alpha-fetoprotein, carcinoembryonic antigen (CEA) etc. Liver biopsy is associated with a risk of tumour seeding along the biopsy track, hence should be done with necessary precautions.

13. Following liver transplantation

    Liver histology post liver transplantation is necessary to determine cause of liver function abnormalities. It helps in differentiating rejection, viral infection,

reperfusion injury, drug toxicity, invasive CMV infection, recurrent disease, and other causes of transplant rejection.

14. Research

Has a role in studying the stages of progression of various diseases, studying pathophysiology of viruses and development of new drugs.

## **CONTRAINDICATIONS** (4,6,7,10,11,15,17,18,20)

1. Uncooperative patient

   Patient's co-operation is very essential to perform liver biopsy as any untoward movement can lead to tear in the parenchyma and hepatic capsule with subsequent bleeding. Sedatives like benzodiazepines can be used to allay patient's anxiety prior to the procedure. If the patient is still uncooperative and the benefits of biopsy outweigh the risk, biopsy can be done under general anaesthesia (18).

2. Extra-hepatic Biliary obstruction

   There is a serious risk of biliary peritonitis, septicaemic shock and death in patients with extra-hepatic biliary obstruction undergoing percutaneous biopsy. One study showed serious complications in ~ 2% of patients and significant complications in 4 % of patients following percutaneous liver biopsy (21). Transjugular liver biopsy is a safe option in patients with extra-hepatic biliary obstruction.

3. Bacterial cholangitis

   In a patient with bacterial cholangitis undergoing liver biopsy there is increased risk of inducing peritonitis and septic shock. One study showed a bacteraemia in 14% of patients undergoing percutaneous liver biopsy (22). These findings suggest increased risk of disseminated infection in patients with bacterial cholangitis undergoing liver biopsy.

4. Abnormal coagulation profile

There are varying opinions at which abnormal coagulation profile becomes contraindication to liver biopsy. Number of studies have shown that there is no correlation between the degree of bleeding and the peripheral coagulation profile when the coagulation indices are modestly elevated. However it should be remembered that during blind percutaneous biopsy the liver along with the skin and subcutaneous tissue is punctured and hence there can be bleeding from these sites.

A. Prothrombin time

Several studies have shown that there is no significantly increased risk in bleeding in patients with increased prothrombin time, upto 4 seconds above controls. The largest retrospective study conducted by Piccinino, Sagnelli et al. showed no significant increased risk of bleeding in patients with increase in prothrombin time upto 7 seconds above the controls (23).

In 1991, BSG (British Society of Gastroenterology) audit of biopsy practice in UK showed that there is increased risk of bleeding if the INR was raised. The study showed there is 3.3 % increased risk of bleeding when INR was in between 1.3 - 1.5, and 7.1% increased risk of bleeding when INR was more than 1.5 (24). However as 90% cases of the bleeding occurred in patients with normal INR values, normal INR or Prothrombin time does not necessarily mean there is no risk of bleeding.

B. Thrombocytopenia

There is a varied opinion regarding the level at which thrombocytopenia is a contraindication to liver biopsy. Menghini, 1976 proposed platelet level of 100,000/ mm3 as safe (24) whereas Mayo clinic regards platelet counts as low as 56,000/mm3 as safe limit (25). Sharma, Mc Donald et al. 1982 showed that patients with a platelet count less than 60,000 are more prone to bleed following the procedure. Though many studies have set the cut off limits, there is no clear consensus for the cut off limit and also no account is taken of the function of the platelets.

The absolute value of platelet count may not be important to determine the risk of bleeding. For a percutaneous liver biopsy the minimum platelet considered safe is 60,000/mm3 (24).

C. Platelet function/ Bleeding time (BT)

Though ingestion of antiplatelet drugs a week prior to invasive intervention is reported as a contraindication, there is no convincing evidence to suggest that it is a contraindication to liver biopsy. Patients with renal dysfunction are at an increased risk (~50 %) for haemorrhagic complications following liver biopsy due to functional impairment of platelet function (26)

5. Ascites

Tense ascites is considered a contraindication due to various reasons like,

a. There is increased risk of failure of procedure as there is increased distance between the abdominal wall and the liver

b. There is increased risk of uncontrollable bleeding

c. Increased mobility of the liver in the free fluid

However there is evidence to support the fact that there is no increased complication rates in patients with ascites under imaging guided liver biopsy (27,28). Despite these studies it seems logical that partial paracentesis can be performed in a patient with tense ascites prior to percutaneous liver biopsy to avoid various complications.

6. Amyloidosis

The diagnosis of amyloidosis on liver biopsy was first used in 1928 (Waldenstrom, 1928). Volwiler and Jones reported mortality due to haemorrhage in a patient with amyloidosis who underwent liver biopsy (29). Several other cases were reported subsequently where increased risk of bleeding was documented in patients with amyloidosis. Stauffer stated that liver biopsy plays an important role in the diagnosis of amyloid liver disease in patients with hepatomegaly of unknown etiology. However in a patient with hepatomegaly, if amyloidosis is strongly suspected then one would need a good indication for performing liver biopsy. Other less invasive procedures like rectal biopsy should be considered.

| | Disease | Diagnosis | Staging/Prognosis | Treatment |
|---|---|---|---|---|
| 1 | Hepatitis B | - | +++ | ++ |
| 2 | Hepatitis C | - | +++ | +++ |
| 3 | Autoimmune hepatitis | +++ | +++ | +++ |
| 4 | Primary sclerosing cholangitis | +++ | +++ | +++ |
| 5 | Primary biliary cirrhosis | ++ | +++ | - |
| 6 | Overlap syndrome | +++ | +++ | ++ |
| 7 | Nutritional – toxic/ alcoholic Steatohepatits | + | +++ | + |
| 8 | NAFLD/NASH | +++ | +++ | ++ |
| 9 | Iatrogenic – toxic | +++ | + | + |
| 10 | Haemochromatosis | +++ | +++ | +++ |
| 11 | Wilsons disease | +++ | +++ | _ |
| 12 | Alpha 1Antitrypsin deficiency | + | ++ | - |
| 13 | Acute liver failure | +++ | ++ | - |
| 14 | Liver transplantation (rejection/ reinfection) | +++ | ++ | +++ |
| 15 | Tumour:<br>HCC<br>Liver cell adenoma<br>Metastases | <br>++<br>+++<br>+++ | <br>-<br>-<br>- | <br>-<br>-<br>- |

(9)

Table : Common indications for liver biopsy

## TYPES OF LIVER BIOPSY

1. Percutaneous liver biopsy
2. Transjugular liver biopsy
3. Laparoscopic liver biopsy
4. Transgastric liver biopsy

1. Percutaneous liver biopsy (PLB)

It is either performed directly or under imaging assistance, in which case ultrasound or computerised tomography is utilised. Imaging assisted PLB has lesser complication rates, has better sample yield, requires lesser passes, is associated with lesser pain related morbidity and is only marginally expensive than the direct PLB.

Complications like pneumothorax or injury to visceral organs or gall bladder are very rare under imaging assisted PLB. The most common complication is pain which can be managed conservatively. In a study conducted by Piccinino et al. 61% of the complications related to PLB were seen during first 2 hours, 82% in first 10 hours and 96% in first 24 hours (23). Therefore the patients have to be monitored strictly for at least 24 hours following the procedure. The major complication rates range from 0.09% - 2.3 %, severe complications in 0.57% and mortality in 0.03% - 0.11% (25,30,31). The complications associated with imaging assisted PLB are low as compared to direct PLB however they are technique and operator dependent. Several studies show 0.5% vs 2.2% for severe complications and 1.8-2% vs. 4-7.7% for total complications (14–16).

2. Transjugular liver biopsy (TJLB)

TJLB was first described by Dotter in 1964 (32–34) on an experimental model and was used clinically for the first time by Hanafee in 1967 (6,35). It involves gaining access to hepatic veins by endovascular approach typically via jugular vein. The risk of complications such as haemorrhage are usually less as the hepatic veins return blood back into the circulation. The specimens obtained by TJLB were initially thought to be suboptimal as compared to percutaneous liver biopsy due to smaller size and increased fragmentation, however with the development of newer instruments and techniques the results are comparable. The complication rates in TJLB are low despite being performed on patients with contraindications for percutaneous liver biopsy. Common indications are coagulopathy, ascites, renal dysfunction, shrunken cirrhotic liver, acute liver failure, morbid obesity, patients after liver transplantation, peliosis hepatis etc. There are no specific absolute contraindications for TJLB. The bleeding parameters should be corrected before performing TJLB. In case of gross ascites the ascitic fluid should be drained prior to the procedure. Other ancillary procedures like hepatic vein wedge pressure measurement can be performed simultaneously (6,36).

Minor complications include local pain, neck haematoma, carotid puncture, abdominal pain and transient cardiac arrhythmia during manipulation of the catheter. Other uncommon complications that have been described in the literature are Horner's syndrome, dysphonia, paraesthesia of arm, hypotension, subclinical capsular perforation, small hepatic haematoma, hepatico-portal vein fistula, hepatic artery

aneurysm, biliary fistula, haemobilia. Major complications that can be seen are large hepatic haematoma, intraperitoneal haemorrhage, IVC perforation, renal vein perforation, persistent ventricular arrhythmia, pneumothorax, intraperitoneal haemorrhage, respiratory arrest and death. The complications rates associated with TJLB range from 0.5– 15 % (4,5). The mortality rate is < 0.1 % in adults and ~ 0.1 % in children (6).

3. Laparoscopic liver biopsy

Several techniques are described for laparoscopic liver biopsy like percutaneous liver biopsy under laparoscopic view, laparoscopic liver biopsy under laparoscopic view, combined laparoscopic liver biopsy and additional procedure. This procedure is usually done under general anaesthesia using special laparoscopic suite which comprises of insufflation devices for distending the abdomen and laparoscopic instruments for performing the procedure. Pneumoperitoneum is created using Veress needle, inserted in the periumbilical region usually on the left side. The second port is inserted on the right side using a trocar through which 16 G Tru-cut needle is inserted and under laparoscopic guidance biopsy is taken. In order to prevent complications like bleeding, the biopsy sites can be cauterized using a cautery.

Laparoscopic liver biopsy allows direct visualisation of the liver surface, morphology and the biopsy sites which aid in acquiring adequate biopsy samples

including wedge resection. It helps us to visualise complications like haemoperitoneum, bile leakage, subcapsular haematoma and also aids in achieving haemostasis.

The advantages of laparoscopic liver biopsy as compared to percutaneous liver biopsy are

- Visualise the complications
- Identifying the site of bleed
- Achieving haemostasis either by cauterisation or compression

The disadvantages are

- Set up time is generally long for initiating the procedure
- Insufflation of gas to create an appropriate operating field
- Preparation of various laparoscopic instruments
- Need for an operating theatre

In general it is appropriate when we need both pathological diagnosis involving the liver and also procedures related to intra-abdominal pathology (36). According to Beckmann et al. majority of the complications associated with laparoscopic liver biopsy are bleeding and bile leakage and the complication rates are 2.7%, comparable to that of percutaneous liver biopsy (3%) and TJLB (2.9%) (37).

4. Transgastric Liver biopsy (TGLB)

Hollerbach et al. described an endoscopic USG guided fine needle aspiration biopsy for liver lesions. It can be used as an alternative to percutaneous liver biopsy especially in patients who have small hepatic lesions and are at risk for bleeding, however limiting factor would be the location of the lesion.

Natural orifice transluminal endoscopic surgery (NOTES) which has been recently introduced aims at performing scar less abdominal operations via an endoscope passed through natural orifices. NOTES using Transgastric approach allows direct visualisation of the biopsy site without inducing any scar on the skin surface. For clinical application of NOTES it is necessary to have a safe access to the peritoneal cavity, closure of the access route, correct intra-abdominal orientation, prevent infections, methods to manage complications, adequate skill and training in the procedure. One of the concern of NOTES is infection or bacterial contamination due to Transgastric access to the peritoneum. However studies have not shown significant complications due to Transgastric access.

The procedure is generally performed under general anaesthesia. Forward viewing, double channel endoscope is introduced into the stomach after which the gastric wall is punctured with a 3mm cutting wire needle knife. The puncture site is dilated using 8 mm balloon dilator. The endoscope is then advanced into the peritoneal cavity and air is introduced into the peritoneal cavity for inflation. The endoscope can be retroflexed

for better visualisation of the liver, following which biopsy can be performed from the free edge. Usually biopsy is performed from segment III of the liver, following which haemostasis is achieved either by cauterising the site of biopsy or manually by applying pressure. The access site is then closed using endoscopic clips (36).

Kalloo et al. showed no significant complications like peritoneal infections related to transgastric peritoneoscopy in the long term observation. Hazey et al. has shown no significant infectious complications related to laparosopic Roux-en-Y bypass although minimal contamination was associated during the procedure (14).

## COMPLICATIONS OF LIVER BIOPSY (6,10,11,15,16,18,23,38–43)

1. Pain

   In adult series most commonly reported complication was pain affecting as many as 84% of patients including those with mild discomfort (44). Sometimes the pain can be agonising and some patients remember the procedure as an unpleasant experience. Moderate to severe pain is reported in 1-5% of patients. The common sites of pain are at the site of biopsy and at the right shoulder tip . The mechanism of pain may be related to skin puncture, subcapsular haematoma stretching the liver capsule and irritation of the diaphragm due to blood or bile in sub diaphragmatic region. Use of imaging guidance, premedication with anxiolytics and analgesics significantly decreased the incidence of post biopsy pain from 47% to 35% (44).

2. Bleeding

   The risk of major bleeding is seen in 0.16% of cases. Major bleeding is severe bleeding defined clinically by significant haemodynamic alteration, radiographic evidence of intraperitoneal bleed that require hospitalisation with likelihood of transfusion or even radiologic intervention or surgery. Such bleeding is reported to occur in 1 in 2500 to 10,000 cases following percutaneous liver biopsy (18). Minor bleeding is characterised by less severe bleeding associated with pain, drop in blood pressure or tachycardia but not requiring transfusion or any intervention. Minor bleeding is seen in 1 in 500 cases (18). Severe bleeding is usually seen within 2 to 4 hours following liver biopsy, however bleeding can occur even upto 1 week

following biopsy. Bleeding can manifest as haemoperitoneum (0.23 – 0.7 %), intrahepatic haematoma (0.59 – 23 %) or haemobilia (0.058 – 0.2%) (45). Conservative treatment with close follow up on ultrasound is generally sufficient in minor bleeding cases. The least common complication among these is haemobilia. It presents with classical triad of pain, gastrointestinal bleeding and jaundice. It may appear acutely following simultaneous perforation of blood vessels and intrahepatic bile ducts or more commonly after 5 days following erosion of haematoma or pseudoaneurysm into a bile duct. Large quantity of haemobilia can cause acute pancreatitis (45).

5. Infective complications

   Transient bacteraemia has been reported in 5.8 to 13.5% of cases following liver biopsy (23,45). Intrahepatic abscess, septicaemia and septic shock are rare and occur in patients with biliary obstruction, cholangitis or due to accidental puncture of colon. Though there is risk of infections following the liver biopsy prophylactic antibiotics are not recommended, except for cases with valvular heart disease.

6. Thoracic complications

   Pneumothorax, haemothorax, subcutaneous emphysema, leakage of ascitic fluid into the pleural space occur following puncture of the pleura during liver biopsy. Haemothorax can occur even under ultrasound guidance if the patient takes deep breath or if the patient moves. Pneumothorax is a serious complication and timely identification is crucial for patient management (7,23).

7. Puncture of other Viscera

   This complication is very rare (~ 0.01 to 0.1 %) and involves puncture of the gall bladder, right kidney, colon etc. The incidence is less common when the biopsy is performed under ultrasound guidance. Biliary complications like bile peritonitis, biloma etc. are relatively more common in patients with biliary obstruction.

8. Miscellaneous complications

   Intrahepatic AV fistula, neuralgia, ventricular arrhythmia with transvenous biopsy, reactions to analgesic or anaesthetic drugs, arterio-portal fistula, breakage of needle etc.

9. Death

   It is very rare following liver biopsy ranging from 0.009% to 0.11% in percutaneous liver biopsy and ~ 0.09% in transvenous liver biopsy which may be related to higher risk patients selected for transvenous liver biopsy (11,23,25,45). The main cause of death after liver biopsy is due to intraperitoneal haemorrhage frequently occurring in patients with malignancy or cirrhosis.

   The incidence of fatal complications can be reduced by careful post procedure monitoring, prompt recognition of bleeding and active intervention if required.

## **RELEVANT HEPATIC ANATOMY** (40,46,47)

Liver is the largest gland in the body, located in the right hypochondrium with both exocrine and endocrine functions. It normally weighs 1.2-1.4 kg in females and 1.4-1.6 kg in males. Its exocrine secretions consist of bile which drains through capillaries, branching ducts and finally into the hepatic duct. From the hepatic duct the bile drains either into gall bladder via cytic duct or is carried to the duodenum via the common bile duct where it helps in digestion. The endocrine secretions are concerned with metabolism of carbohydrate, proteins, fats and other nitrogenous products that are transported to the liver via portal vein from the digestive tract. It plays an important role in haematopoiesis during fetal life.

### LOBES:

The right lobe is separated from the left lobe by the falciform ligament on its superior surface, by the left sagittal fossa on its inferior surface and umbilical notch anteriorly. It is somewhat quadrilateral in shape and is about 6 times larger than the left lobe. The quadrate lobe is situated on the undersurface of the liver. Anteriorly it is bounded by the anterior margin of the liver; posteriorly by the porta; medially by the fossa for umbilical vein and laterally by the fossa for gall bladder. The caudate lobe also called spigelian lobe is situated on the posterior surface of right lobe of the liver. It is bounded by the porta inferiorly, inferior venacava on the right and fossa for ductus venosus on the left. The left lobe is smaller and occupies the epigastrium and left hypochondrium.

## LIGAMENTS

The liver is attached to the diaphragm and the anterior abdominal wall by five ligaments; the falciform ligament, the coronary ligament, the round ligament and two lateral ligaments. The falciform ligament is a sickle shaped peritoneal fold that is attached to the left lobe of liver posteriorly and peritoneum lining the right rectus muscle and the diaphragm anteriorly. It is obliquely placed so that one surface faces anteriorly and the other faces posteriorly. It is composed of two layers of peritoneum folded upon each other and contains round ligament and paraumbilical veins at its free edge.

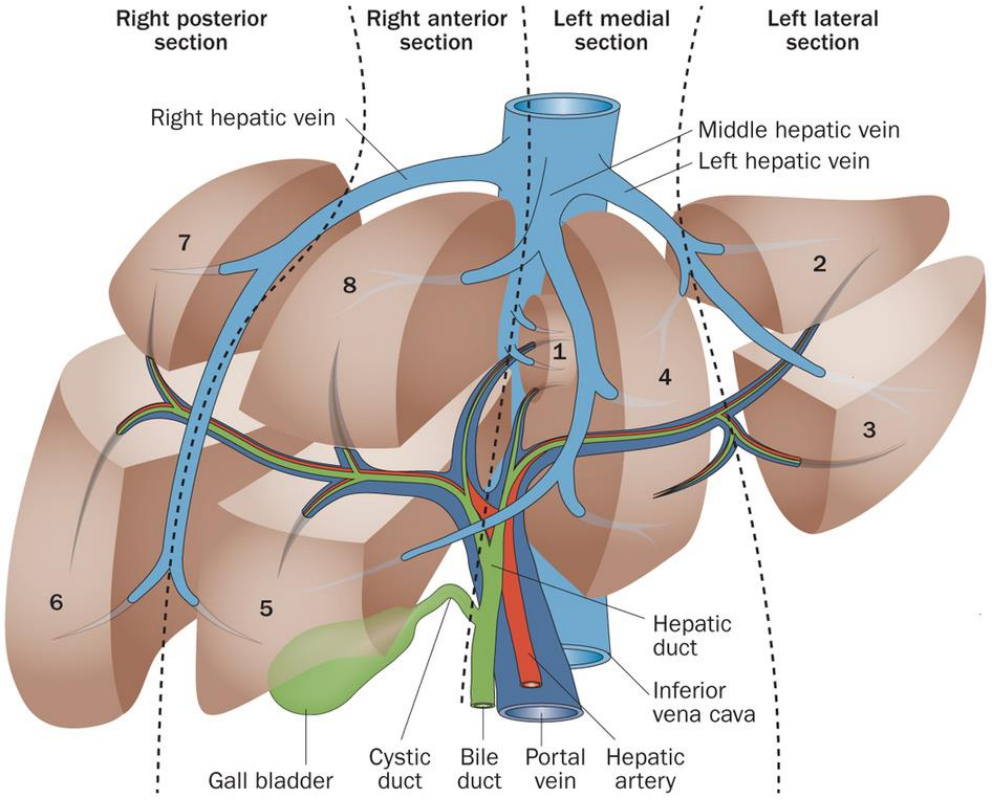
The coronary ligament consists of two layers. The reflection of peritoneum from the upper margin of bare area of the liver onto the diaphragm forms the upper layer and from the lower margin of bare area to the right kidney and adrenal forms the hepatorenal ligament. There are two triangular ligaments, the right triangular ligament connects the right extremity of bare area of liver to the diaphragm; the left triangular ligament connects the posterior aspect of the superior surface of liver to the diaphragm. The round ligament is obliterated umbilical vein and is seen as a fibrous cord along the free margin of the falciform ligament connecting the umbilicus with the umbilical notch of the liver (46).

## SEGMENTS OF THE LIVER

The liver is divided into the right and left lobe by the principal plane which is delineated by three landmarks: The IVC groove, gall bladder fossa and the middle

hepatic vein. The portal vein divides the liver into superior and inferior portions. Based on vascular supply the liver is further divided into Couinaud segments (40).

The left lobe is classified into segments IVa, IVb, II, III and the right lobe is classified into segments V, VI, VII,VIII. The caudate lobe (segment I) has dual supply from both the branches of portal vein.




(48)

Figure : Segments of the human liver and current surgical nomenclature of liver sections

# STRUCTURE OF THE LIVER

The liver is composed of numerous lobules which are held together by a fine areolar tissue. The hepatic ducts, hepatic artery, portal vein, lymphatics and nerves are embedded within the substance of the liver. It is further invested by a serous and fibrous coat which is also called the Glisson's capsule.

The lobules are hexagonal shaped structure which form the functional unit of the liver and are composed of

a. A thick plate of hepatocytes arranged in radial fashion. The hepatocytes, stellate cells and the Kuppfer cells form the reticuloendothelial cells. The Kupffer cells are phagocytes which line the sinusoids and play a role in destruction of erythrocytes.
b. Irregular spaces between the hepatic plates which are occupied by sinusoids and are lined by endothelial cells. They convey the blood from periphery to centre and ultimately empty into intralobular vein.
c. Bile capillaries which are located in-between the hepatocytes.

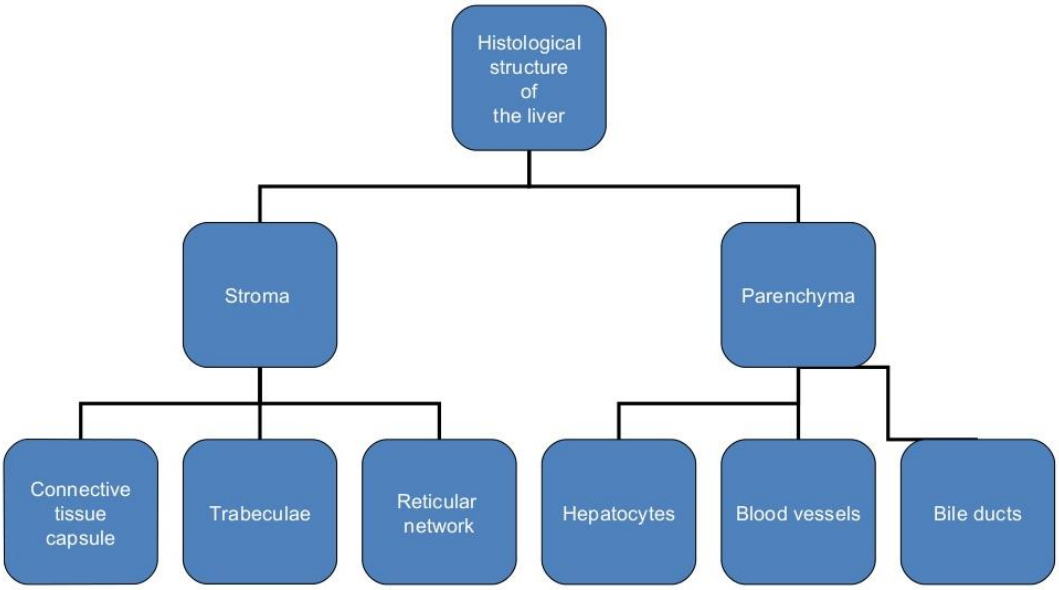



Figure: HEPATIC ARCHITECTURE

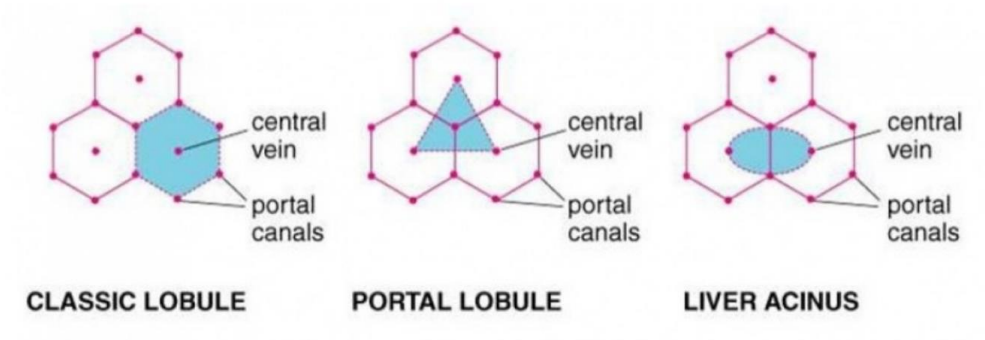



Figure: HEPATIC LOBULES

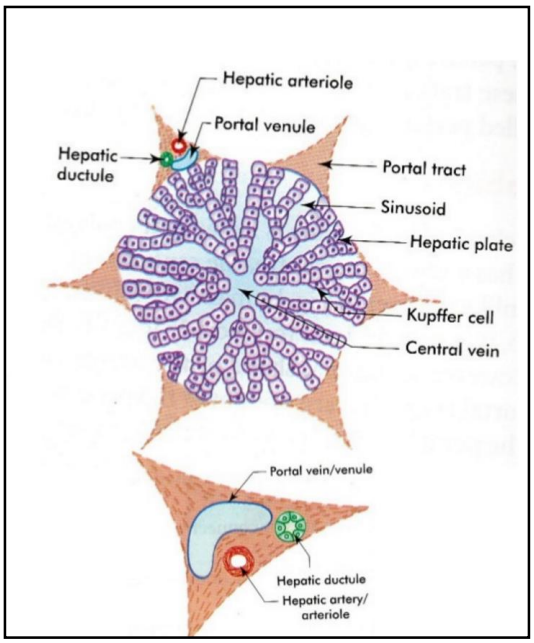



Figure: CLASSIC LOBULE

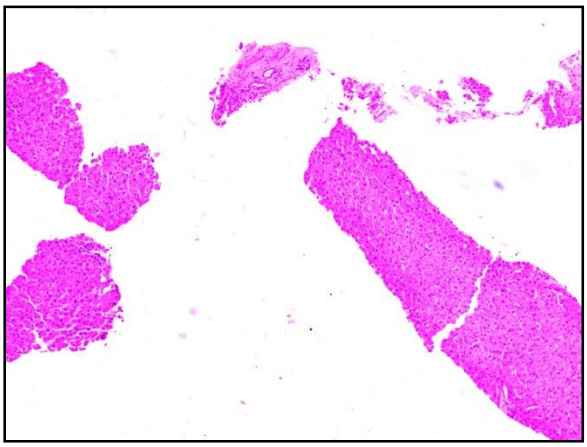


Figure: Fragmented pieces of histological normal Liver. H&E 40X

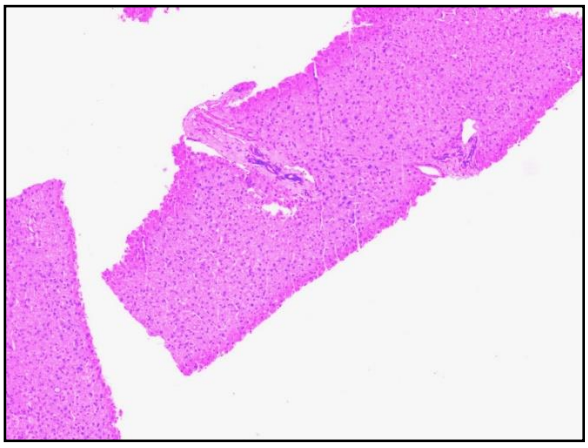


Figure: Liver biopsy with two normal portal tracts. H&E 40X

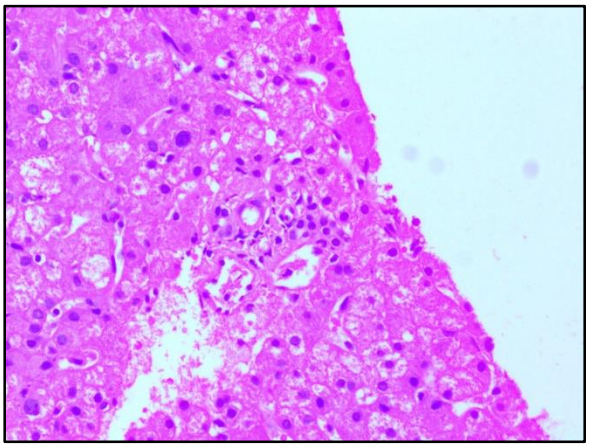


Figure: Liver biopsy with a normal portal tract containing bile duct, hepatic arterioles and portal vein branch. H&E stain 200x.

## THE VESSELS:

The liver has dual supply from the portal vein and hepatic artery. Approximately 2/3$^{rd}$ of blood supply to the liver is by the portal vein and the remaining 1/3$^{rd}$ by the hepatic artery. The venous drainage is primarily by the right, middle and left hepatic veins which drain into the inferior vena cava. The pressure difference between IVC and hepatic wedged pressure is approximately 4-8 mm Hg (40,46).

## VARIATIONS OF VASCULAR ANATOMY:

The common hepatic artery which is branch of the coeliac trunk continues as the main hepatic artery after giving off the gastroduodenal artery. The main hepatic artery divides into the right and left hepatic arteries. Variations of the hepatic arterial supply are classified according to the Michel's and Hiatt's classification.(40,49) The three major hepatic veins drain into the IVC in upto 70% of the cases. In approximately 30% of the cases accessory hepatic veins may be present

- 19% have 2 left hepatic veins
- 8% have 2 right hepatic veins
- 2% have 2 middle hepatic veins

Sometimes IVC can be absent in certain conditions associated with complete sinus inversus, in which cases the hepatic veins drain into the one of the cardia atria via the azygous vein (40,50).

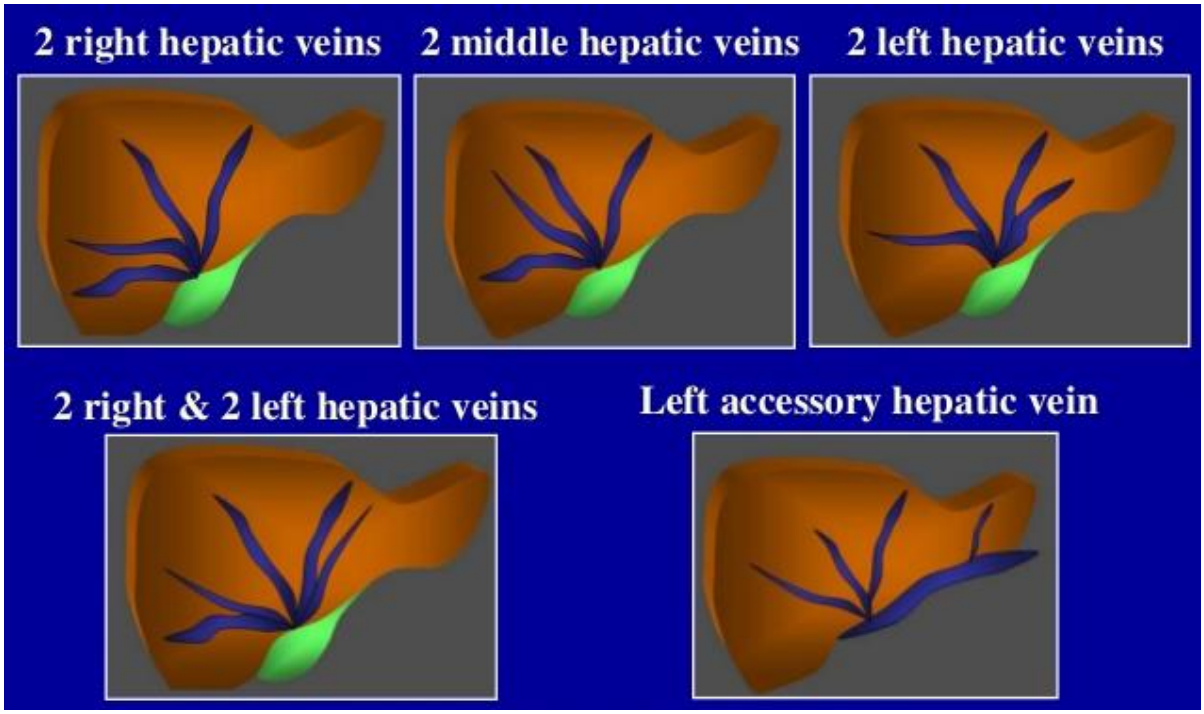



Figure: HEPATIC VEIN VARIANTS

## DEVELOPMENT

The liver primordium appears as a diverticulum from the distal foregut and is lined by endoderm. The diverticulum consists of hepatic cells that proliferate and penetrate the septum transversum which is the mesodermal plate between the vitelline duct and pericardial cavity. The mesodermal plate forms the Kupffer cells, haematopoietic cells and connective tissue. The epithelial further invade the umbilical and vitelline veins and break them into sinusoids which form the venous capillaries. The original hepatic diverticulum narrows and forms the common bile duct from which the cystic duct and gall bladder arise. The liver cords line the bile ducts after differentiating into parenchyma (46,51).

# A GLIMPSE AT VARIOUS LANDMARK STUDIES

A. In a systematic review done by George Kalambokis et al. the complication rates in 7469 patients who underwent TJLB was 7.1%. Complications related to liver puncture was 3.5 % and unrelated to liver puncture was 3.3%. The complications were classified into major and minor according to Society of Interventional Radiology criteria (SIR). Minor complications were seen in 6.5% of patients which were neck pain, haematoma, bleeding, pneumothorax, carotid puncture etc. In adult population complications were seen in 6.7% of patients of which 0.5% were major complications and mortality was 0.09%. The cause of death was either due to ventricular arrhythmia or due to intraperitoneal haemorrhage. In paediatric population the total complication rate was higher as compared to adult population (minor - 20%, major - 1.9%, mortality – 0.6%). The review also showed that the complication rates were lower with the use of Tru-cut and thin biopsy needles.

The fragmentation rate was 34.3%, median length of the biopsy sample was 12 mm (range 3.3-28, mean 12.8 ) and median complete portal triad number was 6.5 (range 2.7 – 11, mean - 6.8 ). Specimens were technically adequate for histological diagnosis in 96.1%. Type of needle used also played a significant role in achieving histopathological diagnosis. Tru-cut needle (98%) had a higher percentage of success as compared to Menghini needle (77%). Fragmentation rate was higher with Menghini needle. The size of the biopsy sample was significantly longer with Tru-cut needle as compared to Menghini needle with comparable number of passes. The

complication rates were also significantly higher with the use of Menghini needle which may be related to difficulty in controlling the depth of puncture.

Fragmentation rate had no significant correlation with adequacy of specimen for histopathological diagnosis. Histopathological diagnosis had significant association with mean length and complete portal tract number. However in cirrhotic liver disease the mean length had a greater role in achieving the diagnosis as compared to number of complete portal tracts (11).

B. In a retrospective study done by Mammen et al. complication rate in 601 patients who underwent TJLB was 2.49%. Mortality occurred in 1 patient. Most of the complications occurred within 24 hours of the procedure. The procedure was considered as successful when they were able to get a tissue sample. Technical success rate was 98.8 %. Histopathological adequacy was achieved when sample was sufficient enough to make a histopathological evaluation (complete portal tracts more than 6) which was ~ 97%. Major complications encountered were hemoperitoneum and haemobilia which were managed by supplementing blood products, performing diagnostic hepatic angiography followed by embolization using coils if the source was identified. One patient had cutaneous pseudoaneurysm which was managed by manual compression followed by thrombin injection and surgical repair. Few patients had fever in whom the blood cultures were negative and were managed conservatively using antipyretics.

In paediatric population which comprised 48 patients, the technical success rate was 98%. One patient had technical failure due to shrunken liver and acute

angulation between hepatic vein & IVC confluence. Histopathological inadequacy was seen in 10.4% (5 patients). Fever was the only complication in paediatric population and was seen in 3 patients. The fever was however transient and settled with antipyretics within 24 hours (15).

C. Behrens et al. in his review article 'Transjugular Liver biopsy' has stated that the technical success rate ranges between 87 to 97%. The most common reason for technical failure is difficulty in cannulating the hepatic vein. The other reason is lack of access to jugular vein, however access through alternate venous routes helps us to overcome this problem. The biopsy sample of 15 mm, containing 6-10 portal tracts was sufficient in most cases to achieve histopathological diagnosis of diffuse liver disease. Sample fragmentation rate was seen in 14 to 25% of patients which can interfere in making histopathological evaluation for reaching diagnosis. Complication rates ranged between 1.3-6.5%. Most of the complications encountered are minor complications like neck pain, abdominal pain, bleeding at puncture site, subscapular haematoma. Major complications are observed in 0.6% of patients. Mortality is seen in less than 0.1% of adults and ~ 0.1% of paediatric population and is related to ventricular arrhythmia during access to hepatic veins, perforation of the hepatic artery and haemorrhage from extracapsular liver puncture. Other complications documented are haemobilia, pseudoaneurysm etc (6).

D. In a retrospective study done by Halil Donmez et al. complication rates in 97 patients who underwent TJLB was 1%( 1 patient), which was neck haematoma at puncture

site. Technical success rate was 95.8% (93 patients). Two patients in whom the biopsy was not successful had Budd Chiari syndrome. Histopathological evaluation could be done in 98.9% (92 of 93) patients (20).

E. In a retrospective study done by Patel et al. 154 consecutive patients were reviewed between March 2003 and November 2011. Complications related to the procedure were seen in 8 out of 154 patients (5.2%) of which all but one were self-limiting requiring no further intervention. One patient had a procedure related mortality which was due to hepatic capsular perforation with subsequent uncontrollable intraperitoneal haemorrhage. This patient had systemic lupus erythematosus with deranged liver function and coagulation profile.

   Technical success was defined as ability to perform the procedure and obtain the liver tissue. The technical success rate was 98.7% (152 out of 154 procedures) and adequate material for diagnosis was obtained in 149 out of 152 (98.0%) technically successful procedures. The technical failure was due to shrunken liver. Indications for biopsy were coagulopathy (82.4%), ascites and post liver transplantation. Specimens were adequate for histopathological evaluation in 149 patients (98%). The mean range of specimen length ranged between 5.7 and 10.6 mm. Average number of complete portal tracts was determined was 6.9 (41).

F. In a prospective study done by Pathak et al. 67 transjugular liver biopsies were performed between January 2004 and February 2012. Technical success was achieved in 64 patients (96%). In 3 patients the TJLB could not be performed. In one

case due to inability to negotiate acutely angled hepatic vein, narrowed suprahepatic IVC and small hepatic vein ostium. In 2 patients (3%) the tissue obtained was judged insufficient for complete histopathological evaluation. Multiple passes were made in 4 patients (6%) in order to obtain adequate tissue sample. No major complications were seen in this group. In 3 patients (5%) minor complications were encountered; pneumothorax in one and fever in two patients. Pneumothorax was due to accidental puncture of the pleura and was managed conservatively (52).

G. In a retrospective study done by George Behrens et al. 233 consecutive patients who underwent TJLB were reviewed. Two automated TJLB sets were used, 18 G Quick core (Cook) and 18 G Flexcore (Dextera surgical needle). A total of 194 samples were available for review; 117 were performed with Cook's needle and 77 with Dextera's needle. Technical success rate was 99.6% (232 of 233 cases). Technical failure rate was due to anatomic variation where angulation of the hepatic vein was very acute. Sample fragmentation rate was 24.9% with Cook's needle and 14.3% with Dextera's. Mean complete portal tract triad was 10 +/- 4.6 using Cook's needle and 12.2 +/- 6.1 using Dextera's and mean length of the sample was 2.8cm+/- 1 with Cook's needle and 2.9 cm +/-0.9 using Dextera's needle. The diagnostic rates for submitted liver tissue were 98.7% using Dextera's needle and 94.9% using Cook's needle(14).

The complications were viewed from medical records and were classified into major and minor according to SIR guidelines. Major complications were seen in 7

patients (2.6%) using LABS-100/Quick-core set and in 6 patients (7.8%) using TLAB/Flexcore system. Patients who are having multiple co-morbidities had higher complications. LABS-100/ Quick core group had 2 deaths and TLAB/Flexcore group had single death. These deaths were seen in patients who had severe hepatic failure and were not attributed to the procedure (14).

H. In a retrospective study done by Rathod K et al. 145 patients who underwent TJLB from May 2007 to November 2007 were reviewed. Technical success rate was 98.62 %. Two procedures were unsuccessful due to failure to cannulate the hepatic veins. Out of 143 biopsies, 4 (2.8%) were inadequate for histopathological analysis, therefore the technical adequacy was 97.2%. Minor complications occurred in 2 patients (1.4%)(17).

I. In a retrospective done by A. Dohan et al. 341 consecutive patients who underwent TJLB were retrospectively analysed. Technical success rate was 97.07%. The technical failure was seen in 10 patients (2.93%).In nine patients failure was due to acute angulation between the right hepatic vein and IVC. They also had atrophy of the liver and severe ascites. In one patient the histopathological analysis showed that the sample was of renal tissue. 2 patients (0.59%) had major complications in the form of intraperitoneal bleed and had severe abdominal pain during the procedure with drop in blood pressure and tachycardia. In one patient the bleeding was self-limiting and the other patient had ongoing bleeding which was demonstrated on venogram and required 2 units of blood transfusions. Total minor complication rate

was 20.5% (70 out of 341 patients). The minor complications encountered were abdominal pain (35 patients, 10.26%), intrahepatic haematoma (12 patients, 3.52%), AV fistula (1 patient, 0.29%) supraventricular arrhythmia (15 patients, 4.4%), limited cervical haematoma (5 patients, 1.47%), hypotension (2 patients, 0.59%)(5).

J. In a study done by Antonio Carlos Maciel et al. to compare the rate of histological diagnosis obtained by trasjugular liver biopsy with an automated Trucut needle and with a modified Ross needle 85 patients were studied. Technical success rate was 91% with Trucut needle and 70% with modified Ross needle. The overall complications occurred in 19% with the use of Trucut needle and 22% with the use of Modified Ross Needle (53).

K. In a study done by Bruzzi et al to assess the safety and efficacy of the quick core biopsy needle 50 consecutive patients who were subjected to Transjugular liver biopsy were evaluated. TJLB was successful in 49 out of 50 patients. Technical adequacy was achieved in 100% of patients. Mean no of portal tracts was 10.4. There were no procedure related complications (54).

# MATERIALS AND METHODS

## STUDY DESIGN:

This is a hospital based prospective, observational study approved by the Institutional Research Board (IRB). IRB study number 22Y598

## SETTING:

Christian Medical College, Vellore is tertiary care hospital and also an educational and research institute located in north Tamil Nadu. This institute was established in the year 1900 and is now a 2700 bedded multispecialty hospital. The annual outpatients and inpatients handled is around 2.4 million and 1,40,000 respectively. The department of radiology was established in 1936. Digitalisation of the system by introduction of Picture Archival and Communication System (PACS) was done in the year 2000. The Department of Radiology has around 75 radiologists and about 120 radiographers.

The radiological investigations done on routine basis are radiographs, Barium studies, Intravenous Urogram, Ultrasound, Mammography, Computerised Tomography, Magnetic Resonance Imaging and a variety of interventional procedures.

# TRANSJUGULAR LIVER BIOPSY

Transjugular liver biopsy was first described by Dotter in 1964. This procedure involves gaining access to the hepatic veins by endovascular approach. Complications such as haemorrhage and post-procedural pain are less using this technique. In case of accidental bleeding, the blood is drained via hepatic veins into the circulation. Studies have shown that the samples obtained by Transjugular liver biopsy using newer techniques like Tru-Cut (Cook, Quick core biopsy, Bloomington needles) are comparable to that obtained by percutaneous technique .

## INDICATIONS (4,6,11,13,16)

1. Ascites
2. Coagulopathy/ deranged bleeding parameters to the extent that percutaneous liver biopsy is contraindicated
3. Small shrunken liver - There is increased space between the skin surface and the liver surface, hence increased risk of complications while performing percutaneous liver biopsy
4. Gross obesity
5. Peliosis hepatis – It is an uncommon condition where multiple vascular spaces are in the liver (11,11)
6. Renal dysfunction - Uremia causes functional impairment of the platelets as a result of which there is higher tendency for bleeding

7. Acute liver failure, liver transplantation etc. where haemostatic abnormality is usually present (42,43)

## CONTRAINDICATIONS (16)

Thrombosis of the right internal jugular vein in which cases access can be gained by alternate approaches like right external jugular vein, left internal jugular vein or the femoral vein. These approaches have greater risk as compared to access through the right internal jugular vein and should be performed by an experienced interventional radiologist.

* In case of gross ascites the ascitic fluid can be drained prior to the procedure
* Thrombosis of hepatic veins or Budd Chiari syndrome
* Hydatid cyst
* Cholangitis
* Uncooperative patients

# METHODOLOGY:

## SAMPLE SIZE:

The range of complications has been reported to be 1-15 % for minor and 1-3 % for major (4). Therefore the range of complications has been assumed to be around 10 %. As the range is very wide, precision is taken as 5 %

The sample size was calculated using the formula– 4 p q / d^2

- (4 x 10 x 90) / (5 x 5)
- 144 patients

* p = prevalence in percentage, q = (100-p)

## INCLUSION CRITERIA:

All patients who will be undergoing transjugular liver biopsy in the Department of Radiodiagnosis, CMC Vellore during the study period.

## EXCLUSION CRITERIA:

Patients who do not want to be a part of this study

## SAMPLING AND CONSENT:

All patients who are undergoing TJLB in the department of radiology and who fulfilled the inclusion criteria were included in the study.

An informed consent was taken from the patient prior to the procedure as per Institutional Review Board guidelines. These patients were followed up post biopsy for any complications. These patients were assessed during and after the procedure by clinical, lab parameters and imaging techniques to determine the exact complication rates. 5 ml of blood sample was taken from the patient, usually 6 hours after the procedure to determine the haemoglobin level. Patients were also subjected to clinical and USG assessment to look for any complications after the procedure. Consent was also obtained to view the medical records if needed (see appendix 2 and 3).

TIMING:

The study period was from May 2015 to July 2016. The liver biopsy was performed by skilled interventional radiologist in the department of radiology. The procedural complications were assessed by the interventional radiologist and were documented if there were any. Assessment of the patient after the procedure was done by the principal investigator within 24 hours of TJLB as studies have demonstrated that majority of the complications occurred within 24 hours. The concerned treating physician was informed about the complications if there were any so that adequate measures were taken.

VARIABLES:

The various variables studied were:

- Patient's age,
- Gender,

- Indication for the procedure: common indications are listed below
    - Deranged bleeding parameters
    - Low platelets
    - Renal failure
    - Ascites
    - Shrunken liver

- Pre procedural variables:
    - Blood pressure, Haemoglobin, Platelets, Bleeding parameters – PT/INR, aPTT, Creatinine, Transfusions of blood/ blood products.

- Intra and Post procedural variables:
    - Arrhythmias, Blood pressure, Haemoglobin, complications like neck pain, neck haematoma, puncture site infection, carotid puncture, abdominal pain, intra-abdominal haemorrhage, hepatic subcapsular haematoma, hepatic parenchymal haemorrhage, fever, pneumothorax and vomiting
- Biopsy – complete portal tracts, size of biopsy sample.
- If TJLB was contributory to the diagnosis

Some of the variables are described as below

1. Blood pressure

a. Hypotension – less than 90/ 60 mm Hg of BP
b. Hypertension – more than 140/90 mm HP or significant increase above the baseline.

2. Drop in Haemoglobin
    a. Less than 0.5 gm/dL – less significant
    b. 0.5- 1 gm/dL – moderately significant
    c. More than 1gm/dL – highly significant

* For practical purposes drop in haemoglobin < 0.5 gm/dL were excluded as many patients had minor variations in haemoglobin levels post procedure which may be attributed to hydration status, prior blood transfusions, sampling or technical errors.

3. Intra-abdominal hemorrhage
    a. Low suspicion – drop in Hb 0.5 - 1 gm/dL with free fluid in abdomen
    b. High suspicion –
        i. drop in Hb 0.5 - 1 gm/dL + free fluid with internal echoes or free fluid with no previous documented ascites.
        ii. drop in Hb > 1 gm/dL + free fluid in the abdomen

4. Neck Pain and Abdominal pain

    Graded according to visual analog scale (55).

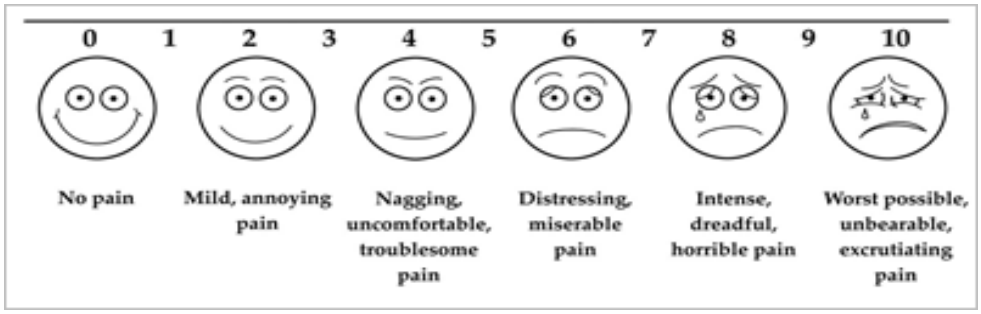



Figure: Visual analog scale for pain

a. No pain - 0 – 4 mm,
b. Mild pain - 5– 44 mm,
c. Moderate pain - 45–74 mm,
d. Severe pain - 75–100 mm

* For practical purposes patients having mild pain are excluded as mild neck pain was seen as part of the procedure in many patients and warranted no additional measures or interventions.

5. Temperature
    a. < 100 deg F – mild
    b. 100 – 102 deg F – moderate
    c. > 102 deg F - severe

* For practical purposes patients having temperature < 100 deg F are excluded as mild rise in temperature may be related to procedure or interventions during the procedure and the patients needed no additional measures or interventions.

* Patients with fever were generally not subjected to TJLB.

The procedural complication were categorised into major and minor based on Society of Interventional Radiology criteria.

Complication risk is based on Society of Interventional Radiology (SIR).
* SIR classification system for complications according to outcome is classified as follows (1)

- Minor complications
  a) No therapy , no consequences
  b) Nominal therapy, no consequences includes overnight admission for observation
- Major complications
  c) Require therapy minor hospitalization (< 48 hr)
  d) Require major therapy, unexplained increase in the level of care, prolonged hospitalization (>48 hr)
  e) Permanent adverse sequelae
  f) Death

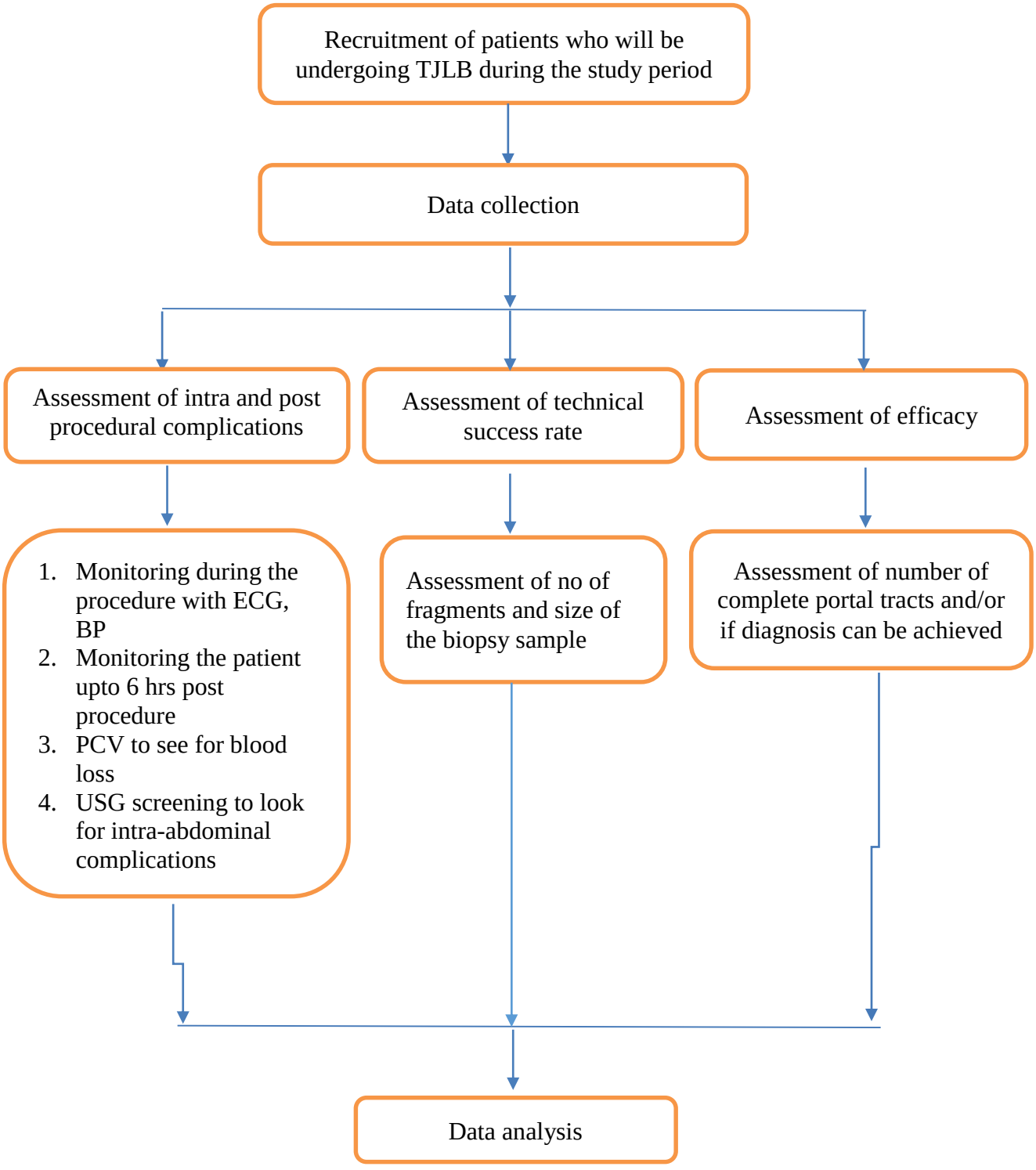
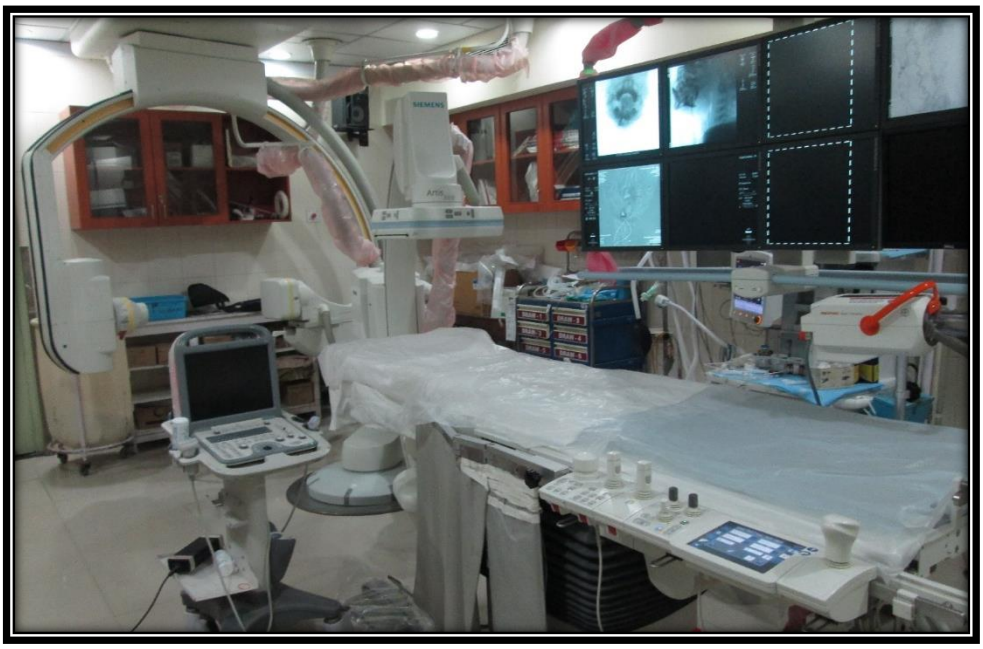



Figure 7: Diagrammatic Algorithm of the operating procedure

TECHNIQUE

## 1. SETUP AND MATERIALS

a. Angiography suite with ultrasound machine



b. TJLB set (LABS 100, Cook), 9F Short sheath, Catheters (Multipurpose, cobra, head hunter), and guide wires (0.035 inch guide wire and stiff guide wire)

Figure: TJLB SET

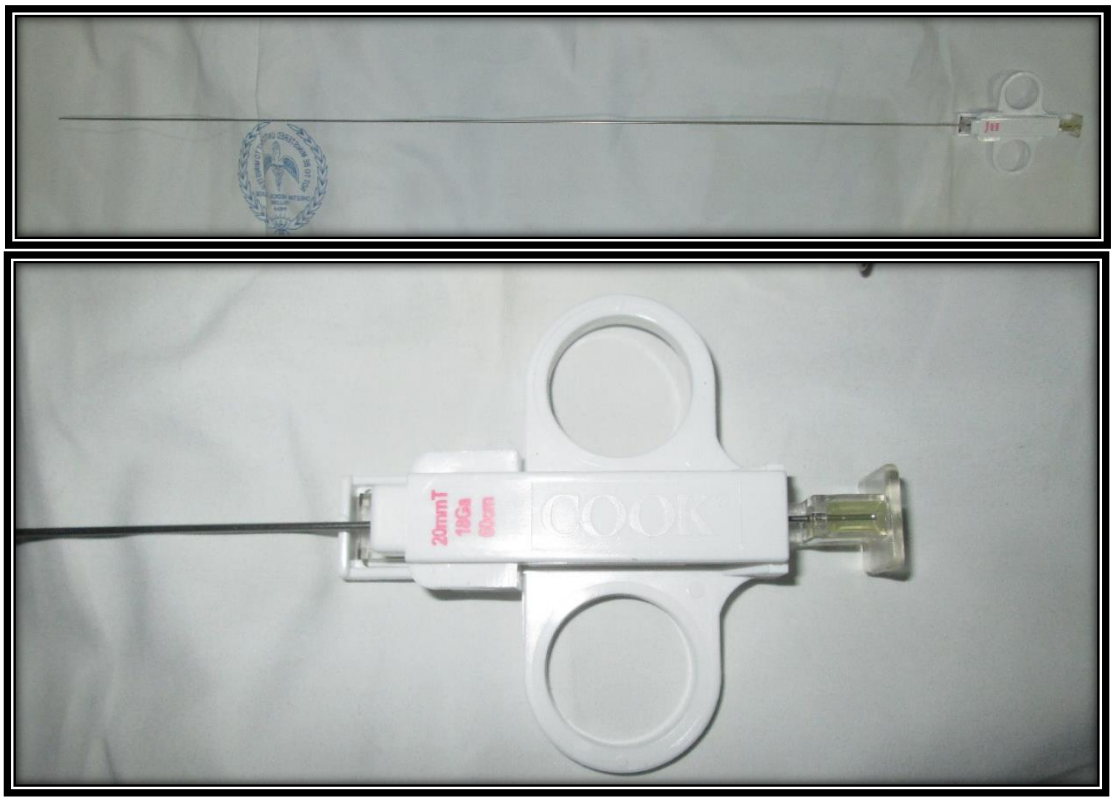



Figure: TJLB BIOPSY NEEDLE

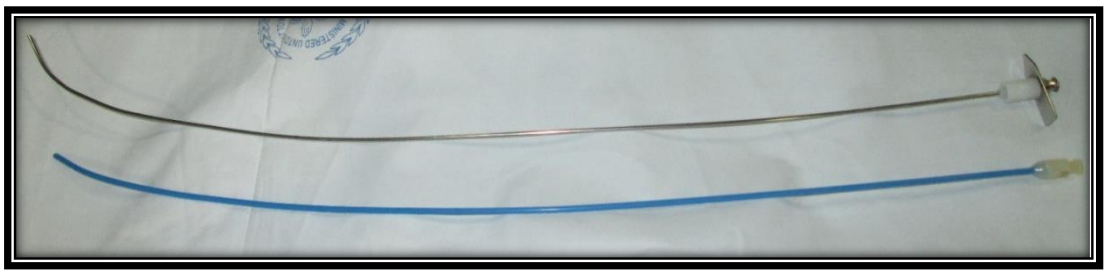


Figure: TJLB CANNULA

## 2. PATIENT PREPARATION

### PRIOR TO THE PROCEDURE

The patient is admitted in the hospital prior to the procedure. Blood investigations such as haemoglobin, platelet count, PT/ INR, aPTT, serum creatinine and blood borne virology screening are done. Any derangement in platelets or bleeding parameters are corrected prior to the procedure. Ultrasonography of the abdomen is done to assess the liver morphology and also to look at any focal lesions if any. Doppler study is done to assess hepato-portal system. The patient is generally sedated before the procedure. If the patient is a child then general anaesthesia may be required. Patient is required to fast 4-6 hrs prior to procedure to reduce the risk of aspiration.

Acceptable laboratory values at our institution beyond which blood products are given:

- INR < 1. 7 times the control
- Platelet count > 35,000
- aPTT( ½ Patient + ½ control) > 42.5 secs

## 3. PROCEDURE:

### IN THE DSA ROOM

Patients are made to lie comfortably in a supine position with head turned towards the left side. ECG leads, BP cuff and pulse oximeter are attached to the patient to monitor the vitals. The operators work from the head end of the table. USG screening of the right internal jugular vein is done to determine the site of puncture and to determine the patency of the lumen. After confirming the patency of internal jugular vein a point 3-5 cm above the clavicle, in between the heads of the sternocleidomastoid is marked for the puncture. Care should be taken not to puncture the carotid artery or the pleura. If necessary the patients head can be turned to the contralateral side. When necessary the patient can be asked to perform valsalva maneuver or foot end elevation to distend internal jugular vein sufficiently.

After cleaning and draping the neck of the patients using sterile techniques, local anaesthesia (2-5 ml of 2% lignocaine) is injected subcutaneously and intradermally. The right IJV is punctured under USG guidance using an insyte or an 18G metallic needle. In children and in patients with deranged bleeding parameters a micropuncture needle (21G) can be used. A syringe, partially filled with saline needs to be connected to the needle for aspirating the blood, to confirm intravenous access and also to prevent air embolism. Aspiration of venous blood confirms jugular venous access. If right IJV is not accessible the left IJV or femoral vein can be accessed. After obtaining venous access a suitable guidewire (0.035 inch for 18 G) is passed through it followed by a 9F sheath.

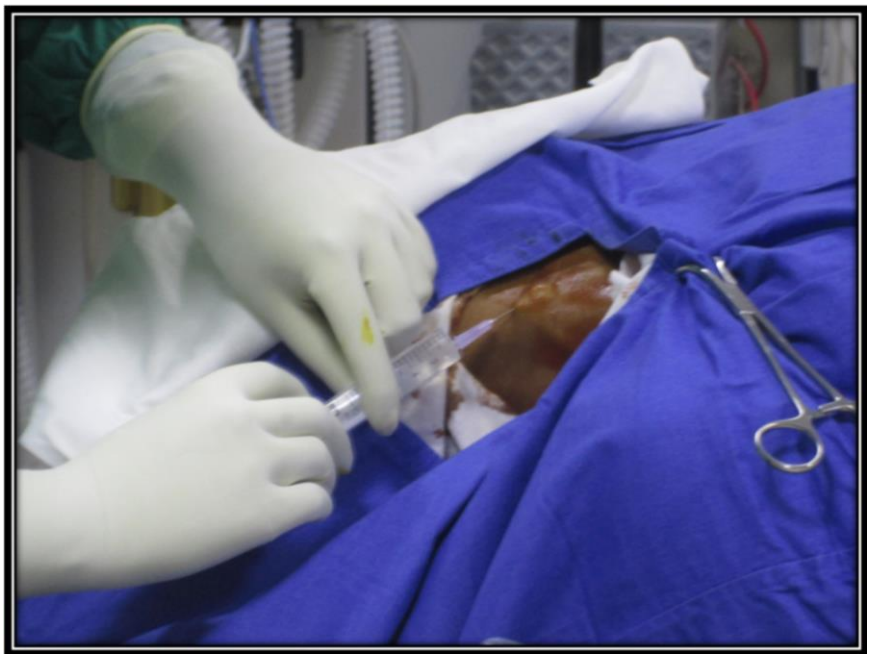


Figure: Site of skin puncture

Figure: Insertion of biopsy needle through the TJLB cannula

RIGHT HEPATIC VEIN ACCESS

A combination of 5Fr multipurpose catheter and guide wire is used to navigate through the SVC, right atrium, IVC into the right hepatic vein. Monitoring for arrhythmias is necessary during transit through the right atrium. Most of these

arrhythmias are transient and subside once the catheter wire reaches the IVC. Sometimes the guide wire or catheter can form a loop in the right atrium. Care should be taken to prevent this from happening.

Following methods can be tried if there is any difficult in bypassing the right atrium

- Different guide wires can be used like J tip, straight tip or a glide wire
- Attempts can be made to pass the guidewire during different phases of respiration i.e. deep inspiration
- Directing the catheter postero-laterally from the right atrium into the IVC
- Changing the angle of the fluoroscopy intensifier may be attempted

The right hepatic vein is located at the level of cavoatrial junction. Accessing the RHV can be difficult at times. Following methods can be attempted if there is any difficulty in accessing the right hepatic vein.

- Attempts can be made to pass during different phases of inspiration i.e. deep inspiration
- Minimal anterior or posterior angulation can be done at cavo-atrial junction
- Different catheters can be used i.e. headhunter, cobra catheter and a 0.035 inch glide wire can be used instead of a regular one
- If there is difficulty in locating the level of hepatic veins, a pig tail catheter is positioned near the cavo-atrial junction and pigtail run is taken. As the contrast is injected, filling of the hepatic veins or washout of contrast from unopacified vein is looked for.

The catheter should be advanced along the main RHV which is oriented along the axis of the ribs. Post cannulation, 5-10 ml of contrast is injected and a hepatic venogram is performed to confirm the position of the catheter.

Special conditions:

- If right hepatic vein cannot be accessed the middle or left hepatic vein can be attempted.
- If there is gross volume redistribution, biopsy can be performed via the left hepatic vein.
- In case of situs inversus the procedure can be performed in an anatomically reverse fashion

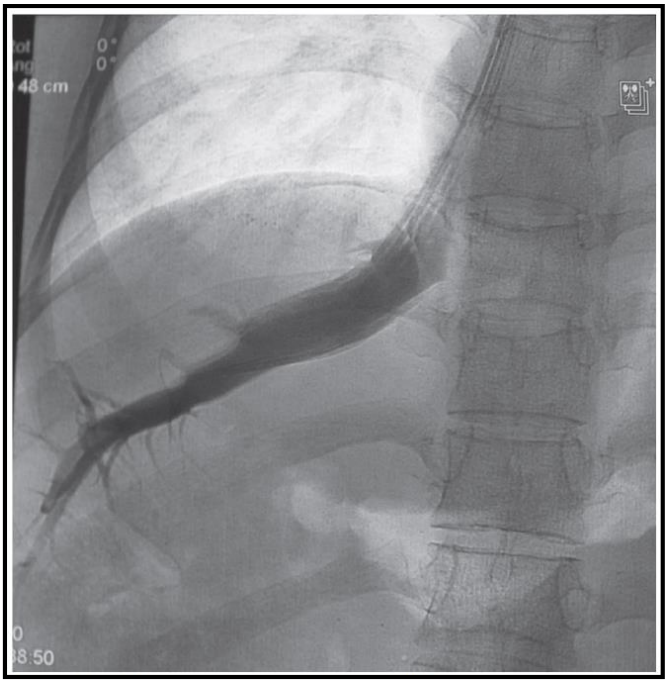



Figure : Right hepatic venogram

The catheter is then exchanged for a TJLB stiffening cannula-7F sheath assembly. The stiffening cannula provides support and guidance for the quick core biopsy needle. There is a directional arrow at the hub, which points towards the gentle curve at the other end of the cannula. The tip of the cannula is then placed in the middle third of the right hepatic vein.

Difficult in passing the cannula is usually encountered at the IVC-RHV junction, in which cases following methods can be tried

- Using stiff guide wire like 0.035 inch Amplatz guide wire instead of 0.035 inch guide wire.
- Using coaxial 5F catheter which can guide the cannula and also by changing the angle of the cannula.
- Attempts can be made to pass the cannula in different phases of respiration i.e. deep respiration.
- Gently maneuvering the cannula antero-posteriorly on the right side at the IVC – RHV confluence can be helpful at times.

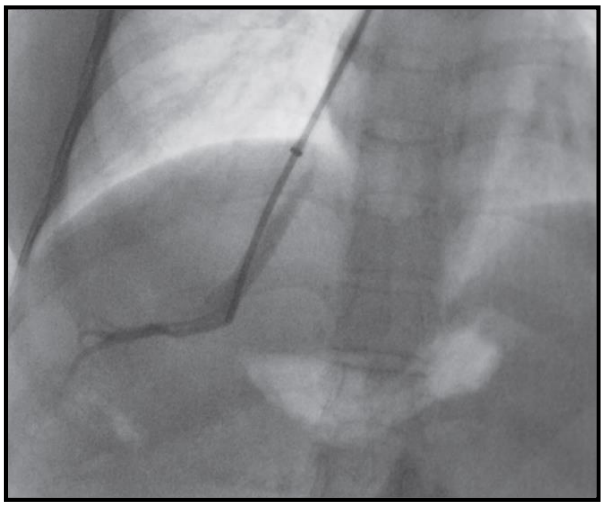


Figure 8: TJLB cannula within the right hepatic vein

Figure: Steps of TJLB

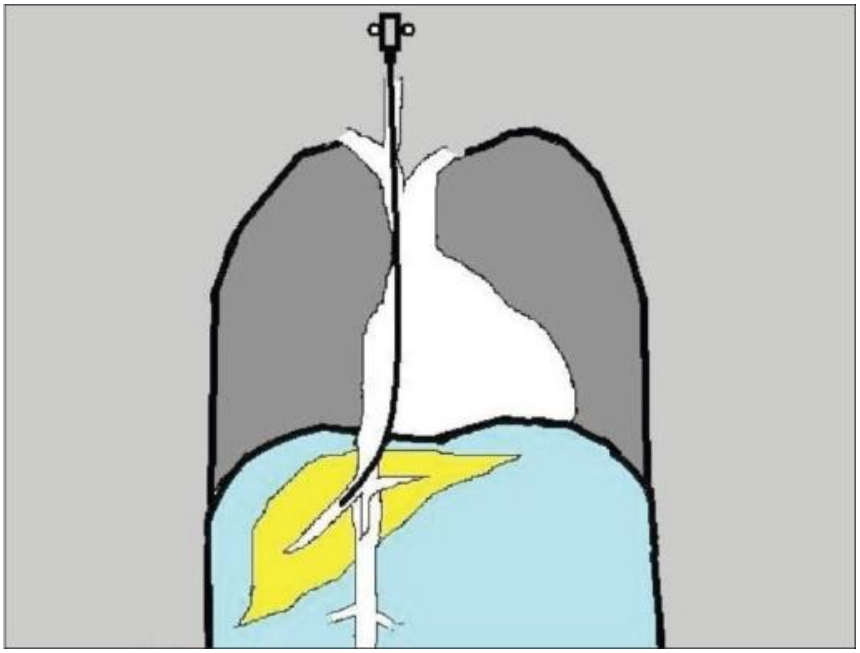


Figure: A line diagram showing orientation of TJLB needle vein

## BIOPSY

The trucut needle is loaded by pulling the plunger till a firm click is heard. The loaded trucut needle is then passed through the stiffening cannula so that the tip of the needle is just visible. The peripheral one third of the vein is better avoided in order to reduce the risk of trans-capsular puncture. If the cannula is in the right hepatic vein it is rotated anteriorly and if it is in the middle hepatic vein it is rotated to the right. This helps in wedging the cannula against the liver parenchyma as well as in directing the needle towards the region where there is more liver tissue. Patient is asked to hold their breath at the time of biopsy to minimize injury to the liver. The needle is withdrawn into the stiffening cannula after the biopsy and is subsequently taken out and the specimen collected. The cannula is kept closed in between biopsies either by check flo valve or by a syringe in order to prevent air embolism and extravasation of blood.

For histopathological analysis three passes are generally sufficient. More samples may be required for estimation of iron /copper and for culture and sensitivity

## POST BIOPSY CARE

- Check venogram to look for extravasation of contrast
- Patient is made to sit or kept in a semi-recumbent position
- Manual compression at the puncture site to achieve haemostasis
- Monitoring pulse and blood pressure, 1 hourly for 6-12 hours.
- Monitoring abdominal girth using a tape

- Post procedure haemoglobin
- Clinical examination to look for pain, abdominal distension, neck swelling, tachypnoea
- USG screening of neck and abdomen to look for local complications

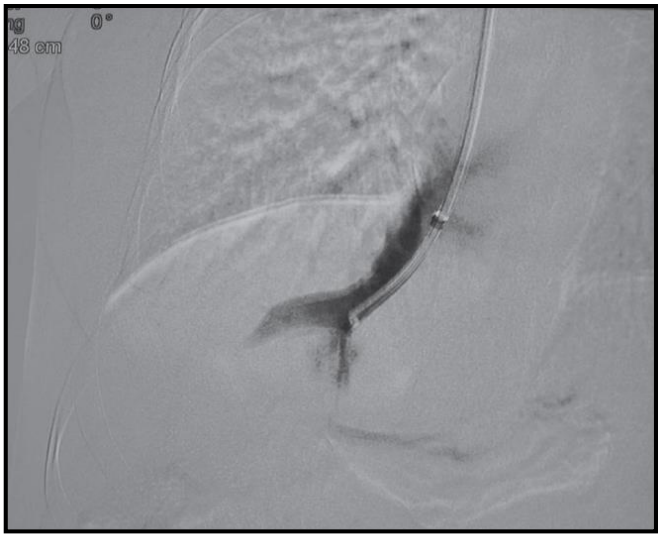



Figure: Post TJLB check venogram

The average fluoroscopy time is 4 minutes. The mean duration of the procedure is 40 minutes and the radiation dose ranges from 0.5 – 1 mSv.

## Special situations:

- In patients with gross volume redistribution biopsy can be attempted from the left lobe of the liver via the left hepatic vein.
- Due to various anatomical factors if none of the hepatic veins can be cannulated, a transcaval biopsy can be attempted. It is mandatory to confirm the intrahepatic position of the cannula by trans-abdominal ultrasonography prior to performing the biopsy.

- In children general anaesthesia becomes necessary as they are not very cooperative.
- In case of situs inversus the procedure can be performed in an anatomically reverse fashion.

## Management of complications:

During routine clinical or radiological examination if any complications are identified the treating physician is alerted so that necessary steps can be taken to manage the complications.

Post procedure bleeding if not detected and managed promptly can be disastrous. Bleeding can be either into peritoneal cavity when it is called haemoperitoneum or into the biliary tree when it is called haemobilia. If the patient develops pain and abdominal distension following the procedure intraperitoneal hemorrhage should be suspected. The site of bleeding can be identified by performing a venogram following which the bleeding can be controlled by embolizing the bleeder.

Endoscopy can be performed if bleeding into the gastrointestinal tract is suspected to differentiate variceal bleeding from haemobilia. Selective hepatic artery angiogram may be done to look for hepatic artery pseudoaneurysm or a biliary fistula in which case embolization can be done. In case when the site of bleeding cannot be identified empirical embolization of the right hepatic vein branches can be performed to control the bleeding (16).

# STATISTICAL ANALYSIS

The data was entered into excel sheet and analysis was done using SPSS version 18 software.

Continuous variables (e.g age) were expressed in terms of mean and standard deviation. Categorical variables were expressed in terms of numbers and percentages. Associations were generated using Chi Square test.

## RESULTS

70 patients who underwent transjugular liver biopsy (TJLB) during the study period between May 2015 and June 2016 were included in the study. The patients were mainly from hepatology, medicine, paediatrics and nephrology departments. The spectrum of cases included Hepatitis B & C, NCIPH, acute hepatic failure, autoimmune hepatitis, Wilsons disease, alcoholic liver disease, patients who needed clearance for renal transplant, patients with pyrexia of unknown origin etc.

### AGE DISTRIBUTION:

A total of 70 patients underwent TJLB. Study population had patients between 11 to 75 years with a mean age of 35.7 years and median age of 37 years.

### GENDER DISTRIBUTION

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | Female | 31 | 44.3 | 44.3 | 44.3 |
| | Male | 39 | 55.7 | 55.7 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

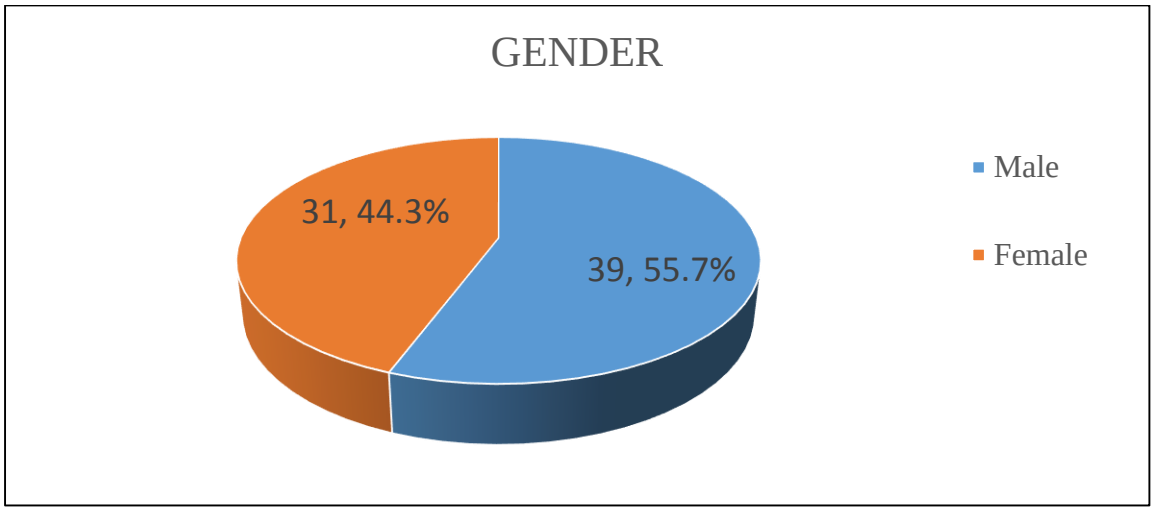



Fig: Pie diagram showing gender distribution among the study population

Of the 70 patients who underwent TJLB, 55.7% were males and 44.3% were females

## IJV ACCESS

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | LEFT | 5 | 7.1 | 7.1 | 7.1 |
| | RIGHT | 65 | 92.9 | 92.9 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

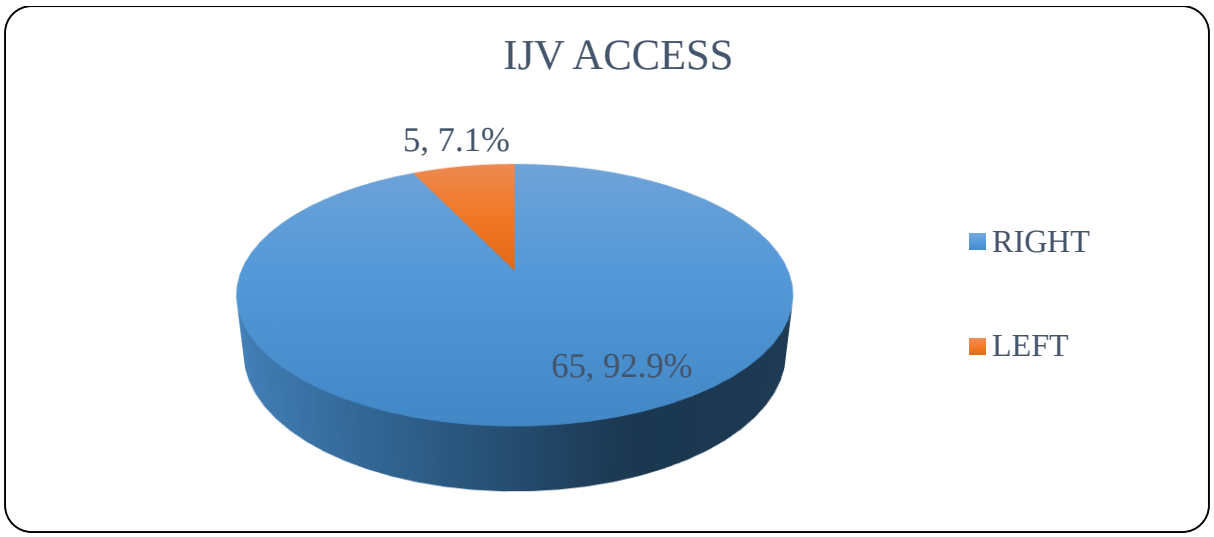



Fig: Pie-diagram showing the side of IJV access

Of the 70 patients who underwent TJLB, 65 patients (92.9%) had right IJV access and 5 (7.1%) patients had left IJV access. Of the 5 patients who had left sided IJV access 2 patient has right IJV thrombosis, 1 patient had right brachiocephalic vein thrombosis, 1 patient had a central line and 1 patient had Hickman's catheter in the right IJV.

## INDICATION

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | Deranged bleeding parameters | 8 | 11.4 | 11.4 | 11.4 |
| | Low platelets | 18 | 25.7 | 25.7 | 37.1 |
| | High creatinine | 14 | 20.0 | 20.0 | 57.1 |
| | Ascites | 8 | 11.4 | 11.4 | 68.6 |
| | More than 2 factors | 22 | 31.4 | 31.4 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

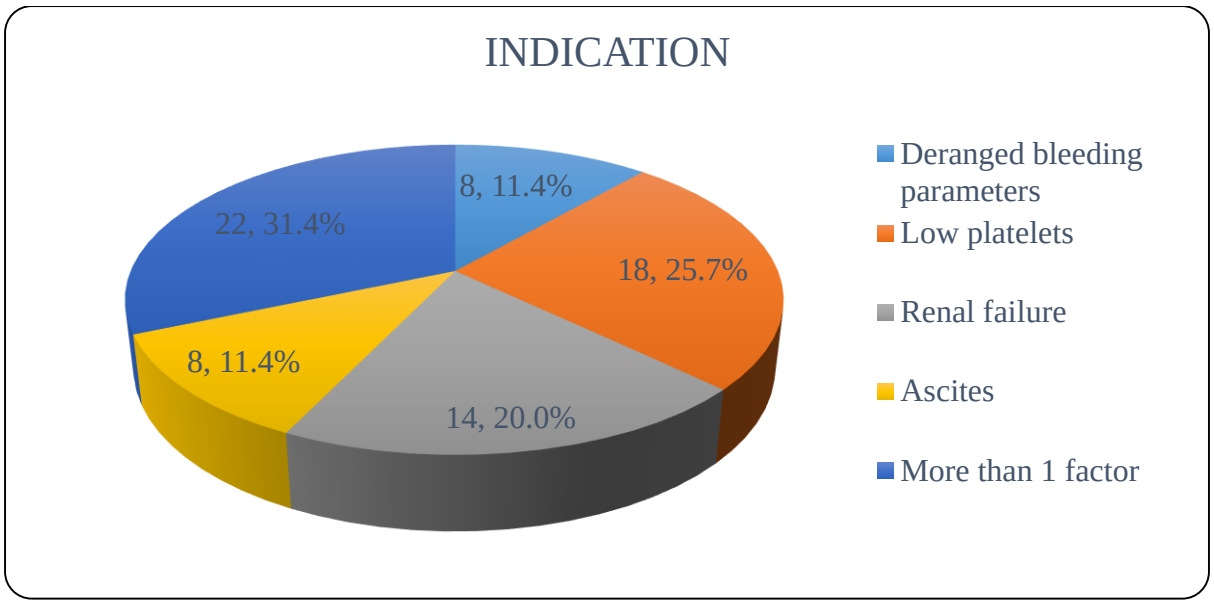



Fig: Pie diagram showing frequency distribution of common indications for TJLB

22 patients had more than one indication of which 17 patients had 2 indications and 5 patients had 3 indications

**TRANSFUSIONS**

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | NO | 42 | 60.0 | 60.0 | 60.0 |
| | YES | 28 | 40.0 | 40.0 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

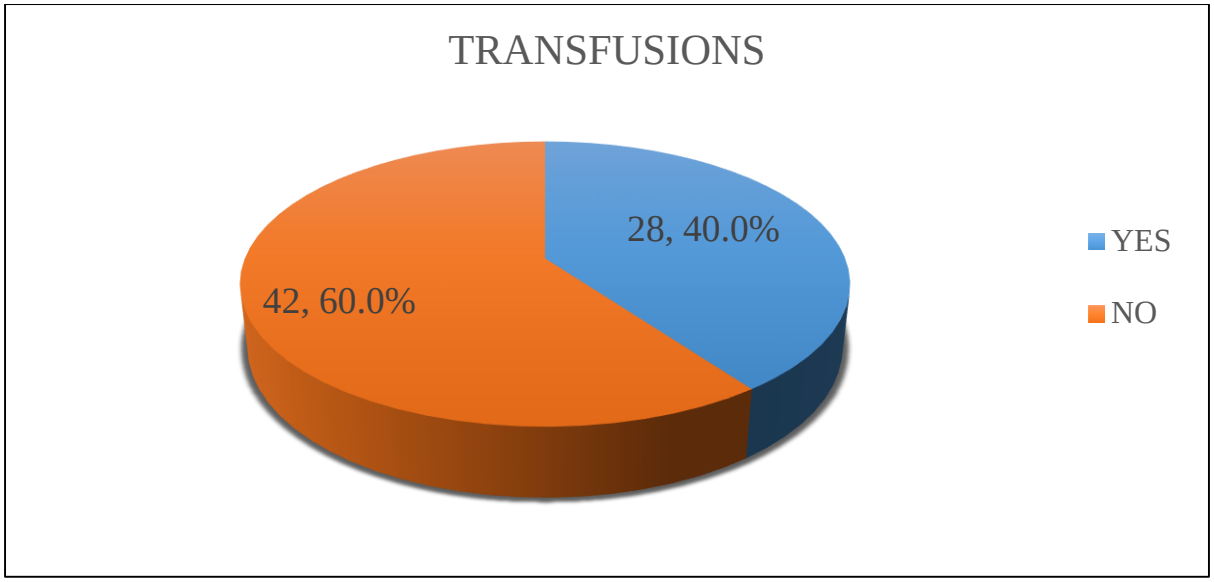



Fig: Pie diagram showing the frequency distribution of the patients who had blood product transfusions prior to the procedure

28 patients out of 70 had transfusions prior to the procedure

## COMPLICATIONS:

### NECK PAIN

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | NO | 56 | 80.0 | 80.0 | 80.0 |
| | MILD | 11 | 15.7 | 15.7 | 95.7 |
| | MODERATE | 3 | 4.3 | 4.3 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

* No patients had neck haematoma post procedure during the study period

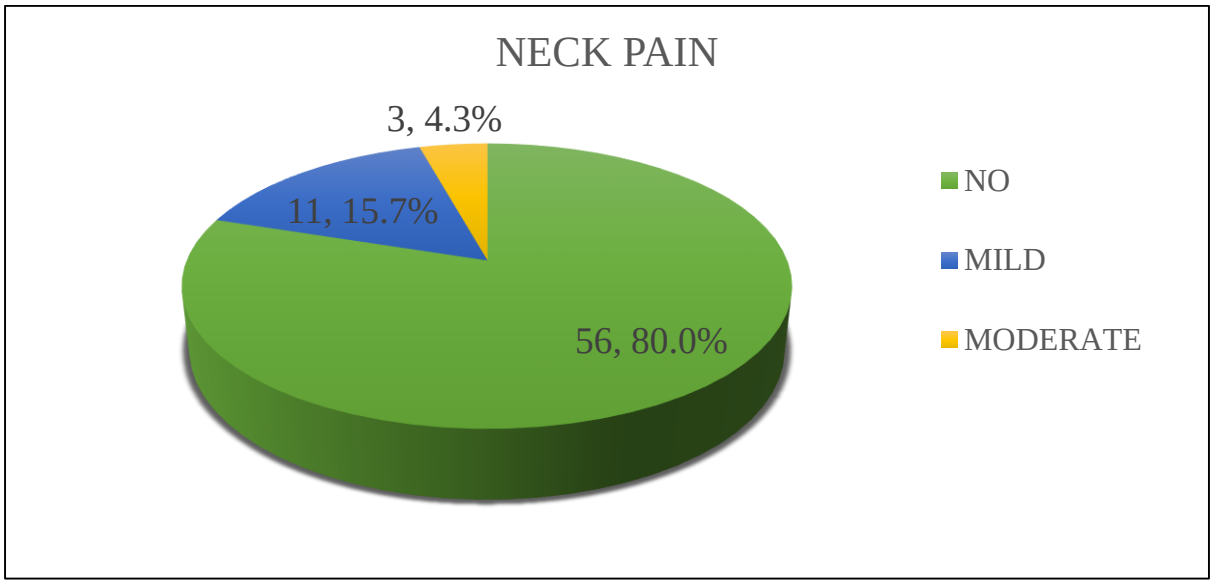
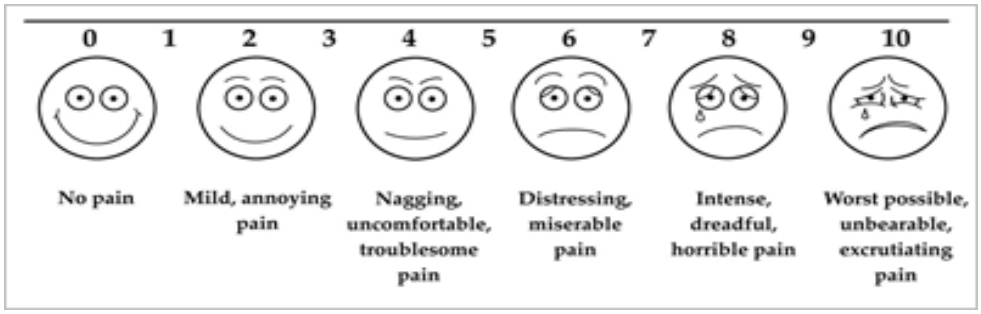



Fig: Pie diagram showing neck pain among population

Visual analog scale for pain was used to qualify the severity of pain. The severity of pain was assessed 6 hours after the procedure as per visual analog scale.




Grading of neck pain:

a. No pain - 0 – 4 mm,
b. Mild pain - 5– 44 mm,
c. Moderate pain - 45–74 mm,
d. Severe pain - 75–100 mm

Of the 70 patients, 11 patients had mild neck pain and 3 patients had moderate neck pain.

* For practical purposes mild neck pain was not considered complication of the procedure as mild neck pain was seen as part of the procedure in many patients and warranted no additional measures or interventions

## ABDOMINAL PAIN

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | No | 68 | 97.1 | 97.1 | 97.1 |
| | Mild | 1 | 1.4 | 1.4 | 98.6 |
| | Moderate | 1 | 1.4 | 1.4 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

The severity of abdominal pain was graded using visual analog scale as described above

1 patient has mild abdominal pain and another patient had moderate abdominal pain post TJLB. Both the patients were managed conservatively.

**TEMPERATURE**

| | | Frequency | Percent | Valid Percent | Cumulative Perc |
|---|---|---|---|---|---|
| Valid | NORMAL | 66 | 94.3 | 94.3 | 94.3 |
| | <100 | 2 | 2.9 | 2.9 | 97.1 |
| | 100-200 | 2 | 2.9 | 2.9 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

* For practical purposes temperature < 100 deg F was not considered as complication as mild rise in temperature may be related to procedure or interventions during the procedure and the patients need no additional measures or interventions

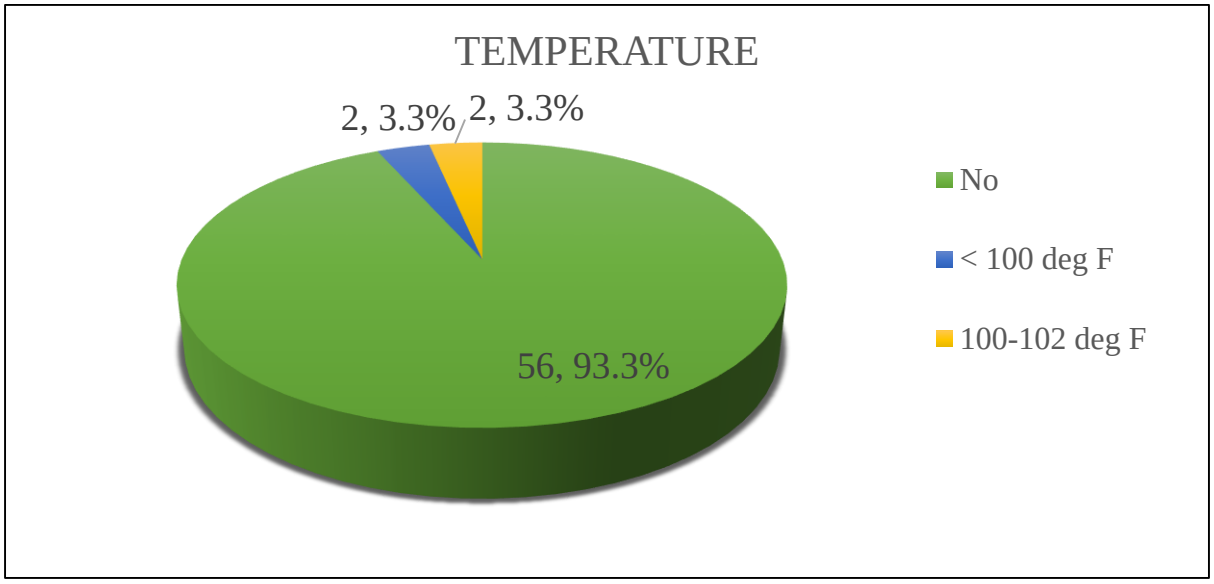



Fig: Pie diagram showing frequency distribution of patients with rise in temperature post TJLB

.

Only 4 patients had rise in temperature post procedure. 2 patients had temperature < 100 deg F and needed no interventions. The other two patients who had temperature ranging between 100-102 deg F were managed using anti-pyretics. Blood cultures were also taken which were negative.

## DROP IN HAEMOGLOBIN (gm/dL)

Drop in haemoglobin was categorized into 3 groups as described below

a. Less than 0.5 gm/dL – less significant
b. 0.5- 1 gm/dL – moderately significant
c. More than 1gm/dL – highly significant

* For practical purposes drop in haemoglobin < 0.5 gm/dL were excluded as most of the patients had fluctuations in haemoglobin levels post procedure which may be attributed to hydration status, prior transfusions or technical errors.

| Drop in Hg (gm/dL) | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | | 28 | 40.0 | 40.0 | 40.0 |
| | 0-0.5 | 15 | 21.4 | 21.4 | 61.4 |
| | 0.5-1 | 12 | 17.1 | 17.1 | 78.6 |
| | >1 | 15 | 21.4 | 21.4 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

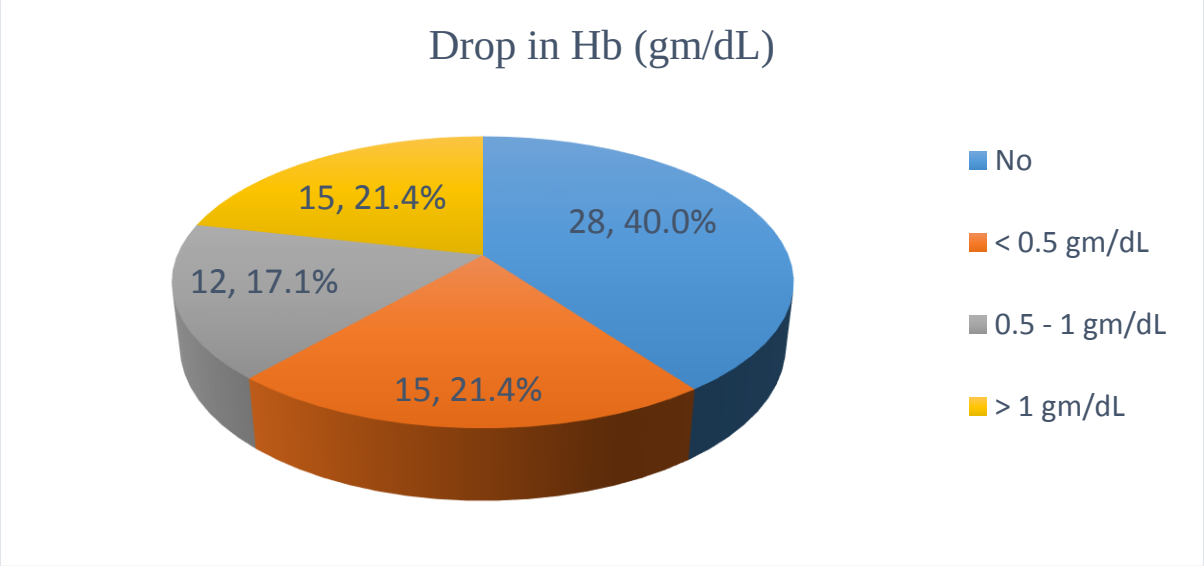



Fig: Pie diagram showing frequency distribution of drop in Haemoglobin levels post procedure

Of the 70 patients 15 had drop in haemoglobin of less than 0.5 gm/dL, 12 had drop in Haemoglobin levels between 0.5-1 gm/dL and 15 had drop in haemoglobin level more than 1 gm/dL.

## INTRA-ABDOMINAL BLEED

The probability of intra-abdominal bleed was categorized based on drop in haemoglobin levels and USG screening post biopsy procedure

a. Low suspicion – drop in Hb 0.5 - 1 gm/dL
b. High suspicion –
    d. drop in Hb 0.5 - 1 gm/dL + free fluid with internal echoes or free fluid with no previous record of ascites.
    e. drop in Hb > 1 gm/dL + free fluid in the abdomen

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | No bleed | 56 | 80.0 | 80.0 | 80.0 |
| | Low suspicion | 5 | 7.1 | 7.1 | 87.1 |
| | High suspicion | 9 | 12.9 | 12.9 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

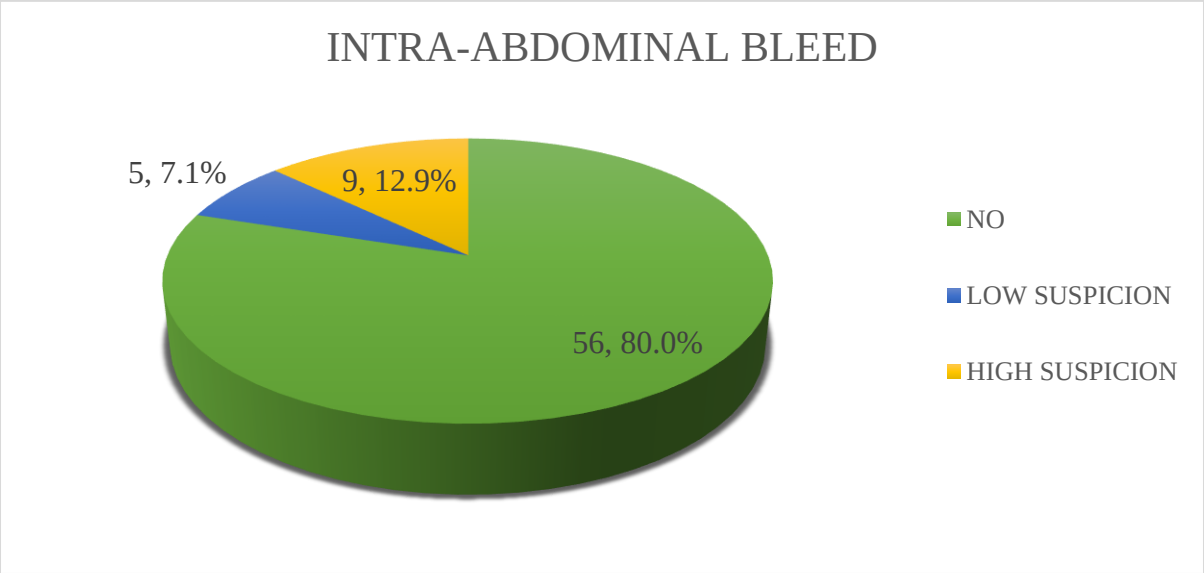



Fig: Pie diagram showing frequency distribution of patients who suspicion of intra-abdominal bleed

.

Of the 70 patients who underwent TJLB, 5 patients (7.1 %) had low suspicion of intra-abdominal bleed and 9 patients (12.9%) had high suspicion of intra-abdominal bleed. No interventions or measures were taken for patients with low suspicion of intra-abdominal bleed. Patients with high suspicion for intra-abdominal bleed were monitored clinically and with serial haemoglobin levels. One patient needed blood transfusion as there was serial drop in haemoglobin levels with mild fluid in the abdomen.

## BLOOD PRESSURE

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | HIGH | 5 | 7.1 | 7.1 | 7.1 |
| | NORMAL | 65 | 92.9 | 92.9 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

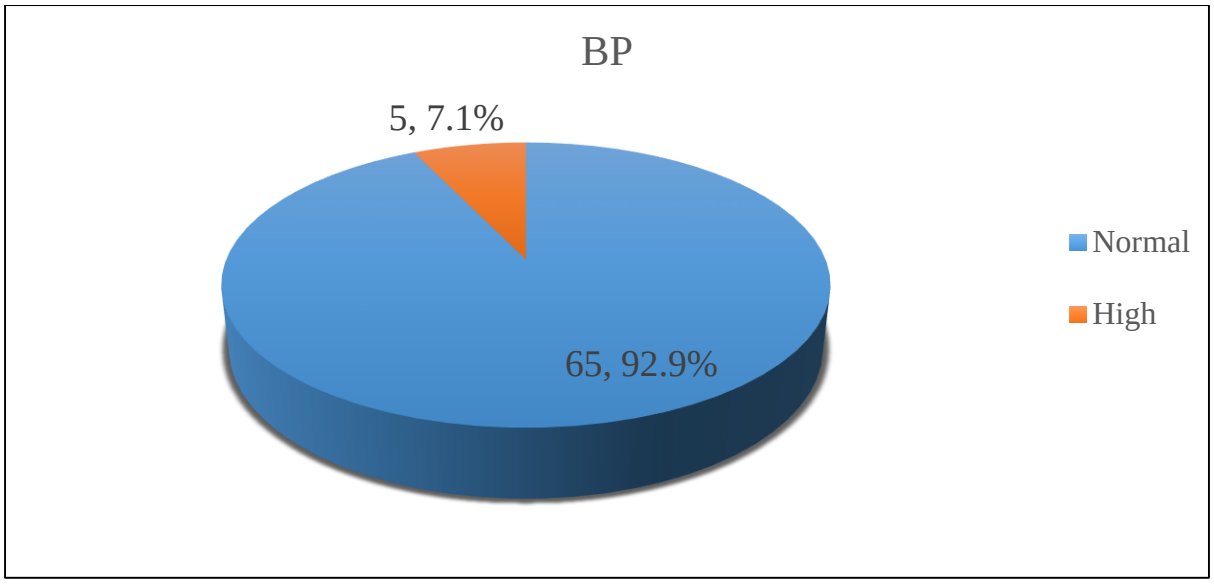



Fig: Pie diagram showing frequency distribution of patients who had hemodynamic instability.

5 out of 70 patients (7.1%) had elevated blood pressure post TJLB

## ARRHYTHMIA

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | NO | 69 | 98.6 | 98.6 | 98.6 |
| | YES | 1 | 1.4 | 1.4 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

1 patient had transient ventricular arrhythmia while coursing through the heart which was self-limiting. The procedure was performed successfully without any further interventions.

## TOTAL COMPLICATION RATES

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | No | 52 | 74.3 | 74.3 | 74.3 |
| | Yes | 18 | 25.7 | 25.7 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

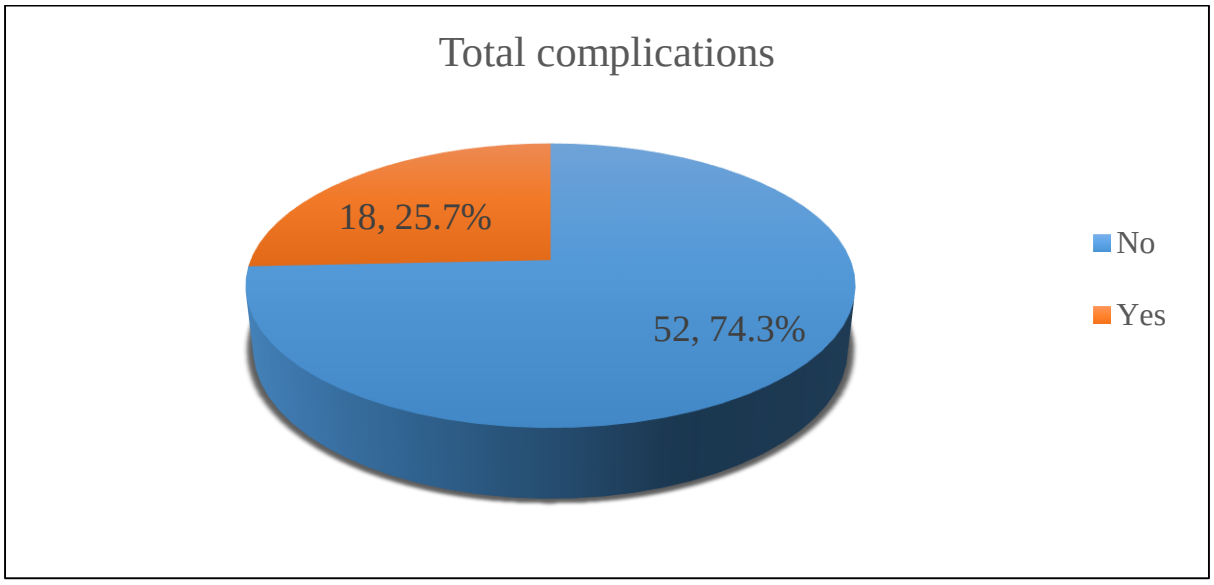



Fig: Pie diagram showing frequency distribution of patients who had complications.

Total complication rates in patients undergoing TJLB was ~ **25.7 %**

**17 patients (24.3%)** had **minor complications** as per SIR criteria.

**1 patient (1.4%)** had **major complication** in the form of serial drop in haemoglobin post TJLB from 9.3 gm/dL to 7.6 and 7.1 gm/dL. There was minimal free fluid in the abdomen. The patient was transfused one unit of packed red cells after which the haemoglobin level reached 8.9 gm/dL and remained stable thereafter. The risk factors postulated in this patient were thrombocytopenia and left IJV access.

## TECHNICAL SUCCESS RATE

* Technical success rate of TJLB is calculated by using the formula

  - (Number of patients in whom TJLB is successful / Total number of patients undergoing TJLB ) x 100

* TJLB is a called technically successful when sample size is more than or equal to10 mm in length

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | No | 11 | 15.7 | 15.7 | 15.7 |
| | Yes | 59 | 84.3 | 84.3 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

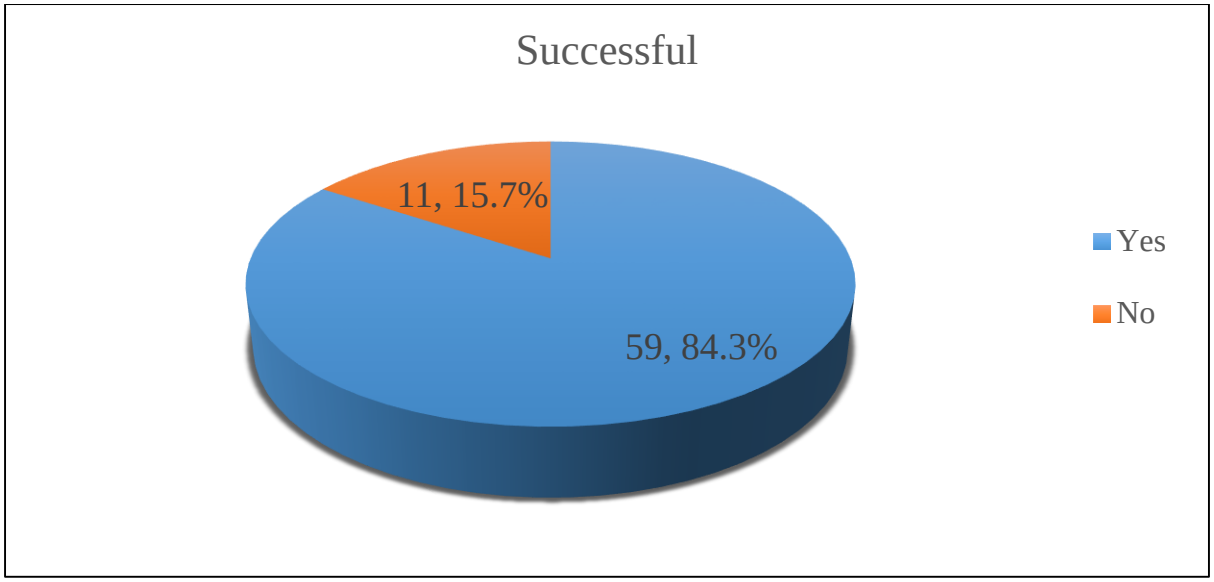



Fig: Pie diagram showing frequency distribution of patients who had technically successful TJLB

59 out of 70 patients (84.3 %) had technically successful TJLB.

**Median sample length was 16 mm.**

**Technical success rate was ~ 84.3%**

* Note: All patients posted for TJLB had successful procedure however the biopsy sample was more than 10 mm in 59 patients (84.3%)

## EFFICACY

* Efficacy of TJLB is calculated using the formula

- (Number of patients with adequate biopsy sample / Total number of patients undergoing TJLB) x 100

* The biopsy sample is called adequate when there are at least 5 complete portal tracts (non – cirrhotic cases) or if histopathological analysis was contributory to diagnosis or management

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|---|
| Valid | No | 9 | 12.9 | 12.9 | 12.9 |
| | Yes | 61 | 87.1 | 87.1 | 100.0 |
| | Total | 70 | 100.0 | 100.0 | |

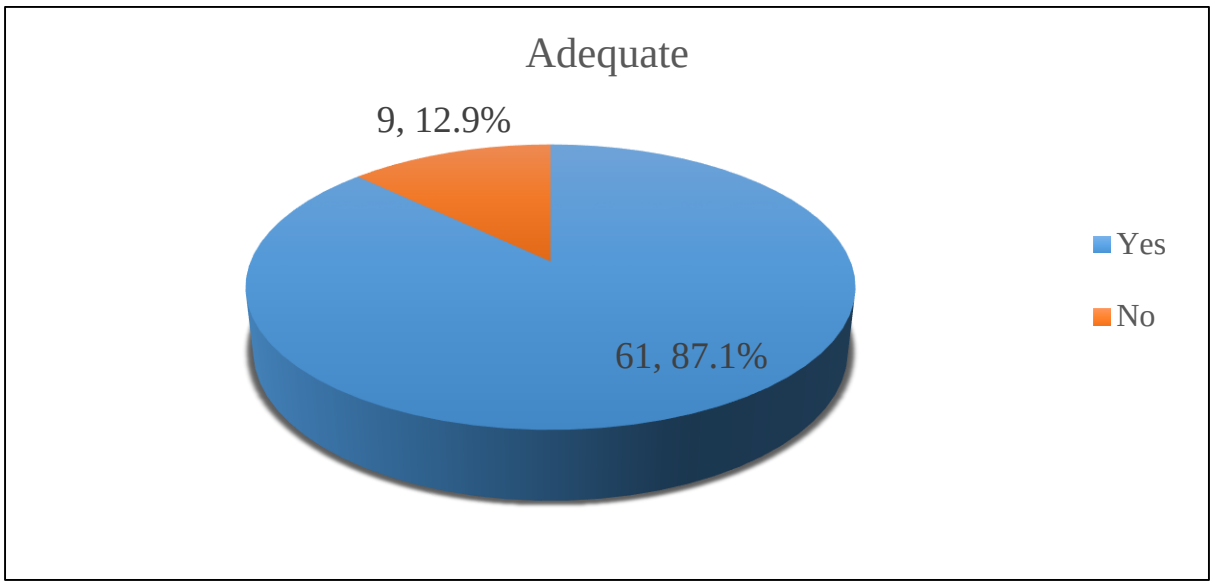



Fig: Pie diagram showing frequency distribution of patients who had adequate biopsy sample

61 out of 70 patients (87.1%) had adequate TJLB.

**Efficacy of TJLB is ~ 87 %**

# ASSOCIATIONS

1. Age category vs complication rates

| | | Complication | | Total |
|---|---|---|---|---|
| | | no | yes | |
| Age category ( in years) | less than 35 | 23 | 8 | 31 |
| | | 74.2% | 25.8% | 100.0% |
| | 36 and more | 29 | 10 | 39 |
| | | 74.4% | 25.6% | 100.0% |
| Total | | 52 | 18 | 70 |
| | | 74.3% | 25.7% | 100.0% |

Chi square – 0 and P value – 0.987

From the table we can conclude that there is no significant statistical association between age category and complication rates.

2. Gender vs complication rates

| | | Complication | | Total |
|---|---|---|---|---|
| | | yes | no | |
| Sex | Female | 3 | 28 | 31 |
| | | 9.7% | 90.3% | 100.0% |
| | Male | 15 | 24 | 39 |
| | | 38.5% | 61.5% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Odds ratio 0.171 (0.044 – 0.664)

Chi square – 7.49* and P value – 0.006*

Odds of developing complications among females is 0.17 times when compared to males and it is statistically significant.

3. Side of IJV access vs complications

| | | Complication | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| IJV access | Left | 2 | 3 | 5 |
| | | 40.0% | 60.0% | 100.0% |
| | Right | 16 | 49 | 65 |
| | | 24.6% | 75.4% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 0.575 and P value – 0.448

From the table we can conclude that there is no significant statistical association between side of IJV access and complication rates

4. Transfusions vs complications

| | | Complications | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Transfusions | No | 10 | 32 | 42 |
| | | 23.8% | 76.2% | 100.0% |
| | Yes | 8 | 20 | 28 |
| | | 28.6% | 71.4% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 0.199 and P value – 0.655

From the table we can conclude that there is no significant statistical association between transfusion of blood products and complication rates.

5. Indication vs complications

| | | Complication | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| No of indication | Multiple indication | 9 | 13 | 22 |
| | | 40.9% | 59.1% | 100.0% |
| | Single indication | 9 | 39 | 48 |
| | | 18.8% | 81.3% | 100.0% |
| Total | | 18 | 52 | 70 |

Chi square – 3.88 and P value – 0.049

There is significant association between number of indications and complication rates.

6. Deranged bleeding parameters vs complications

| | | Complications | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Deranged bleeding Parameters | Yes | 8 | 17 | 25 |
| | | 32.0% | 68.0% | 100.0% |
| | No | 10 | 35 | 45 |
| | | 22.2% | 77.8% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 0.8 and P value – 0.370

From the table we can conclude that there is no significant statistical association between deranged bleeding parameters and complication rates.

7. Thrombocytopenia vs complications

| | | Complications | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Thrombocytopenia | Yes | 7 | 26 | 33 |
| | | 21.2% | 78.8% | 100.0% |
| | No | 11 | 26 | 37 |
| | | 29.7% | 70.3% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 0.662 and P value – 0.416

From the table we can conclude that there is no significant statistical association between thrombocytopenia and complication rates.

8. Renal failure vs complications

| | | Complications | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Renal failure | Yes | 7 | 11 | 18 |
| | | 38.9% | 61.1% | 100.0% |
| | No | 11 | 41 | 52 |
| | | 21.2% | 78.8% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 2.2 and P value – 0.138

From the table we can conclude that there is no significant statistical association between renal failure and complication rates.

9. Ascites vs complication

| | | Complication | | Total |
|---|---|---|---|---|
| | | Yes | No | |
| Ascites | Yes | 6 | 15 | 21 |
| | | 28.6% | 71.4% | 100.0% |
| | No | 12 | 37 | 49 |
| | | 24.5% | 75.5% | 100.0% |
| Total | | 18 | 52 | 70 |
| | | 25.7% | 74.3% | 100.0% |

Chi square – 0.128 and P value – 0.72

From the table we can conclude that there is no significant statistical association between ascites and complication rates.

10. Gender vs Technical adequacy

| | | Adequate | | Total |
|---|---|---|---|---|
| | | N | Y | |
| Sex | Female | 3 | 28 | 31 |
| | | 9.7% | 90.3% | 100.0% |
| | Male | 6 | 33 | 39 |
| | | 15.4% | 84.6% | 100.0% |
| Total | | 9 | 61 | 70 |
| | | 12.9% | 87.1% | 100.0% |

Chi square – 0.5 and P value – 0.479

From the table we can conclude that there is no significant statistical association between gender and technical adequacy.

11. Gender vs Technical success

| | | Successful | | Total |
|---|---|---|---|---|
| | | N | Y | |
| Sex | Female | 3 | 28 | 31 |
| | | 9.7% | 90.3% | 100.0% |
| | Male | 8 | 31 | 39 |
| | | 20.5% | 79.5% | 100.0% |
| Total | | 11 | 59 | 70 |
| | | 15.7% | 84.3% | 100.0% |

Chi square – 1.5 and P value – 0.216

From the table we can conclude that there is no significant statistical association between gender and technical success.

12. Age category vs technical adequacy

| | | Adequate | | Total |
|---|---|---|---|---|
| | | N | Y | |
| Age category | less than 35 | 4 | 27 | 31 |
| | | 12.9% | 87.1% | 100.0% |
| | 36 and more | 5 | 34 | 39 |
| | | 12.8% | 87.2% | 100.0% |
| Total | | 9 | 61 | 70 |
| | | 12.9% | 87.1% | 100.0% |

Chi square – 0 and P value – 0.992

From the table we can conclude that there is no significant statistical association between age category and technical adequacy.

13. Age category vs technical success

| | | Successful | | Total |
|---|---|---|---|---|
| | | N | Y | |
| Age category | less than 35 | 2 | 29 | 31 |
| | | 6.5% | 93.5% | 100.0% |
| | 36 and more | 9 | 30 | 39 |
| | | 23.1% | 76.9% | 100.0% |
| Total | | 11 | 59 | 70 |
| | | 15.7% | 84.3% | 100.0% |

Chi square – 3.6 and P value – 0.058

From the table we can conclude that there is no significant statistical association between age category and technical success.

14. Side of IJV access vs technical adequacy

| | | Adequate | | Total |
|---|---|---|---|---|
| | | N | Y | |
| IJV access | Left | 1 | 4 | 5 |
| | | 20.0% | 80.0% | 100.0% |
| | Right | 8 | 57 | 65 |
| | | 12.3% | 87.7% | 100.0% |
| Total | | 9 | 61 | 70 |
| | | 12.9% | 87.1% | 100.0% |

Chi square – 0.245 and P value – 0.620

From the table we can conclude that there is no significant statistical association between side of IJV access and technical adequacy.

15. Side of IJV access vs technical success

| | | Successful | | Total |
|---|---|---|---|---|
| | | No | Yes | |
| IJV access side | Left | 2 | 3 | 5 |
| | | 40.0% | 60.0% | 100.0% |
| | Right | 9 | 56 | 65 |
| | | 13.8% | 86.2% | 100.0% |
| Total | | 11 | 59 | 70 |
| | | 15.7% | 84.3% | 100.0% |

Chi square – 0 and P value – 0.992

From the table we can conclude that there is no significant statistical association between side of IJV access and technical success.

16. Technical success Vs Adequacy

| | | Successful | | Total |
|---|---|---|---|---|
| | | N | Y | |
| Adequate | No | 4 | 5 | 9 |
| | | 44.4% | 55.6% | 100.0% |
| | Yes | 7 | 54 | 61 |
| | | 11.5% | 88.5% | 100.0% |
| Total | | 11 | 59 | 70 |
| | | 15.7% | 84.3% | 100.0% |

Chi square – 6.436 and P value – 0.011
Odds ratio – 6.171 (1.33 – 28.572)

From the table we can infer that the odds of achieving an adequate sample in a technically successful procedure is 6.436 times and is statistically significant.

TABLES SHOWING SUMMARY OF FINDINGS

| Variables | | Complications | | Odds ratio (CI) & Chi Square P value |
|---|---|---|---|---|
| | | Yes | No | |
| 1. Age category | < 35 years | 23 (74.2%) | 8 (25.8%) | 0.99 (0.33 – 2.27) P - 0.98 |
| | > 35 years | 29 (74.4%) | 10 (25.6%) | |
| 2. Gender | Female | 3 (9.7%) | 28 (90.3%) | 0.17 (0.04 – 0.66) 0.006 * |
| | Male | 15 (38.5%) | 24 (61.5 %) | |
| 3. IJV access | Left | 2 (40 %) | 3 (60 %) | 2.04 ( 0.31 – 13.3) 0.448 |
| | Right | 16 (24.6%) | 49 (75.4 %) | |
| 4. Transfusions | No | 10 (23.8%) | 32 (76.2%) | 0.78 ( 0.26 – 2.31) 0.65 |
| | Yes | 8 (28.6 %) | 20 (71.4%) | |
| 5. Indication category | Multiple | 9 (40.9 %) | 13 (59.1 %) | 3 ( 0.98 – 9.16) 0.049 * |
| | Single | 9 (18.8 %) | 39 (81.3 %) | |
| 6. Deranged bleeding parameters | Yes | 8 (32 %) | 17 (68 %) | 1.64 (0.55 – 4.93) 0.37 |
| | No | 10 (22.2%) | 35 (77.8 %) | |
| 7. Thrombocytopenia | Yes | 7 (21.2%) | 26 (78.8%) | 0.63 (0.21 – 1.89) 0.416 |
| | No | 11 (29.7%) | 26 (70.3%) | |

| | | | | |
|---|---|---|---|---|
| 8. Renal failure | Yes | 7 (38.9 5) | 11 (61.1%) | 2.37 (0.74 – 7.55) 0.138 |
| | No | 11 (21.2 %) | 41 (78.8%) | |
| 9. Ascites | Yes | 6 (28.6 %) | 15 (71.4 %) | 1.23 ( 0.39 – 3.89) 0.72 |
| | No | 12 (24.5 %) | 37 (75.5 %) | |

* Significant statistical association

| Variables | | Technical adequacy | | Odds ratio (CI) & Chi Square P value |
|---|---|---|---|---|
| | | No | Yes | |
| 1. Age category | < 35 years | 4 (12.9 %) | 27 (87.1 %) | 1 (0.24 – 4.12) 0.992 |
| | > 35 years | 5 (12.8%) | 34 (87.2 %) | |
| 2. Gender | Female | 3 (9.7 %) | 28 (90.3 %) | 0.59 (0.13 – 2.57) 0.479 |
| | Male | 6 (15.4 %) | 33 (84.6 %) | |
| 3. IJV access | Left | 1 (20%) | 4 (80 %) | 1.78 ( 0.17-17.99) 0.62 |
| | Right | 8 (12.3 %) | 57 (87.7 %) | |

| Variables | | Technical success | | Odds ratio (CI) & Chi Square P value |
|---|---|---|---|---|
| | | No | Yes | |
| 1. Age category | < 35 years | 2 (6.5%) | 29 (93.5 %) | 0.23( 0.046 – 1.15) 0.058 |
| | > 35 years | 9 (23.1%) | 30 (76.9%) | |

| | | | | |
|---|---|---|---|---|
| 2. Gender | Female | 3 (9.7 %) | 28 (90.3 %) | 0.41 (0.1 – 1.72) |
| | Male | 8 (20.5 %) | 31 (79.5 %) | 0.216 |
| 3. IJV access | Left | 2 (40 %) | 3 (60 %) | 4.15 (0.60 – 28.37) |
| | Right | 9 (13.8 %) | 56 (86.2%) | 0.122 |
| 4. Adequacy * | No | 4 (44.4%) | 5 (55.6%) | 6.17 (1.33-28.57) |
| | Yes | 7 (11.5 %) | 54 (88.5%) | 0.011 |

* Significant statistical association

PHOTOMICROGRAPHS OF LIVER BIOPSY

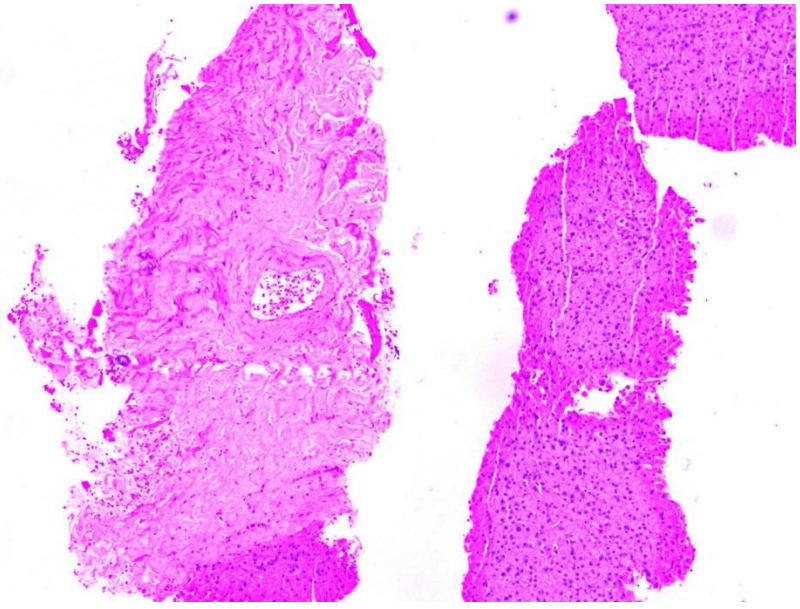


Figure: Part of wall of vein adherent to liver tissue, which can normally be expected in TJLB. H&E stain 40x.

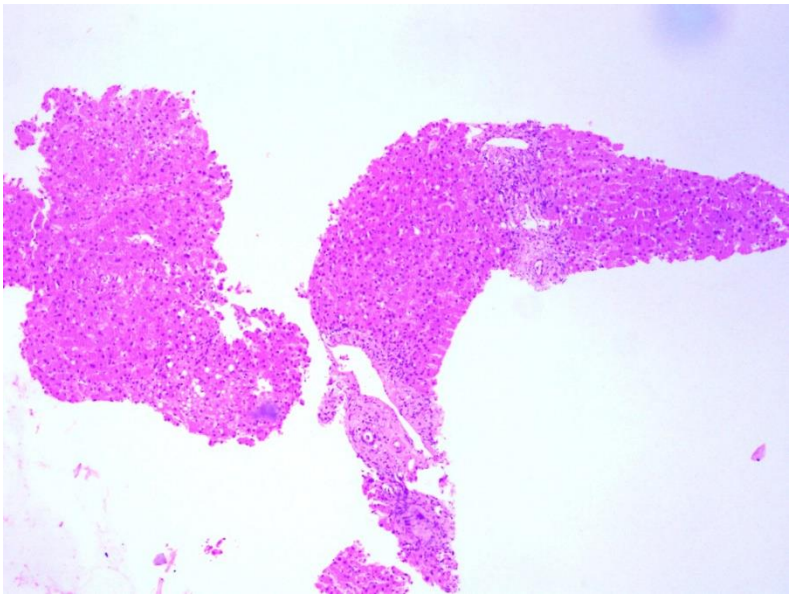


Figure: Liver biopsy with 2 portal tracts displaying mild inflammation and mild expansion. H&E stain 40x.

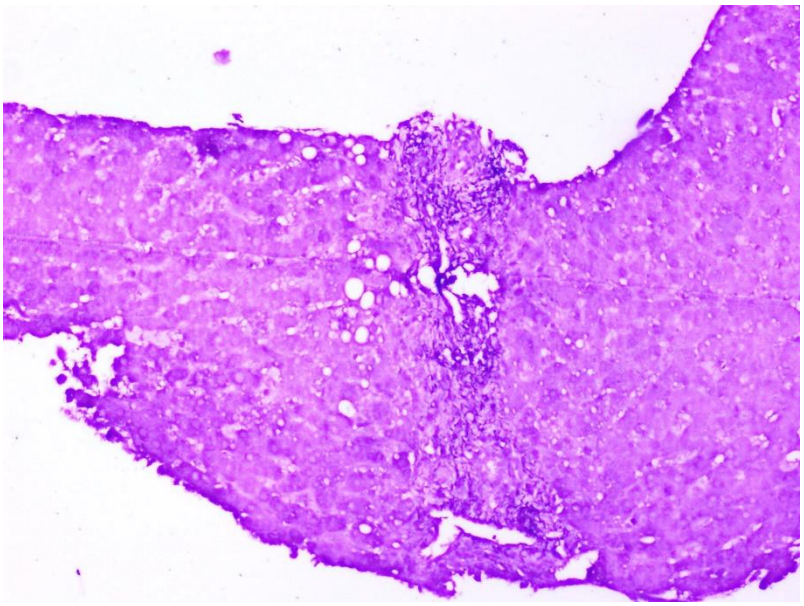


Figure: Liver biopsy of portal tracts displaying mild fibrous expansion. Orcein stain 40x.

# DISCUSSION

Liver biopsy is considered the gold standard in evaluating various conditions affecting the liver and has become a central investigation in evaluating and managing liver disorders. Liver biopsy can be performed through various approaches like percutaneous, Transjugular, laparoscopic & Transgastric routes. Though percutaneous technique is the most common route for performing liver biopsy, in certain circumstances when percutaneous biopsy has higher risk of complications, other routes of biopsy like Transjugular route can be considered. The complication rates associated with TJLB are significantly lower despite being cone in patients with increased risk. The complication rates associated with TJLB range from 0.5-20.5%. The mortality rate is less than 0.1% in adults and ~ 0.1% in children.

Though data is available regarding complications rate, technical success rate and histopathological adequacy in patients undergoing TJLB, many of the studies are retrospective studies from which the exact complication rates is difficult to determine as some of the minor complications would have been overlooked or missed. Through this hospital based, prospective, observational study we tried to determine the precise complication rates, technical success and efficacy rate of TJLB.

| | STUDY | Design | No of cases. | Compli-cation rates | Success | Adequacy |
|---|---|---|---|---|---|---|
| 1 | Transjugular liver biopsy: A systematic review (George Kalambokis etal, Journal of Hepatology 47 (2007) 284–294) | Systemic review | 7649 | 7.1% | 98% | 96.1% |
| 2. | Transjugular liver biopsy: A retrospective analysis of 601 cases (Mammen et al. J Vasc Interv Radiol 2008; 19:351–358) | Retrospect-tive study | 601 | 2.49% | 98.8% | 97% |
| 3. | Transjugular Liver Biopsy: Results of 97 Patients. (Halil Donmez et al. Balk Med J. 2012 Jun;29(2):129–32) | Retrospect-ive study | 97 | 1 % | 95.8% | 98.9% |
| 4. | Single centre experience of transjugular liver biopsy in 152 patients. (Patel et al. Ann Acad Med Singapore. 2014 Mar;43(3): 160-5) | Retrospect-ive study | 152 | 5.2% | 98.7% | 98% |
| 5. | Transjugular liver biopsy (Pathak et al. Med J Armed Forces India. 2013 Oct;69(4):384-7) | Prospective | 67 | 5% | 96% | |
| 6. | Transjugular Liver Biopsy: Comparison of sample adequacy with the use of two automated needle systems (George Behrens, J Vasc Interv Radiol 2011; 22:341–345) | Retrospect-ive study | 233 | 2.6% - 7% (major) | 99.6% | 98.7% |
| 7. | Transjugular Liver Biopsy using Tru-cut biopsy needle: KEM experience (K Rathod et al. JAPI • VOL. 56 • JUNE 2008) | Retrospect-ive study | 145 | 1.4% (minor) | 98.62% | 97.2% |

| | STUDY | Design | No of cases. | Compli-cation rates | Success | Adequacy |
|---|---|---|---|---|---|---|
| 7. | Transjugular biopsy of the liver in pediatric and adult patients using an 18-gauge automated core biopsy needle: a retrospective review of 410 consecutive procedures(56).<br>( Smith T et al. AJR. 2003;180:167-172) | Retrospec-tive | 410 | 2.4% | | 89% |
| 8. | Major complications due to transjugular liver biopsy: Incidence, management and outcome<br>( A. Dohan et al. Diagn Interv Imaging. 2015 Jun;96(6):571–7) | Retrospec-tive | 341 | 20.5% (minor)<br>0.59% (major) | 97% | |
| 9. | Transjugular liver biopsy: histological diagnosis success comparing the trucut to the modified aspiration Ross needle (Maciel et al. A Arq Gastroenterol. 2003;40(2):80–84) | Prospective | 85 | 19% (Trucut needle)<br>22% (Ross) needle) | 91% (Trucut needle)<br>70% (Ross) needle) | |
| 10. | 'Transjugular liver biopsy' Behrens et al. | Review Article | - | 1.3 – 6.5 % | 87 – 97 % | |
| 11. | Transjugular liver biopsy in patients with end-stage renal disease (57). (Ahmad A et al., J Vasc Interv Radiol. 2004 Mar;15(3):257-60) | Prospective | 46 | 12% | 100% | 100% |
| 12 | Transjugular liver biopsy: assessment of safety and efficacy of the Quick-Core biopsy needle(54) (Bruzzi JF et al, Abdom Imaging. 2002 Nov-Dec;27(6):711-5. | Prospective | 50 | 0% | 98% | 100% |

## Demography

A total of 70 patients who underwent TJLB during the study period from May, 2015 to July 2016 were included in the study. Age of the study population ranged between 11 to 75 years with a median age of 37 years. Of the 75 patients who underwent TJLB 39 were male and 31 were female.

## Indications and Complications

Common indications in our study on TJLB were thrombocytopenia, deranged bleeding parameters, ascites and renal failure. Most common indication was thrombocytopenia (33 cases, 47%) followed by deranged bleeding parameters (25 cases, 32.5%), ascites (21 cases, 30%) and renal failure (18 cases, 25.7%). 48 patients (68.6%) had single indication and 22 patients (31.4%) had multiple indications. There is increased complication rates in patients with multiple indications (chi square – 3.88, p value – 0.049). Female gender is found as protective factor (Odds ratio – 0.17(CI - 0.044 to 0.664), Chi Square P value – 0.006). There is no significant statistical correlation between complication rates and age, side of IJV access, transfusions and individual indication for the procedure.

Total complication rate in patients undergoing TJLB was ~ 25.7 % (18 patients). 17 patients (24.3 %) had minor complications as per Society of Interventional Radiology criteria and 1 patient had major complication (1.4%) in the form of intra-abdominal bleed with significant drop in haemoglobin levels, post TJLB requiring blood transfusion. Minor complications seen were moderate neck pain (3 patients,

4.3%), moderate abdominal pain (1 patient, 1.4%), elevated temperature, 100-102 deg F (2 patients, 2.9%), intra-abdominal bleed (low suspicion – 5, 7.1% & high suspicion – 9, 12.9%), hypertension (5, 7.1%) and transient ventricular arrhythmia (1, 1.4%) which was self-limiting. No mortality was encountered during the study.

In all the important retrospective studies which we reviewed it was found that minor complications ranged between 0 - 7% (6,11,14,15,17,20,56) with the exception of one (5). The study conducted by Dohan et al. showed minor complication rate of 20.5% (5). Review of various prospective studies showed complication rates ranging between 5 - 22% (52,54,57,58) which is comparable with our results. The reasons for higher incidence of minor complications in prospective studies can be attributed to

- Documentation of minor complications using a standard proforma.
- Increased sensitivity by health care workers in terms of being a study patient.
- Overlooking some of the minor complications like neck pain, neck haematoma in retrospective studies.

Technical success rate:

TJLB was possible in all patients who were posted for the procedure but the sample had to be sufficient enough for histopathological evaluation. We wanted to see if TLJB was a second rate biopsy as compared to percutaneous liver biopsy. In our study we defined the technical success rate as biopsy sample length more than 10 mm (Our institutional practice is to accept sample length of 10 mm for fair

histopathological analysis). Technical success was achieved in 84.3% (59 out of 70 patients) in this study.

Review of various landmark studies showed a success rate ranging between 90 – 100% (5,11,14,15,17,20,52,57,59,60). Many of these studies have defined success as being able to obtain liver tissue by the procedure. None of these studies have used our definition of success. By their definition we have achieved 100% success.

Efficacy rate:

Biopsy sample was considered adequate when the number of complete portal tracts were more than 5 or if the histopathological report was contributory to the diagnosis. The pathologists determined the length of the sample and number of complete portal tracts and hepatologists determined if the histopathology was contributory to the diagnosis based on clinic-pathological correlation. Efficacy was defined as the percentage of number of patients with adequate biopsy sample to the total number of patients undergoing liver TJLB. Efficacy of TJLB was 87 % in our study.

# CONCLUSION

- Transjugular liver biopsy (TJLB) is an innovative way of performing liver biopsy when percutaneous route is considered unsafe. It has a very high technical success and efficacy rate.
- The complication rate (25.7 %) seen in this prospective study was comparable with other prospective studies.
- Patients with multiple indications for TJLB had higher complication rates as compared to patients with single indication.
- TJLB is superior to other methods of liver biopsy in view of assessment of hepatic wedge pressure for evaluating portal hypertension and its pharmacological response.

# LIMITATIONS

- Small number of patients in this study
- Accurate comparison with other landmark studies was not possible due to difference in definition of variables.
- Time period was inadequate to achieve the sample size (This study will be continued till the sample size is reached)

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Appendix 1

## TRANSJUGULAR LIVER BIOPSY

### Questionnaire

Name Age

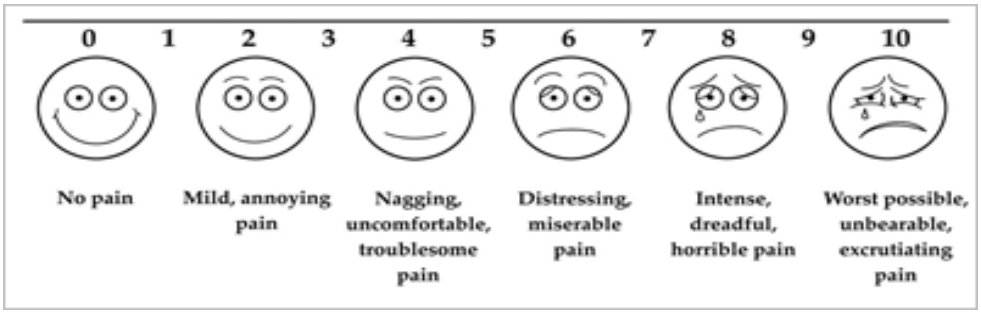
Hospital No. Study No.

Indication for the procedure:

| | Pre-procedure | During | Post-procedure | |
|---|---|---|---|---|
| | | 0 hrs | 6 hrs | 24 hrs (if available) |
| 1. Pulse | | | | |
| 2. BP | | | | |

3. Hb :
4. PT/ aPTT
5. Blood transfusions
6. ECG
7. Visual analogue scale for pain

   Neck




   Abdomen

8. No of attempts :
9. Size of the sample / No of fragments :

10.No of portal tracts :

11. Biopsy interpretation :

12. Successful TJLB (i.e. sample size >10mm in size) :

13. Adequate biopsy :

14. Chest X ray ( if done)

15. USG assessment :

12. Complications:

| | Complications | Consequences | Interventions | Risk |
|---|---|---|---|---|
| 1 | Neck pain | | | |
| 2 | Abdominal pain | | | |
| 3 | Temperature | | | |
| 4 | Neck haematoma | | | |
| 5 | Carotid puncture | | | |
| 6 | Arrhythmias | | | |
| 7 | Hypotension | | | |
| 8 | Hepatic capsular perforation | | | |
| 9 | Intraperitoneal haemorrhage | | | |
| 10 | Pneumothorax | | | |
| 11 | Subcapsular/ parenchymal haematoma | | | |
| 12 | Others | | | |
| 13 | | | | |
| 14 | | | | |
| 15 | | | | |

Appendix 2

**CONSENT SHEET**

I _____ son/ daughter/_____of_____ , am aware that I am being asked to participate in this study "Assessment of yield and procedural complications in patients undergoing transjugular liver biopsy (TJLB) : a prospective study"

The data collected for this study can be used for publication purposes. As a part of this study I will be assessed during and after TJLB procedure by clinical assessment, lab parameters (PCV) and by imaging techniques (USG) to determine the complication rates.

(i) I confirm that I have read and understood the information sheet 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 Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect to 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. [ ]

(iv) 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/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Appendix 3

## STUDY TITLE

## ASSESSMENT OF YIELD AND PROCEDURAL COMPLICATIONS IN PATIENTS UNDERGOING TRANSJUGULAR LIVER BIOPSY: A PROSPECTIVE STUDY

## PATIENT INFORMATION

Liver biopsy is considered the gold standard for the evaluation of acute and chronic liver disorders. It provides information regarding the diagnosis, disease progression and response to therapy in patients with various liver diseases. TJLB is one of the method of liver biopsy which involves accessing liver tissue using neck (jugular) venous access. TJLB is mainly indicated for patients in whom percutaneous liver biopsy is contraindicated due to various reasons like bleeding disorders, free fluid in abdomen acute liver failure etc. This approach reduces the risk of bleeding after biopsy because the bleeding resulting from the biopsy needle will drain back into the veins. However due to limited availability of prospective data determination of exact complications rates in patients undergoing TJLB is limited. This study aims to determine the exact complication rates in a tertiary care centre in India. Some of the complications related to the procedure are -

Minor complications - neck pain, neck haematoma, carotid artery puncture, change in voice, minor disturbances in rhythm of heartbeat, drop in blood pressure, abdominal pain, small hepatic hematoma etc.

Major complications - large hepatic haematoma, intra-abdominal bleed, pneumothorax, serious disturbances in rhythm of heartbeat, respiratory arrest, death etc.

We will assess the patient during and after the procedure by clinical, lab parameters (PCV) and by imaging techniques and the exact complication rates will be determined. This study is an observational study and will not influence your treatment. Recruitment is purely voluntary and at no cost to you or your relative. You/ your relative may choose to withdraw from this study at any time. The care provided to you/ your relative will not be affected by your decision to participate in this study. As a part of the study you will have to give 5 ml of blood after the procedure and may have to visit the radiology department for ultrasound screening. However if you are unable to visit the radiology department due to various medical reasons then bedside USG can be done. By participating in the study you might have an additional benefit of free USG and PCV estimation after the procedure as a part of the study, if you are willing to participate. The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However your medical record may be reviewed by doctors associated with the study, without your additional permission.