Comprehensive Analysis of Liver Biopsies in a Tertiary Care Hospital: A Retrospective Histopathological and Clinical Correlation Study

Nekta Anand[1], Aditya Kumar[2], V. P. Mane[3]

[1]*Assistant Professor, Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, India*
[2]*Assistant Professor, Department of Radiology, Hind institute of medical sciences Barabanki, India*
[3]*Head of Department and Professor, Department of Pathology, Bharati Vidyapeeth (Deemed to be University) Medical College and Hospital, India*
Email: Nektaaditya27@gmail.com
Corresponding Author: Nekta Anand

KEYWORDS
Liver biopsy, histopathological analysis, liver disease diagnosis, tertiary care hospital, retrospective analysis, liver pathology.

ABSTRACT
Liver biopsy (LB) served as a vital diagnostic tool for cases with notable alterations in liver function tests and for diagnosing a range of liver diseases, including chronic liver disease, cirrhosis, primary biliary cirrhosis, and hepatic neoplasms. Patients presenting with liver pathology often exhibited nonspecific symptoms, such as abdominal discomfort, nausea, vomiting, fever, indigestion, and flatulence. Based on patients' clinical history and radiological findings that suggested liver disease, a liver biopsy was frequently recommended, as it provided definitive diagnostic insights. Histopathological analysis of liver biopsies offered critical information on disease severity, grading, staging of liver tumors, and the presence of any coexisting hepatic conditions.This study retrospectively examined liver biopsies submitted to the Department of Pathology, correlating histopathological findings with clinical and radiological data. Through this integration, the research contributed to improved diagnosis, management, and follow-up of liver disease cases in a tertiary care setting.

1. Introduction

The global prevalence of liver diseases continues to rise across all age groups, sexes, regions, and races. Liver biopsy remains a widely utilized and well-established technique, offering high sensitivity for the definitive clinical management of hepatic lesions【1】【2】. Liver biopsy and its histological assessment are considered the gold standard in diagnosing and managing certain conditions such as autoimmune hepatitis, cirrhosis, and hepatocellular carcinoma. Histopathology interpretation is particularly valuable when non-invasive diagnostic methods, including clinical, radiological, and serological findings, fail to provide sufficient information for diagnosis, management, treatment, or prognostication.

There are several methods for performing liver biopsy, with the most commonly used being transthoracic percussion-guided liver biopsy, which is based on clinical evaluation and radiological workup【1】. Other methods employed for liver biopsies include transthoracic image-guided, subcostal, and real-time image-guided techniques. Additionally, advanced techniques such as transvenous or transjugular liver biopsies, performed through the jugular or femoral veins under fluorescence guidance, are also increasingly advocated.

Indications for liver biopsy are generally classified into three main categories. First, it is primarily used for diagnostic purposes, including conditions such as autoimmune hepatitis, nonalcoholic steatohepatitis (NASH), overlap syndrome, and for diagnostic challenges such as distinguishing cholangiocarcinoma from hepatocellular carcinoma and focal nodular hyperplasia【3】【4】【5】. Second, liver biopsies serve as important prognostic tools for diseases such as advanced fibrosis, cirrhosis, NASH, and other chronic liver conditions【5】. Lastly, liver biopsies are recommended for the follow-up of certain diseases, such as autoimmune hepatitis, to assess disease activity and predict relapse, thus also aiding in the monitoring of treatment effectiveness【5】【6】.

The aim of this study is to profile liver biopsies from a tertiary hospital, with objectives including the demographic distribution of liver biopsies, clinical presentations, radiological investigations, and exploring the correlation between clinical and radiological findings.

2. Methodology

This prospective descriptive study was conducted in the Department of Pathology, in collaboration with the

Departments of Medicine and Radiology, at a tertiary care center in Western India. Given that liver biopsy is an invasive procedure with rare associated complications, patients were fully informed about the procedure and its risks. Written informed consent was obtained from each patient included in the study. All liver biopsies performed at our institute between October 2019 and January 2021 were included, while cases without consent were excluded. The study received approval from the Institutional Ethical Committee (IEC) with approval number IEC/323/20.

Liver biopsies were performed by the Departments of Medicine and Pediatrics, and specimens were preserved in 10% neutral buffered formalin, or in 95% alcohol for suspected cases of storage disorders in children. Gross descriptions of the tissues were recorded, followed by routine tissue processing, block preparation, and sectioning with a microtome. Sections were prepared and stained with Hematoxylin and Eosin (H&E) and, as required, special stains such as Ziehl-Nielsen, Grocott's silver methenamine, Congo Red, Rhodamine, and orcein, according to established protocols.

The stained slides were examined under a light microscope, and diagnoses were made by correlating clinical, biochemical, and radiological findings. Clinical details, radiological findings, and histopathological diagnoses were analyzed, and associations between histopathological diagnoses and clinical and radiological findings were studied.

3. Result:

The present study included 50 cases of liver biopsies performed between October 2019 to January 2021. This table 1 presents the demographic distribution of liver biopsy cases by age and gender. The majority of cases (60%) were among children aged 0-10 years, with a nearly equal distribution of males (7%) and females (8%). The age groups 41-60 and >60 showed smaller but notable case counts, comprising 16% and 18% of cases, respectively, indicating a higher prevalence of liver conditions in pediatric patients and older adults.

Table 1- Demographic profile of cases

Age (year)	Male	Female	Number of cases (n=50)
0-10	14(7%)	16(8%)	30(60%)
11-21	0(0%)	0(0%)	01(02%)
21-40	2(1%)	1(0.5%)	02(04%)
41-60	7(3.5%)	1(0.5%)	08(16%)
>60	7(3.5%)	2(1%)	09(18%)

In Table 2(a), clinical features and associated liver diseases were examined within the study population. The most common clinical feature was hepatomegaly, observed in 66% of cases, frequently linked with hepatocellular carcinoma (18%), cirrhosis (16%), and glycogen storage disease (10%). Additional prevalent symptoms included nausea (62%) and vomiting (60%), each associated with various liver conditions such as cirrhosis, hepatitis, and carcinoma. Other significant clinical presentations included jaundice, splenomegaly, fever, and abdominal pain, showcasing a wide spectrum of symptoms linked to liver disease.

Table- 2(a) Spectrum of clinical manifestation in cases with liver diseases

Clinical feature		Present cases
Hepatomegaly	33(66%)	Hepatocellular carcinoma(18%)
		Cirrhosis(16%)
		Metastasis(10%)
		Glycogen storage disease (10%)
		Liver Abscess(4%)
		Wilsons disease (4%)
		Granulomatous infection(02%)
Nausea	31(62%)	Cirrhosis(18%)
		Hepatitis(18%)
		Hepatocellular carcinoma(10%)
		Liver Abscess(4%)
		Wilsons disease (4%)
		Neonatal hepatitis(4%)
		Viral Hepatitis(4%)
		Metastasis (2%)
Vomiting	30(60%)	Hepatitis(18%)
		Cirrhosis(16%)
		Hepatocellular carcinoma(10%)
		Viral hepatitis (4%)

		Liver Abscess(4%)
		Neonatal hepatitis(4%)
		Hydatid Cyst(2%)
		Metastasis (2%)
Jaundice	29(58%)	Cirrhosis(16%)
		Hepatitis(9%)
		Viral Hepatitis(4%)
Splenomegaly	24(48%)	Hepatitis(18%)
		Cirrhosis(16%)
		Glycogen storage disease (10%)
		Metastasis(4%)
Fever	22(44%)	Hepatitis(18%)
		Viral Hepatitis(4%)
Pain abdomen	20(40%)	Cirrhosis(12%)
		Viral Hepatitis(4%)
		Liver Abscess(4%)

Table 2(b) displays radiological findings across liver disease cases, demonstrating diverse radiologic presentations. Hepatosplenomegaly emerged as the most frequent finding, occurring in 42% of cases, mainly associated with hepatocellular carcinoma (18%) and glycogen storage disease (10%). Interestingly, 14% of cases displayed normal radiological findings despite evident clinical symptoms, with conditions like steatohepatitis and neonatal hepatitis identified in these cases. Hepatomegaly alone was present in 20% of cases, underscoring its prominence in liver disease diagnostics.

Table- 2(b) Radiological distribution

Radiological findings		**No. of cases(50)**
Hepatosplenomegaly	21(42%)	Hepatocellular carcinoma(18%)
		Glycogen storage disease (10%)
		Cirrhosis(08%)
		Wilsons disease (4%)
		Granulomatous infection(02%)
Normal radiological findings	13(14%)	Steatohepatitis(04%)
		Neonatal hepatitis(04%)
		Hepatitis(06%)
Hepatomegaly	10(20%)	Glycogen storage disease (10%)
		Viral Hepatitis(4%)
		Wilsons disease (4%)
		Hydatid Cyst(2%)
Cyst like lesion	01(02%)	Hydatid Cyst(2%)
Hepatic portal enlarged node	01(02%)	Hepatocellular carcinoma(02%)

Table 3 compares the age distribution of liver biopsy cases in this study with those in prior studies (Kalaranjini KV et al., 2018, and Agrawal et al., 2017). This study observed a higher proportion of cases in the 0-10 age group (60%), contrasting with the predominantly older age distributions in the referenced studies, suggesting a unique demographic pattern with a marked concentration of pediatric cases.

Table 3- Demographic distribution of cases among the study population

Age (year)	**Current Study**	**Kalaranjini KV et al (2018) [13]**	**Agrawal et al (2017) 16**
0-10	30 (60%)	-	8 (12.30%)
11-21	01 (2%)	1 (4%)	3 (4.61%)
21-40	02 (4%)	4 (16%)	16 (24.60%)
41-60	08 (16%)	10 (40%)	22 (33.84%)
>60	09 (18%)	10 (40%)	16 (24.61%)

In Table 4, the range of liver diseases diagnosed in this study is compared with previous findings. Cirrhosis and hepatitis were each prevalent in 16% of cases, aligning with the reports by Kalaranjini KV et al. and Katiyar R et al. However, this study presented a higher incidence of glycogen storage disease (8%) and a relatively lower occurrence of viral hepatitis (4%), possibly reflecting the demographic focus on pediatric and elderly populations in the study cohort.

Table 4- Spectrum of diseases among the study population

Sex	**Current Study**	**Kalaranjini KV et al (2018)[13] (25 cases)**	**Katiyar. R et al (2017)[14] (50 cases)**
Cirrhosis	08 (16%)	9(36%)	12 (24%)
Hepatitis	08 (16%)	4 (16%)	7(14%)

Metastasis	07 (14%)	2 (8%)	4(8%)
Hepatocellular carcinoma	04 (8%)	2(8%)	4(8%)
Glycogen storage	04 (8%)	-	3(6%)
Viral Hepatitis	02 (4%)	4(16%)	10(20%)
Wilsons disease	02 (4%)	1(4%)	5(10%)
Steatohepatitis	02 (4%)	3 (12%)	5(10%)

Figure 1 provides visual representations of Glycogen Storage Disease (GSD) through histopathological and radiological images. Panel A, at 40X magnification, illustrates the characteristic mosaic pattern of hepatocytes, which is indicative of glycogen accumulation in the liver. Panel B, also at 40X magnification, shows ballooning degeneration of hepatocytes, a sign of cellular injury often seen in GSD. Panel C, using Periodic Acid-Schiff (PAS) staining at 40X magnification, highlights the glycogen deposits within hepatocytes, marked by bright magenta staining. Finally, Panel D presents a radiograph showing hepatomegaly, a common finding in glycogen storage diseases due to the liver's enlargement caused by excess glycogen.

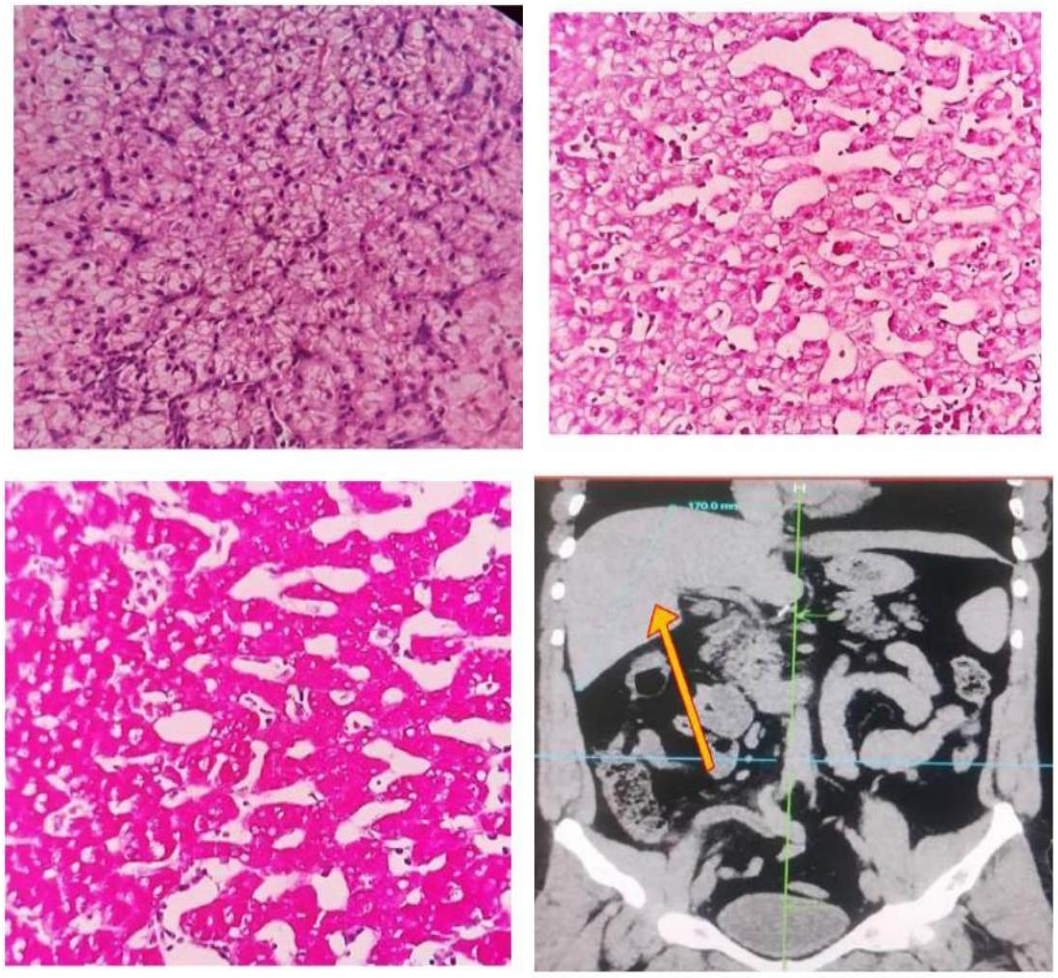

Figure 1-A) 40X-Glycogen storage disease- showing mosaic pattern

B) 40X-Glycogen Storage Disease-Ballooning degeneration of hepatocytes.

C) 40X-Glycogen Storage Disease-PAS stain

D) Radiograph shows- Hepatomegaly

Figure 2 focuses on Hepatocellular Carcinoma (HCC), providing both histopathological and radiological evidence of the disease. Panel A, at 10X magnification, demonstrates the general structural alterations in the liver tissue caused by HCC, with abnormal clusters of malignant cells disrupting the liver's architecture. Panel B, at 40X magnification, zooms in on the cancerous cells, showing their atypical characteristics, including enlarged nuclei and irregular cell sizes, typical of HCC. Panel C displays a radiograph showing hepatomegaly, a common finding in advanced HCC cases as the tumor causes the liver to enlarge. These images collectively

highlight the key histopathological and radiological features essential for diagnosing these liver conditions.

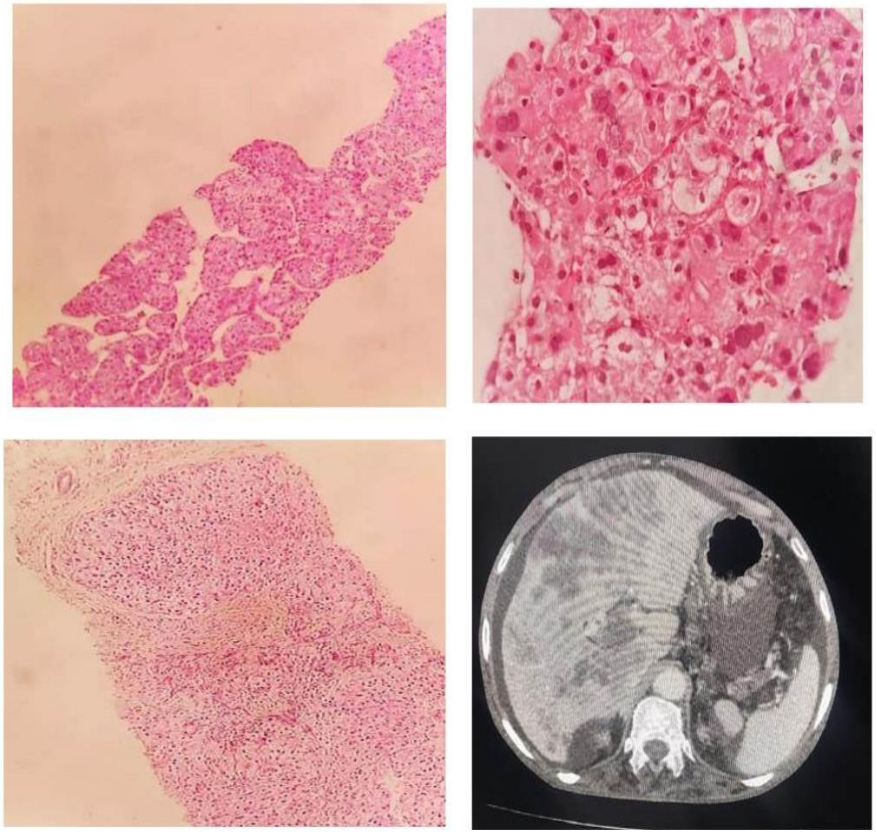

Figure 2 -A) 10X-Hepatocellular carcinoma

B) 40X-Hepatocellular carcinoma.

C) Radiograph shows- Hepatomegaly

4. Discussion: -

In our study, 60% (30/50) of cases were in the 0-10 years age group, followed by 18% (9/50) in the >60 years group, 16% (8/50) in the 41-60 years group, 4% (2/50) in the 21-40 years group, and 2% (1/50) in the 11-21 years age group. A similar study conducted by Kalaranjini KV et al. in 2018 observed 40% (10/25) of cases in both the 41-60 years and >60 years age groups, followed by 16% (4/25) in the 21-40 years age group, and 4% (1/25) in the 11-21 years age group【13】. In a 2017 study that evaluated the histopathological spectrum of hepatic lesions, the majority of cases were found in the 41-60 years age group (33.84%, 22/65) and the >60 years group (24.61%, 23/65), with only 12.30% (8/65) of cases in the <10 years age group【16】. This indicates that the pediatric population (0-10 years) was the most prevalent in our study, whereas other studies reported a higher incidence in the 40-60 years age range.

Regarding gender distribution, our study found that 62% (31/50) of the cases were male and 38% (19/50) were female, with a male-to-female (M

) ratio of 1.6:1. This is in line with Kalaranjini KV et al.'s study (2018), which showed a similar Mratio of 1.5:1【13】. In contrast, a study by Agrawal et al. in 2017 reported a higher female prevalence, with a Mratio of 0.75:1【16】. These findings highlight some variability in gender distribution across different studies, but our results are consistent with Kalaranjini KV et al.'s findings.

The spectrum of liver diseases observed in our study included hepatitis (16%, 8/50), cirrhosis (16%, 8/50), metastasis (14%, 7/50), and glycogen storage disease (8%, 4/50). Other diseases such as Wilson disease, steatohepatitis, liver abscess, and hydatid cyst each accounted for 4% (2/50) of cases. Additionally, 12% (6/50) of cases had no specific lesion. A study by Kalaranjini KV et al. (2018) reported similar findings, with cirrhosis

(28%, 7/25) and viral hepatitis (36%, 9/25) being the most common【13】. The study by Katiyar R et al. (2017) also observed a similar distribution, with cirrhosis (24%, 12/50) and viral hepatitis (20%, 10/50) being the most prevalent【16】.

In terms of clinical features, hepatomegaly was the most common presentation in our study, found in 66% (33/50) of cases, followed by nausea (62%, 31/50), vomiting (60%, 30/50), jaundice (58%, 29/50), splenomegaly (48%, 24/50), fever (44%, 22/50), and abdominal pain (40%, 20/50). These results contrast with those from Kalaranjini KV et al., who observed jaundice in 28% (7/25) of cases, and Sanchez GC et al. (2022), where abdominal pain was the most common symptom (35%, 25/70)【13】【26】. In the latter study, nausea, vomiting, and hepatomegaly were less common.

Radiologically, the most frequent finding in our study was splenomegaly (42%, 21/50), followed by hepatomegaly (20%, 10/50) and normal radiological findings (26%, 13/50). A study by Miller et al. (2020) reported similar findings, with 60.31% (38/63) of cases showing splenomegaly and 7.93% (5/63) showing normal findings【25】. Another study by Garcia-Eulate et al. (2006) reported abscesses in 51% (24/47) of cases, highlighting the regional variability in radiological findings across different studies【30】. These studies indicate that splenomegaly is the most common radiological finding in liver diseases, with varying frequencies of other findings depending on the specific population studied.

5. Conclusion:

Liver biopsy remains a crucial and gold standard diagnostic tool for the identification and management of various liver diseases. For accurate diagnosis and effective treatment planning, clinical and imaging data must be thoroughly correlated with biopsy findings. It is imperative for pathologists to provide comprehensive and clear reports on biopsy results, while also integrating clinical, radiological, and pathological findings before issuing a final report. This collaborative approach enhances evaluation, diagnosis, treatment, and follow-up care throughout the management of liver diseases.

Conflict of Interest:

The authors declare that there is no conflict of interest regarding the publication of this research.

Acknowledgment:

I would like to express my sincere gratitude to the technicians and technical support team in the pathology department for their invaluable assistance and dedication. I would also like to extend my heartfelt thanks to the departments of Medicine and Pediatrics for their expertise and unwavering support, which have been instrumental in facilitating our research. Your commitment to excellence has significantly contributed to our work, and we are deeply appreciative of your efforts. Thank you for your continued support.

References

[1] Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD; American Association for the Study of Liver Diseases. Liver biopsy. Hepatology. 2009 Mar;49(3):1017-44. doi: 10.1002/hep.22742. PMID: 19243014.
[2] Neuberger J, Patel J, Caldwell H, Davies S, Hebditch V, Hollywood C, Hubscher S, Karkhanis S, Lester W, Roslund N, West R, Wyatt JI, Heydtmann M. Guidelines on the use of liver biopsy in clinical practice from the British Society of Gastroenterology, the Royal College of Radiologists and the Royal College of Pathology. Gut. 2020 Aug;69(8):1382-1403. doi: 10.1136/gutjnl-2020-321299. Epub 2020 May 28. PMID: 32467090; PMCID: PMC7398479.
[3] Tannapfel A, Dienes HP, Lohse AW. The indications for liver biopsy. Dtsch Arztebl Int. 2012 Jul;109(27-28):477-83. doi: 10.3238/arztebl.2012.0477. Epub 2012 Jul 9. PMID: 22833761; PMCID: PMC3402072.
[4] Goodman, Z. D. (2007). Grading and staging systems for inflammation and fibrosis in chronic liver diseases. Journal of hepatology, 47(4), 598-607.
[5] https://www.ncbi.nlm.nih.gov/books/NBK470567
[6] Casanovas, Teresa. 'Rethinking the Role of Liver Biopsy in the Era of Personalized Medicine'. Liver Biopsy - Indications, Procedures, Results, InTech, 21 Nov. 2012. Crossref, doi:10.5772/53120.
[7] Lefkowitch, J. H. (2020). Scheuer's liver biopsy interpretation. Elsevier Health Sciences.
[8] Khalifa A, Sasso R, Rockey DC. Role of Liver Biopsy in Assessment of Radiologically Identified Liver Masses. Dig Dis Sci. 2022 Jan;67(1):337-343. doi: 10.1007/s10620-021-06822-9. Epub 2021 Feb 19. PMID: 33604792; PMCID: PMC8999003.
[9] Ahmad M, Afzal S, Roshan E, Mubarik A, Bano S, Khan SA, Hashmi SN. Usefulness of needle biopsy in the diagnosis

of paediatric liver disorders. J Pak Med Assoc. 2005 Jan;55(1):24-8. PMID: 15816692.
[10] Sathiah, P., Basu, D., Kar, R., Jagadisan, B., & Kumaravel, S. (2018). Evaluation of Liver Biopsies using Histopathological Scoring System in Neonatal Hepatitis and Biliary Atresia: Correlation with Clinico- Radiological and Biochemical Parameters. Journal of Clinical & Diagnostic Research, 12(2). https://doi.org/10.7860/JCDR/2018/30685.11212
[11] Desmet, V. J. (2003). Liver tissue examination. Journal of hepatology, 39, 43-49.
[12] Wyatt. J, Hubscher. S, Bellamy. C, The Royal college of pathologists,2020, Vol.3,1-34.
[13] KV Kalaranjini, Glaxon A.J, Vasudeven Sheela et al, Changing role of liver biopsy indication in atertiary care center: A histopathological study,Annals of Pathology and Laboratory Medicine; Vol. 6, Issue 9; 2019;475- 480 https://doi.org/10.21276/apalm.2633.
[14] Katiyar.R, Shashikant C.U. Kumar S.P, Shukla S, Spectrum of liver disease diagnosed on liver biopsy: A study from tertiary care center of Uttar Volume-7 | Issue-9 |September-2017 | ISSN - 2249
[15] Murgod, P. S., Doshi, P. R., & Dombale, V. D. (2019). Spectrum of hepatic lesions-A histopathological study of liver biopsies. IP Journal of Diagnostic Pathology and Oncology, 4(3), 200-3 https://doi.org/10.18231/j.jdpo.2019.042
[16] Agrawal, N. S., Iqbal, M. B., Patil, A. A., Karia, K. M., & Kumar, H. (2018). Study to evaluate the histopathological spectrum of hepatic lesions in liver biopsies in a tertiary care hospital. Annals of Pathology and Laboratory Medicine, 5(3), A228-A233.
[17] Jaiswal D.G. Dakhure. S.D, Clinicopathological correlation in liver biopsy of cirrhosis, International Journal of Medical and Health Research, Volume 5; Issue 8; August 2019; 189-192.
[18] Saleem, T. H., Eltalawy, H. N., Abu-faddan, N. H., Ahmed, A. E., Gamal, Y., & Hassan, M. H. (2016). Clinical and laboratory study on children with glycogen storage disease type-1 in Upper Egypt. Adv Res Gastroenterol Hepatol, 2, 555-578.
[19] Gümüş E, Özen H. Glycogen storage diseases: An update. World J Gastroenterol. 2023 Jul 7;29(25):3932-3963. doi: 10.3748/wjg. v29.i25.3932. PMID: 37476587; PMCID: PMC10354582.
[20] Verma. Abhishek, Sinha. Somya, Panicker K N, The clinicopathological correlation in suspected cases of chronic liver disease with the aid of liver biopsy – a study in tertiary health center,
[21] Santos, B. L., de Souza, C. F., Schuler-Faccini, L., Refosco, L., Epifanio, M., Nalin, T., ... & Schwartz, I. V. (2014). Glycogen storage disease type I: clinical and laboratory profile. Jornal de pediatria, 90, 572-579.
[22] Schlageter, M., Quagliata, L., Matter, M., Perrina, V., Tornillo, L., & Terracciano, L. (2016). Clinicopathological features and metastatic pattern of hepatocellular carcinoma: an autopsy study of 398 patients. Pathobiology, 83(6), 301-307.
[23] Hamilton W, Barrett J, Stapley S, Sharp D, Rose P. Clinical features of metastatic cancer in primary care: a case–control study using medical records. British Journal of General Practice. 2015;65(637);516-22.
[24] Takayasu K, Furukawa H, Wakao F, Muramatsu Y, Abe H, Terauchi T, Winter TC 3rd, Sakamoto M, Hirohashi S. CT diagnosis of early hepatocellular carcinoma: sensitivity, findings, and CT-pathologic correlation. AJR Am J Roentgenol. 1995 Apr;164(4):885-90.
[25] MillerJ.H, Stanley.P, and Gates GF Radiography of glycogen storage diseases, Volume132, Issue 3.
[26] Sanchez GC, Baunsgaard P, Lundborg CJ. A comparison between clinical diagnosis and histopathological findings in liver biopsies. Scand J Gastroenterol. 1980;15(8):985-91
[27] Ronot M, Leporq B, Van Beers BE, Vilgrain V. CT and MR perfusion techniques to assess diffuse liver disease. Abdom Radiol (NY). 2020 Nov;45(11):3496-3506.
[28] Tsushima, Y., & Endo, K. (2004). Spleen Enlargement in Patients with Nonalcoholic Fatty Liver. Digestive Diseases and Sciences, 45, 196-200.
[29] Lyu Q, Lin D, Tang M, Liu D, Zhang J, Wang Y, Shelat VG, Raissi D, Ostwal V, Chen X, Li S. 18F-FDG PET/CT and MR imaging features of liver metastases in gastrointestinal stromal tumors: a cross-sectional analysis. Ann Transl Med. 2022 Nov;10(22):1220. doi: 10.21037/atm-22-5181. PMID: 36544642; PMCID: PMC9761173.
[30] Garcia-Eulate R, Hussain N, Heller T, Kleiner D, Malech H, Holland S, et al. CT and MRI of hepatic abscess in patients with chronic granulomatous disease. AJR Am J Roentgenol 2006 Aug;187(2):482-49