Experience of pediatric liver disease at a university hospital in Western Saudi Arabia

Nawal H. Almohammad, MBBS, SB-Ant.Path,
Rana Y. Bokhary, MBBS, FRCPC.

ABSTRACT

Objectives: To describe the diverse spectrum presented by pediatric liver diseases and prevalence of histopathological patterns and assess the role of histopathological findings in predicting prognosis.

Methods: We carried out a retrospective cohort study of 158 pediatric patients who underwent liver biopsy or resection for liver disease at King Abdulaziz University Hospital, Jeddah, Saudi Arabia (2014-2023). Demographic data, clinical data, and histopathological findings were analyzed using counts and percentages.

Results: The majority of the patients were infants (n=83; 52.5%), with male predominance (n=97; 61.4%). Biopsies were the most common specimen type (n=137; 86.7%). Cholestatic/bile duct disorders were the most prevalent pathological pattern (n=92; 58.2%), with extrahepatic biliary atresia being the most common subtype (n=32; 34.8%). Inflammatory/infectious disorders accounted for 13.3% (n=21) of cases, with chronic active hepatitis-not otherwise specified (n=10; 47.6%) being the most frequent. Metabolic disorders represented 12.0% of cases, with glycogen storage disorders and non-alcoholic fatty liver disease both at 31.6% (n=6). Neoplastic disorders were found in 7.6% (n=12) of cases, evenly distributed between benign and malignant tumors.

Conclusion: This study provides a comprehensive overview of histopathological patterns in pediatric liver diseases, highlighting the predominance of cholestatic disorders and the significance of early diagnosis.

Keywords: histopathological patterns, pediatric liver disease

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Pediatric liver diseases present a substantial challenge in clinical practice due to their diverse etiologies and complex presentations, ranging from metabolic disorders and congenital anomalies to infectious and inflammatory diseases.[1] In terms of non-alcoholic fatty liver disease (NAFLD), a 2015 meta-analysis estimated the prevalence of it in children aged 1-19 years to be 7.6%.[2] Saudi Arabia shows prevalence of NAFLD is projected to surpass 30% by 2030.[3] These statistics highlight the growing burden of studied forms of pediatric liver diseases in the country.

Due to diverse etiologies and complex presentations and scarce prevalence record, pediatric liver diseases therefore, warrant precise diagnostic approaches to ensure appropriate management and treatment.[4] Significant progress has been carried out in understanding the development of liver diseases, leading to the discovery of new therapeutic targets that can improve the progression of these conditions, over the recent decades. In this context, histopathological examination stands out as a critical diagnostic tool in liver diseases. Liver biopsies and resections play a vital role in understanding disease pathology, providing detailed insights into the cellular and structural changes associated with various liver conditions.[5] In pediatric patients, histopathological examination is particularly vital as it helps differentiate between various liver diseases that often present with similar clinical and laboratory findings.[3] Understanding the histopathological patterns associated with different etiologies, especially for a specific demographic like Saudi Arabia with growing burden of pediatric liver diseases, can thoroughly enhance diagnostic accuracy and direct treatment strategies.

This study aims to describe the spectrum and prevalence of histopathological patterns encountered in liver biopsies and resections from pediatric Saudi population. Specifically, the researchers seek to identify the common and specific histopathological patterns and features and their prevalence associated with different etiologies among pediatric liver disease patients as part of contributing to local and global accurate epidemiological data.

Methods. Our study employs a retrospective cohort design, analyzing data from pediatric patients (0-18 years) who underwent liver biopsy or resection for liver disease at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, as one of the main referral centers for pediatric liver disease in the western region of Saudi Arabia, between 2014-2023. We collected demographic data (age, gender, and ethnicity), clinical data when available, and histopathological data, focusing on microscopic findings.

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Ethical approval was requested from the Unit of Biomedical ethics of the Faculty of Medicine at King Abdulaziz University, Jeddah, Saudi Arabia, with approval number of 296-24, in accordance with the Saudi Laws; including, but not limited to, the Saudi Law of Ethics of Research on living creatures and regulations issued by the National Committee of Bioethics, King Abdul-Aziz City for Science and Technology, Jeddah, Saudi Arabia.

Statistical analysis. Data collected in this study were analyzed and visualized using the Statistical Package for the Social Sciences, version 27.0 (IBM Corp., Armonk, NY, USA). Simple descriptive statistics was used to describe the prevalence and distribution of histopathological patterns through a form of counts and percentages.

Results. The age distribution shows that the majority of the patients were infants, with 52.5% (n=83) under one year of age, followed by 22.2% (n=35) aged 1-5 years, and 25.3% (n=40) over 5 years. There was a predominance of male patients, accounting to more than half of the samples analyzed (n=97; 61.4%) compared to females (n=61; 38.6%).

Table 1 shows the distribution of specimen types and pathological patterns. In terms of specimen types, 86.7% (n=137) were small biopsies, while 13.3% (n=21) were large surgical specimens. Pathological patterns identified in the specimens included cholestatic/bile duct diseases (n=92; 58.2%), inflammatory/infectious disorders (n=21; 13.3%), metabolic disorders (n=19; 12.0%), vascular conditions (1.9%), cirrhotic changes (n=4; 2.5%), mixed patterns (n=4; 2.5%), neoplastic disorders (7.6%), near normal biopsies (n=2; 1.3%), and transplant rejection (n=1; 0.6%). Among the large surgical specimens, Kasai procedure accounted for the majority (n=14; 8.7%), followed by hepatectomy (n=5; 3.2%), mass resection (n=1; 0.6%), and abscess drainage (n=1; 0.6%).

Table 2 details the prevalence of specific histopathological patterns and their subtypes. The most common pathological pattern is cholestatic/bile duct disease at 58.2% (n=92). Within this category, extrahepatic biliary atresia was the most frequent (34.8%, n=32), followed by paucity of bile ducts (21.7%, n=20), neonatal hepatitis (10.9%, n=10), progressive familial intrahepatic cholestasis (PFIC)-2 (13.0%, n=12), PFIC-3 (5.4%, n=5), PFIC-1 (3.3%, n=3), choledochal cyst (1.1%, n=1), primary sclerosing cholangitis (3.3%, n=3), and cholestasis, not otherwise specified (NOS, 6.5%; n= 6).

On the other hand, inflammatory/infectious disorders accounted for 13.3% (n=21) of the cases, with chronic active hepatitis, NOS being the most common (47.6%, n=10), followed by autoimmune hepatitis (19.0%, n=4), abscesses (14.3%, n=3), infectious etiologies (14.3%, n=3), and cholestatic hepatitis (4.8%, n=1). Meanwhile, metabolic disorders were present in 12.0% (n=19) of the cases, with glycogen storage disorders and NAFLD both accounting for 31.6% (n=6) of the cases, followed by cystic fibrosis (10.5%, n=10.5), lysosomal storage diseases (5.3%, n=1), alpha-1 antitrypsin deficiency (5.3%, n=1), and

Table 1 - Distribution of specimen types into categories (N=158).

Specimen types	n (%)
Biopsies	137 (86.7)
Surgical specimens (n=21)	
Kasai procedure	14 (8.7)
Hepatectomy	5 (3.2)
Mass resection	1 (0.6)
Abscess drainage	1 (0.6)

Values are presented as numbers and percentages (%).

Table 2 - Prevalence of specific histopathological patterns and their subtypes (N=158).

Pathological patterns	n (%)
Cholestatic/bile duct disorders (n=92)	
Extrahepatic biliary atresia	32 (34.8)
Paucity of bile ducts (syndromic and non-syndromic)	20 (21.7)
Neonatal hepatitis	10 (10.9)
PFIC-1	3 (3.3)
PFIC-2	12 (13.0)
PFIC-3	5 (5.4)
Choledochal cyst	1 (1.1)
PSC	3 (3.3)
Cholestasis, NOS	6 (6.5)
Inflammatory/infectious disorders (n=21)	
Autoimmune hepatitis	4 (19.0)
Abscess	3 (14.3)
Infectious (HCV, fungal)	3 (14.3)
Cholestatic hepatitis	1 (4.8)
CAH, NOS	10 (47.6)
Metabolic disorders (n=19)	
Glycogen storage disorders	6 (31.6)
NAFLD	6 (31.6)
Cystic fibrosis	2 (10.5)
Lysosomal storage diseases	1 (5.3)
A1ATD	1 (5.3)
Metabolic disorders, NOS	3 (15.8)
Neoplastic disorders (n=12)	
Benign	5 (41.7)
Malignant, 1ry	3 (25.0)
Malignant, 2ry	4 (33.3)

Values are presented as numbers and percentages (%).
PFIC: progressive familial intrahepatic cholestasis, PSC: primary sclerosing cholangitis, NOS: not otherwise specified, HCV: hepatitis C virus, CAH: chronic active hepatitis, NAFLD: non-alcoholic fatty liver disease, A1ATD: alpha-1 antitrypsin deficiency

metabolic disorders, NOS (15.8%, n=3). Furthermore, neoplastic disorders were found in 7.6% of the cases, with benign neoplasms constituting 41.7% (n=5), primary malignant neoplasms 25.0% (n=3), and secondary malignant neoplasms 33.3% (n=4).

Discussion. The current study revealed significant demographic trends among pediatric liver disease patients in the western region of Saudi Arabia. The results revealed a diverse range of histopathological patterns, with cholestatic/bile duct disorders being the most prevalent.

Metabolic disorders, notably glycogen storage disorders and NAFLD, accounted for 12.0% of the cases, highlighting the growing burden of these conditions. The demographic analysis showed a predominance of infants under one year and a male bias, reflecting the critical need for early diagnosis and intervention.

In terms of age, the high prevalence of liver disease in infants may be attributable to the frequency of congenital and early-onset liver disorders, underscoring the critical importance of early detection and intervention of such conditions. Similar findings were reported in a 10-year single-center retrospective study carried out by Chen et al,[6] where liver disease in infancy was found to make up the largest group in pediatric liver disease. Of the total 4,313 children recruited, a median age of 0.7 (0.2-4.5) years was found, and 54.5% of the cases were in the 0-1-year age group.

Moreover, a global meta-analysis that combined various diagnostic methods, such as liver chemistry, imaging, and histology, estimated the prevalence of NAFLD in children to be approximately 7.6%. This suggests that the prevalence of NAFLD in the pediatric population is likely to range between 5-10%.[7] These findings, however, are at odds with a survey carried out in California, the United States, which indicated that 50% of childhood liver disease cases occur in the 16-21-year age group.[8] Such regional differences highlight the variability in disease patterns and underscore the influence of local factors on the prevalence of liver conditions in different age groups.

The present study also revealed a notable male predominance (61.4%), which aligns with global trends and suggests potential genetic or hormonal influences in the prevalence of these conditions. Furthermore, Schwimmer et al[9] observed a gender difference in the prevalence of pediatric liver disease, with boys showing a higher rate (11.1%) compared to girls (7.9%). A trend consistent with another retrospective Arab study in 3 tertiary care hospitals in Riyadh, Saudi Arabia (King Abdullah Specialist Children's Hospital, Security Forces Hospital, and King Khalid University Hospital) where 56% (n=65) of male children had higher proportion of NAFLD than female.[10]

Biopsies constituted 86.7% of the specimens, reflecting their primary role in the diagnosis and monitoring of liver diseases. The predominance of liver biopsies, which is a relatively simple bedside procedure over surgical specimens, highlights their diagnostic utility and the preference for minimally invasive procedures.[11-13] Among the surgical specimens, the high number of Kasai procedures (8.7%) reflects the significant burden of biliary atresia (BA) in the studied population.

The relatively lower numbers of hepatectomy, mass resection, and abscess drainage reflect the less frequent need for these surgical interventions compared to biopsies and biliary surgeries. Additionally, the examination of liver diseases in infants is often constrained by their young age and the invasive nature of diagnostic procedures.

According to Arya et al,[14] the most common types of liver disease in children include metabolic disorders, chronic intrahepatic cholestasis, steatohepatitis related to obesity, liver conditions caused by drugs or toxins, and viral hepatitis. These findings are consistent with the conditions identified in the current study.

Cholestatic/bile duct disorders were the most prevalent, comprising 58.2% of the cases. Extrahepatic BA (34.8%) and paucity of bile ducts (21.7%) were the most common subtypes, highlighting their major role in pediatric liver disease in this region. These findings align with the review by Arya et al,[14] which reported that BA occurs in approximately 0.5-1.0% cases per 10,000 live births and is responsible for 30% of all cholestasis cases in young infants. In a Saudi Arabian national study from 2000-2018 that looked into the epidemiology and outcome of BA, it was found that BA cases had an incidence rate of 1 in 44,365 live births, or 2.254 per 100,000 live births, with a range of 0.5-4 per 100,000.[15] Meanwhile, the relatively high prevalence of PFIC-2 (13.0%) further emphasizes the importance of genetic factors in the etiology of cholestatic disorders.

The study provides valuable insights into the histopathological patterns of pediatric liver diseases, geared towards the enhancement of diagnostic accuracy and guide clinical management. The results reported in this study underscore the importance of early and accurate diagnosis. In addition to this, a more effective management approach would include a multidisciplinary care where hepatologists, nutritionists, gastroenterologists, and pediatric surgeons should cooperate to provide regular monitoring (function, growth, and development of liver) and tailored-fit treatment plan. It is also crucial for pediatric patients to include supportive care in terms of nutrition and psychosocial support as part of clinical management. Epidemiologically, this study contributes important

data on the prevalence and distribution of pediatric liver diseases in the studied region, providing a basis for comparison with other populations and contributing to a better understanding of regional disease patterns.

Study limitations. This study's retrospective design and reliance on existing medical records may introduce potential selection bias and limit the generalizability of the findings. Additionally, the lack of statistical data on the prognostic value of histopathological findings and their role in treatment decisions represents a significant gap. Future research should address these limitations by incorporating prospective data collection and evaluating the impact of histopathological findings on patient outcomes.

Future studies should aim to fill the gap in understanding the prognostic value of histopathological findings by including longitudinal data and assessing treatment outcomes. Prospective studies with a larger sample size and comprehensive data collection could provide more robust insights into the utility of histopathological patterns in predicting prognosis and guiding treatment decisions.

In conclusion, this study provides valuable insights into the prevalence and histopathological patterns of pediatric liver diseases in the western region of Saudi Arabia. While the findings align with existing literature on the prevalence and types of liver diseases, they also highlight the need for further research into less common subtypes and their impact on pediatric liver health.

Cholestatic and bile duct disorders, particularly extrahepatic BA, emerged as the most common condition, underscoring the importance of early diagnosis and intervention. Additionally, the significant presence of metabolic and inflammatory disorders, along with the observed age and gender differences, highlights the complex nature of pediatric liver diseases, and the need for tailored healthcare strategies. These insights contribute to the growing body of knowledge necessary for improving clinical outcomes and guiding future research and healthcare policies in the region.

The current work makes an excellent foundation for future studies in the field, with future research addressing its limitations (especially the retrospective design) that could further enhance the understanding and management of pediatric liver disease in the region.

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From the Department of Basic Medical Sciences (Almohammad), Faculty of Medicine, Taibah University, Al-Madinah Al-Munawwarah, and from the Department of Pathology (Bokhary), Faculty of Medicine, King Abdulaziz University, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

Address correspondence and reprints request to: Dr. Nawal H. Almohammad, Department of Basic Medical Sciences, Faculty of Medicine, Taibah University, Al-Madinah Al-Munawwarah, Kingdom of Saudi Arabia.
E-mail: nhmohammadi@taibahu.edu.sa
ORCID ID: https://orcid.org/0000-0002-0784-4826

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