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A Review of Transient Elastography as a Screening Tool in Pediatric Hepatic Diseases

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Abstract. Fatty liver disease is now increasingly being identified in children and adolescents. It has even gained a new call, Metabolic Dysfunction – Associated Steatotic Liver Disease. It entails the entire spectrum, from simple accumulation of fat deposits inside the liver to causing inflammation and liver damage ensuing in cirrhosis. Currently, the gold standard for diagnosis is Liver Biopsy, which is an invasive technique. Suppose Ultrasonography with Transient Elastography is included at the screening stage, along with the routine tests. In that case, the chances of missing Metabolic Dysfunction – Associated Steatotic Liver Disease will be reduced, and corrective interventions can be taken early.

There are numerous studies on Transient Elastography in children with Hepatic Diseases. It is practised worldwide but has yet to become popular in India. In most cases, it is USG Abdomen, stating that the liver is enlarged and has some features. The routine practice of Transient Elastography is performed by a few radiologists and a few centres. However, if Transient Elastography can be added as a feature, many chronic cases can be identified early. Furthermore, it can be used as a routine screening tool in our adolescent populations.

Keywords: Transient Elastography; Screening Tool; Pediatric Hepatic Diseases.

INTRODUCTION

Fatty liver disease is now increasingly being identified in children and adolescents. It has even gained a new call, Metabolic Dysfunction – Associated Steatotic Liver Disease. It entails the entire spectrum, from simple accumulation of fat deposits inside the liver to causing inflammation and liver damage ensuing in cirrhosis. Currently, the gold standard for diagnosis is Liver Biopsy, which is an invasive technique. Suppose Ultrasonography with Transient Elastography is included at the screening stage, along with the routine tests. In that case, the chances of missing Metabolic Dysfunction – Associated Steatotic Liver Disease will be reduced, and corrective interventions can be taken early.

Objective – to review the usefulness of Transient Elastography as a screening tool for pediatric liver diseases.

METHOD

A preliminary scoping exercise confirmed that the topic was heterogeneous to allow a systematic evaluation, so a narrative review was undertaken. The review mainly identified studies from 2018-2023. Although Transient Elastography has been practised abundantly in a few nations for the last few years, it is nevertheless not a general practice worldwide. Studies included in the review were identified using keyword searches of PUBMED, Google Scholar, and Cinahl databases. The

searched keywords included Transient Elastography, Non-Alcoholic Fatty Liver Disease, Chronic Hepatitis, Varices, and Portal Hypertension. This evaluation's primary focus was determining the usefulness of transient elastography in hepatic diseases. These searches revealed three comparative, qualitative studies on the prediction of portal hypertension by Transient Elastography (of which two were about predicting clinically significant varies in portal hypertension), and seven studies were about the usefulness of Transient Elastography in assessing liver fibrosis in known or suspected liver disease, with a few comparing the clinical performance of it with Magnetic Resonance Imaging, Ultrasound, and Biopsy. The hepatic diseases studied were fatty liver disease, chronic hepatitis B or C, and Non-Alcoholic Fatty Liver Disease.

Author	Country	Sample characteristics
6	China	Number – 120; Age – 6.1 -17.8 years; Cases – Obesity without any complications; Investigations Done – Anthropometry, Blood samples, and Transient Elastography
7	Egypt	Number – 50; Age – 5-18 years; Cases- Chronic Viral Hepatitis B or hepatitis C; Investigations done – Transient Elastography.
8	China	Number – 157; Age – 0-6 years; Investigations done – Transient Elastography, Liver Biopsy
9	Korea	Number – 106; Age – 5-15 years; Cases – NAFLD; Investigations Done – Transient Elastography
10	London	Number – 67; Age – 3 months – 18 years; Cases – Chronic Liver Disease, Portal Vein Thrombosis

Table

Author	Country	Sample characteristics
1	India	Age – 6 months to 18 years; Cases – portal hypertension (chronic liver disease, CLD, and non-cirrhotic portal hypertension, NCPH); Investigations Done – Transient Elastography for spleen and liver and Doppler ultrasonography.
2	London	Number – 117 +33 Children; Age – Median age ten years; Cases – Portal Hypertension; Investigations done – Esophagogastroduodenoscopy, vWF, Transient Elastography
3	USA	Number – 55; Age – mean age 15 years; BMI – 36.6; Cases – known or suspected NAFLD; Investigations Done – Transient Elastography MRI, Biopsy.
4	Taiwan	Number – 137; Age – 6-18 years; Cases – Hepatic Steatosis and fibrosis; Investigations Done – Transient Elastography and Abdominal USG
5	Denmark	Number – 117; Age -1-19 years; Cases – known chronic or acute liver disease, suspected liver disease (elevated transaminases of unknown origin), or children with prior liver transplantation, in which liver biopsy and either US, Transient Elastography or MRE, or a combination of the latter three, had been performed

RESULTS AND DISCUSSION

This review identified a few qualitative studies on Transient Elastography. The first group, in which most have focussed, is Liver stiffness measurement and Continued attenuation Parameters. Liver steatosis was measured using the Controlled Attenuation Parameter. At the same time, liver Fibrosis was evaluated by Longitudinal Stiffness Measurement in healthy school children in those with chronic hepatitis B or C [9, 10]. The second group focused on splenic stiffness as an indicator of portal hypertension and the varices assessment [3, 4, 11]. The third group has concentrated on evaluating Transient Elastography findings in obese and non-obese and those with or without findings of Metabolic Dysfunction Associated with Steatotic Liver Disease and Metabolic Dysfunction Associated with Steatohepatitis [6, 8].

Ultrasound devices use sound waves to send vibrations into the liver. The device measures the speed at which the vibrations move through the liver. If there are areas of stiff liver tissue, the vibrations move faster through that area. This identifies fibrosis, the pathology underlying various pathological conditions of the liver. It has long been used for adults but has yet to be standardized in paediatrics.

A study [2] concluded that it is feasible but requires two different types of probes to cover the entire age group and consider the different physiological variables.

Furthermore, research [8] in a single-centre prospective study of 157 children with chronic Hepatitis B, aged 0-6 years, in whom Transient Elastography and Liver Stiffness Measurements were performed along with liver Biopsy, separated by an interval of less than one week. They concluded it was promising for diagnosing advanced fibrosis in chronic hepatitis B children aged 0-6 years [8]. To estimate the accuracy of non-invasive methods for diagnosing liver fibrosis with chronic liver hepatitis, a cross-sectional study was done by [7] for hepatitis B and Hepatitis C patients who underwent liver biopsy within nine months of laboratory tests. They concluded that Transient Elastography was the only method to differentiate mild cases from significant ones. As early as 2007, research [1] conducted a prospective feasibility study on 116 children with a mean age of 10.7 years, comparing Transient Elastography with blood parameters like Aspartate transaminase to platelet ratio index and liver biopsy. They concluded that Liver Stiffness measurements are feasible in pediatric populations and correlated with liver fibrosis [1]. Similar studies were performed in 2013 in the United States from Boston Children's Hospital, with serum biomarkers and Transient Elastography as predictors of liver fibrosis [12].

However, the serum biomarkers were serum Hyaluronic Acid (HA) and human cartilage bioprotein-39 (YKL-40). They predicted the utility of Transient Elastography and HA as non-invasive tools for assessing liver fibrosis. In 2021, research [11] used Transient Elastography to estimate fibrosis in pediatric liver diseases like Biliary Atresia, Alpha-1 Anti-trypsin Deficiency, Alagille Syndrome, and Non-Alcoholic Steatohepatitis. According to them, several confounding factors like obesity, non-fasting state, severe inflammation, and liver congestion should be considered when interpreting the results [13]. Two studies, however, studied the influence of changes in levels of transaminases on Transient Elastography [14, 15].

However, it is not substantiated in pediatric hepatic diseases. Authors [16] in 2008 conducted studies on the accuracy and reproducibility of Transient Elastography for diagnosing fibrosis in pediatric Non-Alcoholic Steatohepatitis of various grades, without fibrosis or significant or advanced fibrosis [28]. A study from Thailand utilized Transient Elastography to predict oesophageal /gastric varices in children with biliary atresia and found it useful [28]. In a survey by [28], a multi-

institutional cohort study enrolled children with biliary atresia, Alagille Syndrome, Alpha 1 Anti-trypsin deficiency, and Transient Elastography was done. They concluded that it was possible to measure Liver Stiffness Measurements in children, especially over two years, which correlated well with liver parameters and Portal hypertension [12]. Authors [18] assessed liver fibrosis by Transient Elastography and compared it with liver biopsy in 31 children with Biliary atresia. They concluded that Transient Elastography can be used as a non-invasive technique to assess liver fibrosis in Biliary Atresia, and using standard cut-off values, cirrhotic patients can be distinguished from non-cirrhotic in cases with biliary atresia [19]. Another study [20], a cross-sectional study in patients undergoing liver biopsy as part of standard clinical care for various liver disorders, had Transient Elastography with Controlled Attenuation Parameter measurements within one year of biopsy.

Further Controlled Attenuation Parameter values were compared across histologic Steatosis grades using standard grading criteria [21] in an observational study of a similar comparison between Transient Elastography and liver biopsy [22], which concluded that Transient Elastography appeared reliable in distinguishing different stages of liver fibrosis in children. However, disease-specific cut-off values for staging are required. Liver Biopsy has also been increasingly used in liver transplantation as a follow-up protocol for various liver diseases. In these cases, a study was done with 36 pediatric patients with a median age of 3.02 years who underwent both Transient Elastography and liver biopsy one year later. They found it a helpful and reliable tool to avoid several protocol biopsies and as an alert to the indication of liver biopsy as and when required [23]. In another study on post-transplant fibrosis [21], Transient Elastography helped assess post-transplant graft fibrosis in children and young adult liver transplant recipients [24]. The most confounding factor associated with Transient Elastography is Obesity. However, Hepatic Transient Elastography in Obesity is a controversial topic. Few comparative studies in normal-weight children and those with obesity have proved that Transient Elastography, especially Two-Dimensional Shear Wave Elastography, provides a useful quantitative imaging biomarker for evaluating liver stiffness in children [25].

Further, there were two exciting studies in adolescents with Extreme Obesity with Non-Alcoholic

Fatty Liver Disease. Liver stiffness was measured using time-harmonic elastography (externally induced continuous vibrations of 30-60 Hz) and real-time B-Mode guided wave analysis covering tissue depths up to 14 cm. They concluded that it allows accurate detection of moderate fibrosis even in pediatric patients with extreme obesity. However, they also suggested more extensive clinical trials to confirm the accuracy [25]. In a prospective study done on a cohort of pediatric patients, 67 consecutive adolescents (age range, 10–17 years; mean body mass index, 34.7 kg/m²; range, 21.4–50.4 kg/m²) with biopsy-proven Non-Alcoholic Fatty Liver Disease were enrolled, and a type of elastography known as US Time-Harmonic Elastography (as before) was done [26]. In this, the patient was put on a trolley that rolled out vibrational waves, which were then measured inside the liver tissue using Ultrasound techniques.

Also, the recent review of Sleman et al. underlined the importance of elastography for assessing the evolution and prognosis of chronic liver conditions in children [9]. Bailey et al. also emphasized the critical role of 2D-SWE as a quantitative biomarker for assessing liver stiffness [26]. In diagnosing Pediatric Non-Alcoholic Fatty Liver

Disease, or the new term Metabolic Dysfunction Associated with Steatotic Liver Disease, research [27] concluded that Controlled Attenuation Parameter and Longitudinal Stiffness Measurement have diagnostic efficacy in children with obesity. Even for Non-Alcoholic Steatohepatitis or the new term Metabolic Associated Steato-Hepatitis, the diagnostic efficacy was good [27].

CONCLUSIONS

There are numerous studies on Transient Elastography in children with Hepatic Diseases. It is practised worldwide but has yet to become popular in India. In most cases, it is USG Abdomen, stating that the liver is enlarged and has some features. The routine practice of Transient Elastography is performed by a few radiologists and a few centres. However, if Transient Elastography can be added as a feature, many chronic cases can be identified early. Furthermore, it can be used as a routine screening tool in our adolescent populations.

Conflict of interests

The authors declare that they have no competing interests.

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