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RESEARCH ARTICLE

LIVER FIBROSIS AND STEATOSIS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A TRANSIENT ELASTOGRAPHY STUDY

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Abstract

Background : The prevalence of non-alcoholic fatty liver disease is notably high among patients with type 2 diabetes mellitus (T2DM). The objective of this study was to assess the potential utility of transient elastography (TE), a technique capable of measuring both fibrosis and liver fat content simultaneously, as a screening tool for hepatic involvement in patients with T2DM.

Material and methods : It's a retrospective study spanned from January 2019 to January 2024 and included all patients diagnosed with T2DM who underwent TE. LSM values were determined using a Fibroscan 502 touch (Echosens SA, Paris, France) with the original M or XL probe selected based on the patient's body weight or subcutaneous adipose tissue thickness, as per the manufacturer's guidelines. TE scans were considered reliable when a minimum of 10 successful acquisitions were obtained, and the interquartile range-to-median ratio of the 10 acquisitions was ≤0.3.

Results : A total of 124 patients with T2DM who underwent TE examination were included. 46 males and 78 females. The mean BMI of the patients was 33.2±6.6 kg/m2. The mean LSM was 7.1±3.4 kPa. LSM values exhibited significant correlations with BMI ($p<0.001$) and AST ($p<0.001$). The mean CAP value was 317±54 dB/m. Univariate correlation analyses demonstrated significant associations between CAP values and BMI ($p<0.001$). We found higher ALT levels ($p<0.05$) in patients with F3/F4 fibrosis. Both patients with mild and severe steatosis had higher ALT levels than those without (both $p<0.05$). However, ALT values did not differ significantly according to steatosis severity ($p=0.69$).

Conclusion : Our results contribute to the existing body of evidence across various studies, approving the clinical utility of LSM and CAP for concurrent screening of liver fibrosis and steatosis in patients with T2DM.

Introduction:-

Patients diagnosed with type 2 diabetes mellitus (T2DM) face a heightened susceptibility to non-alcoholic fatty liver disease (NAFLD), likely attributed to the prevalent occurrence of obesity and insulin resistance within this demographic [1]. Despite the potential progression of NAFLD to advanced fibrosis and cirrhosis, leading to

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increased liver-related mortality [2], most patients remain asymptomatic and are typically identified through elevated liver enzymes [3,4]. Nonetheless, ALT elevation isn't consistently present in NAFLD, and its levels inadequately reflect hepatic fibrosis and fat accumulation [5,6]. Although routine liver ultrasound offers insight into hepatic fat deposition in T2DM, its accuracy in identifying or ruling out fibrosis is limited [7]. Given the inherent limitations of liver biopsy, including invasiveness and sampling errors, there's a growing interest in novel non-invasive screening methods for hepatic fibrosis and steatosis.

Transient elastography (TE) is increasingly favored as a non-invasive, operator-independent, and simple imaging technique to evaluate liver stiffness and hepatic fat content. Liver stiffness measurement (LSM) and controlled attenuation parameter (CAP), have demonstrated reliability as imaging markers for liver fibrosis and steatosis, respectively [8-10]. Recent researchs [11-14] suggest that TE parameters could serve as valuable screening tools for hepatic fibrosis and steatosis among T2DM patients. In this study, recognizing significant NAFLD risk , we examine the prevalence of TE-defined hepatic fibrosis and steatosis in a cohort of Moroccan T2DM patients.

Material and Methods:-

It’s a retrospective study spanned from January 2019 to January 2024. Were included all patients diagnosed with T2DM who underwent TE. Exclusion criteria werechronic liver diseases such as viral hepatitis, autoimmune hepatitis, hemochromatosis, primary biliary cirrhosis, Wilson's disease, sclerosing cholangitis, and biliary obstruction, as well as instances of measurement failure or unreliable TE readings. Clinical and laboratory data were extracted from medical records. Overweight and obesity were defined by BMI >25 kg/m2 and BMI >30 kg/m2, respectively. Patients were instructed to fast for a minimum of 3 hours before undergoing imaging. LSM values were determined using a Fibroscan 502 touch (Echosens SA, Paris, France) with the original M or XL probe selected based on the patient's body weight or subcutaneous adipose tissue thickness, as per the manufacturer's guidelines. TE scans were considered reliable when a minimum of 10 successful acquisitions were obtained, and the interquartile range-to-median ratio of the 10 acquisitions was ≤0.3.

Advanced fibrosis (≥F3) and cirrhosis (F4) were defined using probe-specific LSM cut-off values as follows: M probe: F3=9.6–11.4 kPa, F4 ≥11.5 kPa; XL probe: F3=9.3–10.9 kPa, F4 ≥11.0 kPa. The CAP value (ranging from 100 to 400 dB/m) was calculated as the median of individual measurements. Mild, moderate, and severe steatosis were delineated as CAP values of 222–232 dB/m, 233–289 dB/m, and ≥290 dB/m, respectively.

Results:-

A total of 124 patients with T2DM who underwent TE examination were included. 46 males and 78 females, sex ratio= 0,6. The mean BMI of the patients was 33.2±6.6 kg/m2.

The M and XL probes were utilized in 115 (92.7%) and 9 (7.3%) patients, respectively. The mean LSM was 7.1±3.4 kPa, with the range spanning from 2.9 to 25.1 kPa. 21 (16.9%) and 10 (8.0%) patients were identified with advanced fibrosis (≥F3) and cirrhosis (F4), respectively. LSM values exhibited significant correlations with BMI ($p<0.001$) and AST ($p<0.001$).

The mean CAP value was 317±54 dB/m, with the range extending from 184 to 400 dB/m. TE-defined hepatic steatosis (CAP>222 dB/m) was prevalent in the vast majority of the sample (n=82; 66.1%). Among these, 12, 27, and 42 patients exhibited mild, moderate, and severe steatosis, respectively. Univariate correlation analyses demonstrated significant associations between CAP values and BMI ($p<0.001$).

We studied the ALT levels in patients with T2DM in relation to TE-defined hepatic fibrosis and steatosis.

We compared ALT levels in patients F1/F2 fibrosis and patients with F3/4 fibrosis. We noticed higher ALT levels ($p<0.05$) in patients with F3/F4 fibrosis. Both patients with mild and severe steatosis had higher ALT levels than those without (both $p<0.05$). However, ALT values did not differ significantly according to steatosis severity ($p=0.69$).

Discussion:-

The occurrence of Type 2 Diabetes (T2DM) significantly influences liver-related outcomes. Individuals with T2DM tend to exhibit a higher prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD), advanced fibrosis, and face an

elevated risk of mortality compared to counterparts without diabetes [15, 16]. The issue of screening for NAFLD continues to evoke debate. Nevertheless, there is an increasing alignment among international medical societies supporting for the non-invasive screening of diabetic individuals for liver fibrosis, regardless of pre-existing NAFLD [17–19].

In our research, we found that advanced fibrosis (≥F3) and cirrhosis (F4) were present in 16.9% and 8.0% of the cases, respectively. Additionally, TE-defined steatosis was highly prevalent, affecting over 66% of our patients. Steatosis was mainly moderate-to-severe, with mild forms being less common. Moreover, we identified BMI as an independent predictor of both TE fibrosis and steatosis. In contrast, ALT levels, commonly used in clinical practice to screen for NAFLD, remained unchanged in patients with TE-defined cirrhosis and failed to distinguish between various grades of TE-diagnosed steatosis. Overall, our findings support the utility of TE as a clinically valuable non-invasive screening tool for detecting hepatic involvement in diabetic patients.Due to the notable correlation between BMI and both fibrosis and steatosis observed in our investigation, TE examinations are particularly recommended for overweight or obese patients with T2DM. While TE is recognized as more sensitive than ultrasound, which is nonetheless more cost-effective, it could be a revelant screening tool for this at-risk population due to its established advantages over traditional ultrasound methods : ability to detect fibrosis and even low-grade fat accumulation, as well as its independence from machine and operator variability [20].In an other hand, our current findings strongly indicate that measuring liver enzymes is insufficient for detecting liver damage in patientss with T2DM. Notably, not only were ALT levels not frequently elevated in patients with cirrhosis, but they also failed to differentiate the severity of steatosis [5,6].

We demonstrate an elevated risk of steatosis and advanced fibrosis as detected by TE in patients with T2DM, even in the absence of a prior NAFLD diagnosis, which underscores the importance of screening all diabetic individuals [17].

Indeed, Type 2 diabetes is a well-established risk factor for NAFLD, NASH, and advanced fibrosis. According to a comprehensive meta-analysis spanning 22 countries, the pooled prevalence of T2DM among NAFLD and NASH patients was 23% and 44%, respectively, figures notably higher than those observed in the general population [15]. T2DM emerges as an independent predictor of advanced liver fibrosis [16]. In a European NAFLD registry, the presence of T2DM was significantly associated with advanced fibrosis. Moreover, findings from a study involving serial liver biopsies revealed a significant association between the stage of fibrosis on the initial biopsy and T2DM ($P < 0.001$) [21]. Notably, 80% of patients experiencing fibrosis progression were diabetic, compared to only 25% of those without fibrosis progression ($P = 0.005$).

Nevertheless, the clear correlation between TE findings and the presence of T2DM underscores the necessity for TE access to evaluate liver-related risks by detecting steatosis, advanced liver fibrosis, and cirrhosis in individuals with T2DM.

TE, an approved tool integrated into clinical practice, serves as a crucial means to diagnose patients with liver disease. However, its accessibility to general practitioners remains limited. Improving accessibility to physicians treating patients at risk for NAFLD, such as those with T2DM, is necessary to prevent underdiagnosis.

As observed in European cohorts, noninvasive screening can facilitate appropriate referrals, reduce healthcare costs, and enable early intervention [22–24]. Given the escalating prevalence of NAFLD, screening individuals with T2DM is imperative. International guidelines, including those from AASLD and EASL, advocate for noninvasive fibrosis assessment in patients deemed at high risk for NAFLD, including those with T2DM [19, 25].

Conclusion:-

Our results expand previous evidence supporting the clinical value of LSM and CAP for simultaneous screening of hepatic fibrosis and steatosis in patients with T2DM.

Indeed, transient elastography emerges as a promising tool in the evaluation and management of diabetes-related complications, particularly non-alcoholic fatty liver disease (NAFLD) and its progression to advanced liver fibrosis. Through non-invasive assessment of liver stiffness, transient elastography offers clinicians a valuable method for early detection and risk stratification in diabetic patients, facilitating timely interventions to mitigate hepatic complications.

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