

HISTOPATHOLOGICAL EVALUATION OF NON-ALCOHOLIC FATTY LIVER DISEASEDr. Yahya Azeem Ahmed¹, Dr. Sidra Tahir² and Dr. Muhammad Ikram*³

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ABSTRACT

Introduction: Due to hepatic and extra hepatic entanglements, Non-alcoholic fatty liver disease (NAFLD) will wind up a standout amongst the most significant difficulties to general wellbeing in the coming decades. It is most normal ceaseless liver malady in the industrialized world. **Objective:** To analyze the histopathological evaluation of non-alcoholic fatty liver disease. **Place and Time of study:** Nishtar Hospital Multan from March 2017 to Feb 2018. **Methodology:** Non-alcoholic fatty liver disease (NAFLD) is an ailment identified with liver. Hepatic steatosis (lipid collection in hepatocytes) and fibrosis of the tissue are its basic qualities. A few scores are accessible. The SAF score (Steatosis, Activity, Fibrosis) has as of late been portrayed for a progressively complete evaluation of the hepatic status. From these attributes, the highest quality level for determination of the illness is the histo-pathological assessment after liver biopsy. The reason for this survey is to report the NAFLD utilizing this new score.

KEYWORDS: Steatosis; Fibrosis; Fatty Liver; Histology.**INTRODUCTION**

Because of its hepatic and extra hepatic entanglements, Non-alcoholic fatty liver disease (NAFLD) will wind up a standout amongst the most significant difficulties to general wellbeing in the coming decades. It is most normal ceaseless liver malady in the industrialized world,^[1] Insulin obstruction and inordinate collection of lipids are emphatically connected with non-alcoholic fatty liver disease (NAFLD). NAFLD is an aftereffect of metabolic disorder in the liver. Its obsessive procedures incorporate steatosis to steatohepatitis,^[2] which can advance to fibrosis, cirrhosis and hepatic carcinoma.^[3-5] It is related with stoutness, type II diabetes and dyslipidemia. NAFLD is described by aggregation of fat in hepatocytes more prominent than 5% in hepatic tissue, without critical utilization of liquor, drugs and viral hepatitis.^[6-7] The hepatic appearance of a foundational inadequacy of the insulin system is spoken to by Insulin opposition and intemperate gathering of lipids.^[8] This pathogenesis is multifactorial and incorporates adjustments in lipid digestion, with variant amassing of triglycerides, mitochondrial brokenness, irritation and oxidative stress.^[9]

Hepatic Steatosis

The discretionary limit for treating steatosis as neurotic is the nearness of lipid beads in any event 5% of hepatocytes. Non-alcoholic steatosis is the most well-known type of incessant liver sickness and is portrayed

by amassing of fat in hepatocytes.^[10] Steatosis can be grouped into: macrovesicular, made out of enormous vacuoles that move the core to the fringe of the phone; mid vesicular made out of little and huge vacuoles; and microvesicular steatosis made out of countless little vacuoles with frothy appearance.^[11-12]

MATERIALS AND METHODS

The examination was done in December 2018 in the databases PUBMED and MEDLINE. An audit of the writing was completed so as to address the accompanying inquiry: Which logical creations manage the criteria of histological assessment of the liver? For the qualification of productions, each title and conceptual was perused thoroughly to affirm whether they tended to the directing inquiry of this examination and whether it would meet the consideration and prohibition criteria built up. At that point, it happened to the phase of incorporation of the articles. The choice of studies is appeared Table 1. For the choice of the example, the criteria proposed by Moher et al,^[13] (2009) were isolated into stages: ID, screening, qualification and incorporation. In the distinguishing proof and screening were embraced consideration criteria: be accessible at the electronic location, for nothing out of pocket in full and be uncovered in English, Portuguese or Spanish. In this manner, expositions, theories, reports, news, letters to the proofreader and logical articles were not accessible in full on the web and those that were rehashed in the

databases. Figure 1 demonstrates the flowchart of the entire procedure of recognizable proof and determination of articles. The accompanying watchwords or descriptors were utilized in the Health Sciences Descriptors of the Virtual Health Library: greasy liver, histology, and fibrosis.

Histological Evaluation

Brunt et al (1999) proposed a semi-quantitative assessment framework for the remarkable sores perceived for NASH. The proposed framework depended on the idea that the histological finding of NASH is shaped by a lot of highlights instead of any individual trademark. Right now, liver biopsy, through histo-pathological assessment, is as yet the best quality level for the finding of NAFLD and the assessment of its progression.^[14-15] Histologic assessment remains the main exact methods for evaluating the level of steatosis, necroinflammatory injuries, fibrosis sores and non-alcoholic steatohepatitis (NASH), and fills in as the essential methods for recognizing NASH from a "straightforward" steatosis, or steatosis with inflammation.^[16] In the framework proposed by Brunt et al, the degree of steatosis can be characterized by the level of steatotic hepatocytes: mellow, 0-33%; moderate, 33-66%; and serious, > 66%.^[17] Nonetheless, it was produced for NASH and was not created to include the whole range of NAFLD as characterized by Matteoni et al,^[18] (1999). A few semi quantitative histological scoring frameworks were proposed to analyze and order NAFLD. Everyone has certain points of interest and a few impediments. Barely any writing discoveries underscore the assessment of scores and their pertinence in the determination of hepatic steatosis by the SAF strategy. From 2002, the NASH Clinical Research Network proposed to create and approve a histological assessment framework, described by NAFLD Activity Score (NAS), which would cover the range of NAFLD and could be connected to pediatric NAFLD, and this would permit the assessment of changes with treatment. This framework depended on and further culminated Brunt et al's (1999) grouping proposition. The assessment framework was separated into 4 grades, named 0 > 5%, 1-5% - 33%, 2-> 33% - 66% and 3-> 66%.^[18] The histological qualities were assembled into five general classes: steatosis, aggravation, hepatocellular injury, fibrosis and different attributes. The ongoing scoring framework - Steatosis, Activity, Fibrosis (SAF) calculation proposed by Bedossa et al,^[20] (2012) in light of the discoveries of the American Association for the Study of Liver Disease scored the equivalent histological attributes yet with steatosis ordered independently from the action score (ballooning and lobular aggravation). To assess the new analytic strategy for SAF hepatic steatosis by methods for a survey in the.

writing was the target of this examination.

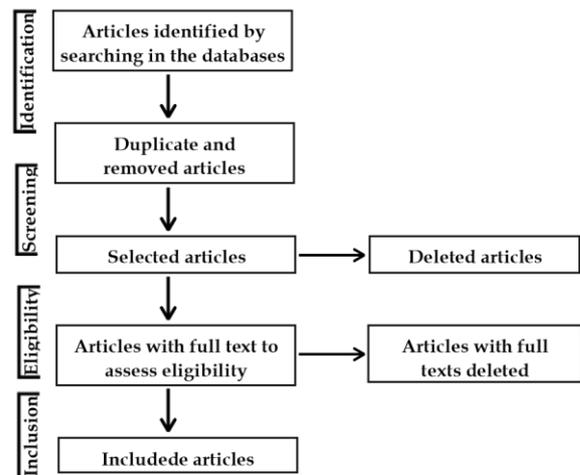


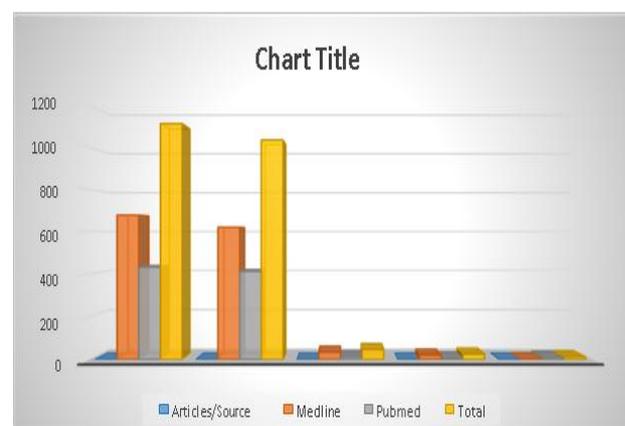
Figure 1: Flowchart of the research phases.

RESULTS AND DISCUSSION

With respect to the histo-pathological assessment of the investigations, one arranged by the level of steatotic hepatocytes (Brunt et al., 1999), eight articles played out the conclusion of NAFLD as indicated by the NAS score (Kleiner et al., 2005; Vajro et al. Concerning periodical and language, all were distributed in universal magazines with English language. Twelve articles were broke down in this examination. The articles were found in the Medline (02) and Pubmed (10) databases. The outcomes are appeared Table 1 and Table 2 for the outcomes acquired by Dowman et al and the utilization of the SAF scores (Bedossa et al, 2012, Singh et al, 2015, and Bedossa P, 2017).

Table 1: Characteristics of studies included in this study.

Articles/Source	Medline	Pubmed	Total
Found	678	432	1110
Articles not related to the theme	621	412	1033
Repeated	35	12	47
Unavailable	20	5	25
Selected	2	10	12



It was conceivable to see that the NAS score is still generally utilized for the determination of NAFLD and that the SAF score, in spite of ordering steatosis and fibrosis independently, is still once in a while utilized. NAS without the incorporation of fibrosis may lose extraordinary unwavering quality in the qualification of liver infections. In view of the discoveries of the American Association for the Study of Liver Disease, Bedossa *et al.*^[20] (2012) proposed the histological calculation of NASH SAF, which arranges dynamic and endless injuries independently, however together as SAF scores. They expanded vulnerability about the incorporation of steatosis in scores. The separate information is displayed in the accompanying table. From the principal portrayal of the neurotic discoveries and the terminology of Ludwig *et al.*^[30] (1980), a few significant obsessive characterizations of NAFLD were created to precisely analyze NASH.^[12,18,19] One such broadly acknowledged point is the NAFLD Activity Score, created by the Pathology Committee of the NASH Clinical Research Network in 2005.^[31] In spite of the fact that this score is straightforward and plainly isolates the three injuries, it is an unknown aggregate of steatosis score, lobular aggravation and hepatocellular ballooning, yet it does exclude a parameter of fibrosis in NAS. The histological scoring frameworks depend on semiquantitative scores of steatosis, ballooning, lobular penetration and fibrosis, and are exceptionally helpful in clinical trials.^[31] Histopathological portrayals and highlight based determination are apparently the most significant, yet the convenience of scoring in clinical preliminaries, similar investigations, and simplicity of comprehension of these results, for the two pathologists and clinicians, cannot be disparaged.

Until this point, the NAFLD score stays questionable, with the need to evaluate the utility and impediments of current frameworks. These outcomes recommend the need to incorporate fibrosis in the all-out score or adjust the last analysis. The utilization of NAS without the consideration of fibrosis would think little of the nearness of noteworthy liver infection and has additionally been accounted for in different investigations. Furthermore, the fibrosis stage was freely connected with general long haul mortality, liver transplantation and liver-related events.^[32-33]

CONCLUSION

It is concluded by the outcomes that the scoring framework that uses the calculation as the SAF score can give down to earth instruments to pathologists that would improve the comprehension of hepatic sores by hepatologists.

REFERENCES

- Della PG. Isocaloric Dietary Changes and Non-Alcoholic Fatty Liver Disease in High Cardiometabolic Risk Individuals. *Nutrients*, 2017; 26: 9(10). pii: E1065. [DOI: 10.3390/nu9101065].
- European Association for the Study of the Liver (EASL). Easl-easd-easo clinical practice guidelines for the management of non-alcoholic fatty liver disease. *J Hepatol*, 2016; 64: 1388–1402. [DOI: 10.1159/000443344].
- Abd El-Kader SM, El-Den Ashmawy EM. Non-alcoholic fatty liver disease: The diagnosis and management. *World J Hepatol*, 2015; 7: 846-58. [DOI: 10.4254/wjh.v7.i6.846].
- Arab JP, Candia R, Zapata R. Management of nonalcoholic fatty liver disease: An evidence-based clinical practice review. *World J Gastroenterol*, 2014; 20: 12182-201. [DOI: 10.3748/wjg.v20.i34.12182].
- Aguirre L, Portillo MP, Hijona E, Bujanda L. Effects of resveratrol and other polyphenols in hepatic steatosis. *World J Gastroenterol*, 2014; 20: 7366-80. [DOI: 10.3748/wjg.v20.i23.7366].
- Chalasanani N. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases. *Hepatology*, 2012; 55: 2005-2023. [DOI: 10.1002/hep.25762].
- Sachin SK, Audrey J, Ronald H. Clements, and Gary a. Abrams. Spectrum of NAFLD and Diagnostic Implications of the Proposed New Normal Range for Serum ALT in Obese Women. *Hepatology*, 2005; 42: 650-656. [DOI: 10.1002/hep.20964].
- Salamone F, Bugianesi E. Nonalcoholic fatty liver disease: The hepatic trigger of the metabolic syndrome. *J Hepatol*, 2010; 53: 1146–1147. [DOI: 10.1016/j.jhep.2010.06.013].
- Takaki A, Kawai D, Yamamoto K. Multiple hits, including oxidative stress, as pathogenesis and treatment target in non-alcoholic steatohepatitis (NASH). *Int J Mol Sci.*, 2013; 14: 20704-28. [DOI: 10.3390/ijms141020704].
- Nagao Y, Kawahigashi Y, Sata M. Association of periodontal diseases and liver fibrosis in patients with HCV and/or HBV infection. *Hepat Mon*, 2014; 14: e23264. [DOI: 10.5812/hepatmon.23264].
- Brunt EM. Nonalcoholic steatohepatitis. *Semin Liver Dis.*, 2004; 24: 3-20. [DOI: 10.1055/s-2004-823098].
- Tiniakos DG, Vos MB, Brunt EM. Nonalcoholic fatty liver disease: pathology and pathophysiology. *Annu Rev Pathol*, 2010; 5: 145–171. [DOI: 10.1146/annurev-pathol-121808-102132].
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med*, 2009; 6: e1000097. [DOI: 10.1371/journal.pmed.1000097].
- Schwimmer JB, Behling C, Newbury R. Histopathology of pediatric nonalcoholic fatty liver disease. *Hepatology*, 2005; 42: 641–649. [DOI: 10.1002/hep.20842].
- Harwood J, Bishop P, Liu H, Nowicki M. Safety of blind percutaneous liver biopsy in obese children: a retrospective analysis. *J Clin Gastroenterol*, 2010;

- 44: e253–e255. [DOI: 10.1097/MCG.0b013e3181cf8358].
16. Vajro P, Lenta S, Socha P, Dhawan A, Mickiernan P, Baumann U. Diagnosis of nonalcoholic fatty liver disease in children and adolescents: position paper of the ESPGHAN Hepatology committee. *J Pediatr Gastroenterol Nutr*, 2012; 54: 700-713. [DOI: 10.1097/MPG.0b013e318252a13f].
 17. Brunt EM, Janney CG, Di Bisceglie AM, Neuschwander-Tetri BA, Bacon BR. Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *Am J Gastroenterol*, 1999; 94: 2467-2474. [DOI: 10.1111/j.1572-0241.1999.01377.x].
 18. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. *Gastroenterology*, 1999; 116: 1413-1419. [PMID: 10348825].
 19. Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, Ferrell LD, Liu YC, Torbenson MS, Unalp-Arida A, Yeh M, McCullough AJ, Sanyal AJ. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. *Hepatology*, 2005; 41: 1313–1321. [DOI: 10.1002/hep.20701].
 20. Bedossa P. Histopathological algorithm and scoring system for evaluation of liver lesions in morbidly obese patients. *Hepatology*, 2012; 56: 1751-1759. [DOI: 10.1002/hep.25889].
 21. Angulo P. Nonalcoholic fatty liver disease. *N Engl J Med* 2002; 346: 1221-1231. [DOI: 10.1056/NEJMra011775]
 22. Singh S, Allen AM, Wang Z, Prokop LJ, Murad MH, Loomba R. Fibrosis progression in nonalcoholic fatty liver vs nonalcoholic steatohepatitis: a systematic review and meta-analysis of paired-biopsy studies. *Clin Gastroenterol H*, 2015; 13: 643-654. [DOI: 10.1016/j.cgh.2014.04.014].
 23. Kishida N, Matsuda S, Itano O, Shinoda M, Kitago M, Yagi H, Abe Y, Hibi T, Masugi Y, Aiura K, Sakamoto M, Kitagawa Y. Development of a novel mouse model of hepatocellular carcinoma with nonalcoholic steatohepatitis using a high-fat, choline-deficient diet and intraperitoneal injection of diethylnitrosamine. *BMC Gastroenterology* 2016; 16:61. [DOI: 10.1186/s12876-016-0477-5]
 24. McPherson S, Hardy T, Henderson E, Burt AD, Day CP, Anstee QM. Evidence of NAFLD progression from steatosis to fibrosing-steatohepatitis using paired biopsies: implications for prognosis and clinical management. *J Hepatol*, 2015; 62: 1148-55. [DOI: 10.1016/j.jhep.2014.11.034].
 25. Auberval N, Dal S, Bietiger W, Pinget M, Jeandidier N, Maillard-Pedracini E, Schini-Kerth V, Sigrist S. Metabolic and oxidative stress markers in Wistar rats after 2 months on a high-fat diet. *Diabetology & Metabolic Syndrome* 2014; 6: 130. [DOI: 10.1186/1758-5996-6-130]
 26. Mohamed AA, Sabry S, Abdallah AM, Elazeem NAA, Refaey D, Algebaly HAF, Fath GAE, Omar H. Circulating adipokines in children with nonalcoholic fatty liver disease: possible noninvasive diagnostic markers. *Annals of Gastroenterology*, 2017; 30: 457-463. [DOI: 10.20524/aog.2017.0148].
 26. Bedossa P. Pathology of non-alcoholic fatty liver disease. *Liver Int*, 2017; 37: 85-89. [DOI: 10.1111/liv.13301].
 27. Zhang QZ, Liu YL, Wang YR, Fu LN, Zhang J, Wang XR, Wang BM. Effects of telmisartan on improving leptin resistance and inhibiting hepatic fibrosis in rats with non-alcoholic fatty liver disease. *Exp Ther Med*, 2017; 14: 2689-2694. [DOI: 10.3892/etm.2017.4809].
 28. Dowman JK, Hopkins LJ, Reynolds GM, Nikolaou N, Armstrong MJ, Shaw JC, Houlihan DD, Lalor PF, Tomlinson JW, Hübscher SG, Newsome PN. Development of Hepatocellular Carcinoma in a Murine Model of Nonalcoholic Steatohepatitis Induced by Use of a High-Fat/Fructose Diet and Sedentary Lifestyle. *Am J Pathol*, 2014; 184: 1550-61. [DOI: 10.1016/j.ajpath.2014.01.034].
 29. Ludwig J, Viggiano TR, McGill DB, Oh BJ. Nonalcoholic steatohepatitis: Mayo Clinic experiences with a hitherto unnamed disease. *Mayo Clin Proc*, 1980; 55: 434-8. [PMID: 7382552].
 30. Kleiner DE, Brunt EM. Nonalcoholic fatty liver disease: pathologic patterns and biopsy evaluation in clinical research. *Semin Liver Dis*, 2012; 32: 3-13. [DOI: 10.1055/s-0032-1306421].
 31. Angulo P. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology*, 2015; 149: 389-393. [DOI: 10.1053/j.gastro.2015.04.043].
 32. Santiago-Rolón A. A Comparison of Brunt Criteria, the Non Alcoholic Fatty Liver Disease Activity Score (NAS) & a Proposed NAS-including fibrosis as Valid Diagnostic Scores for NASH. *Puerto Rico health sciences journal*, 2015; 34: 189. [PMCID: PMC4720965].