Original Article

Non-Alcoholic Fatty Disease of Liver in Obese Persons, an Underappreciated Risk

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ABSTRACT

Objective: To assess the incidence of NAFDL among local obese population, relate it with USG grading of fatty change in liver and to highlight the issue and sensitize both general population and the medical community to recognize its importance for early diagnosis and interventions.

Study Design: Observational cross section study

Place and Duration of Study: This study was conducted at the Rai Medical College teaching Hospital, Sargodha from Jan. 2021 to Dec, 2021 for a period of one-year.

Materials and Methods: The patients attending the medical OPD between the ages of 20-70 years, both genders were selected for this Observational study, convenient sampling. Ideal body weight, BMI and B-Mode USG were recorded to measure hepatic size and parenchymal echogenicity as per standard.

Results: 1010 Patients, 700 females, 310 males participated. All the % calculations are for the total number of patients. When assessed by USG, in the Normal weight category only 3% had normal parenchymal echotexture of liver (nPEL), 19% had Grade 1 Fatty liver (FL), 3% had Grade 2 FL and none had Grade 3 FL. In overweight category none had nPEL, 26% had Grade 1 FL, 32% had Grade 2 FL and none had Grade 3 FL. In obese category none had nPEL, 7% had Grade 1 FL, 10% had Grade 2 FL and none had Grade 3 FL. When assessed by USG, in the <25 BMI category 1% had nPEL, 12% had Grade 1 FL, 4% had Grade 2 FL and none had Grade 3 FL. In 25.0-29.9 BMI category none had nPEL, 25% had Grade 1 FL, 19% had Grade 2 FL and none had Grade 3 FL. In 30-35 BMI category none had nPEL, 16% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL. In >35 BMI category none had nPEL, 8% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL.

Conclusion: Early detection of HPE changes and sensitization to its future implication as a risk factor for CLD and even HCC among both medical community and general public must be the priority in our professional circles. It shall be highlighted in all clinical conferences because early interventions in terms of lifestyle modifications targeted to not only weight reduction but more importantly weight maintenance have a great potential for reversal of all these changes.

Key Words: Obesity, BMI, NAFDL, IR, Metabolic Syndrome

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INTRODUCTION

Inspite of the efforts of all the divine sermons, health professionals' warnings, social reformists appeal, chronic and excessive alcoholism remains the leading cause of CLD followed by chronic HCV infection and its sequel, the CLD, in our population. Excess fat deposition in the liver and other tissues is a well-known metabolic consequence of IR.

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Now Non-Alcoholic Fatty liver technically called Non-Alcoholic Steohepatitis (NASH) and NAFDL are becoming the leading hepatic pathologies in both. [1-3]

Visceral adiposity is an independent risk factor for insulin resistance, Type 2 Diabetes mellitus (T2DM) and associated cardiovascular (CV) risks. Taylor has proposed that ectopic fat deposition in the liver and islets underlies the development of hepatic insulin resistance and βcell dysfunction.[4-6] Grey scale ultrasound is a reliable, non-invasive, cheap and readily available parameter used worldwide for estimation of hepatic fatty change and severity grading.[7, 8]

Obesity is a known phenomenon from the known human history. Untill recently, in most of the cultures it was a desired beauty feature and a reflection of upper socioeconomic class. All the Egyptian, Persian, European and Indian queens and princesses are always portrayed a little bit plump. All the goddess sculptures have quite a contour of tummy and bumps. Industrial

revolution led us into an era of ever-expanding ease of procuring diet, the food and beverage industry packed our dining tables with concentrated calories foods, appetizers and delicacies. This resulted into epidemic of obesity with all its known complication, from metabolic syndrome (MS) making Ischemic Heart disease (IHD) (CHD and Cerebro-vascular Accidents (CVA) being the top killers to a range of pelvic and intestinal malignancies, musculoskeletal issues, fertility and obstetric problem and surgical issues. The worldwide prevalence of overweight and obesity has doubled since 1980 to an extent that nearly a third of the world population, 1.9 billion, and out of these 609 million were adolescents or young adults, a staggering 39%, was classified as overweight or obese by 2015 figures.

MATERIALS AND METHODS

This study was carried out on all of our consenting and affording obese patients presenting to Medical OPD between the ages of 20-70 years, both genders.

After securing informed consent, basic biodata, validating the diagnosis of obesity on anthropometric criteria and applying exclusion criteria, abdominal USG findings were recorded. Ideal body weight, BMI and B-Mode ultrasound evaluation was done to measure hepatic size and assess parenchymal echogenicity as per standard tables and calculations.

Inclusion Criteria: 20-70 years age, both sexes, Obesity.

Exclusion Criteria:

Seriously sick patient or terminally ill patient.
Non treated Chronic HBV and HCV disease
Established cirrhosis of liver
Alcohol use in last 3 years
Any other cause of hepatomegaly or CLD
Pregnancy
Ascites of any etiology
Major end organ disease, liver, kidney, heart, lungs
Active steroid use in last 6 months
Hypothyroidism
Human Immunodeficiency Virus
Gastrointestinal by-pass surgery
History of liver surgery.

Study Design: Observational cross section study.

Study Period: From January to December, 2021.

Sample Size and Sampling Technique: A sample size of 392 patients was calculated as minimum required to maintain a 5% margin of error and 95% confidence interval using WHO sample size calculator.

Statistical Analysis: Data analysis was conducted using Microsoft Excel version 2016 and Statistical Package for Social Sciences software version 25. Descriptive statistics (i.e. frequency distribution, percentages, mean and standard deviations) was the primary analytical methods.

We calculated the incidence of NAFLD in different age decades in both sexes and in different weight and BMI groups.

RESULTS

In this study, out of 1010 patients, 700 were females and 310 were males, completed the study. These were divided into Normal Weight, Overweight and Obese categories as per standard. BMI Groups are divided into <25, 25-29.9, 30-35 and >35.

Table No.1: Ideal Body Weight and Liver Fat. All % calculated for total number of patients in the group. (N 1010)

Weight Category	Total Patients	Liver Fat			
		Nor. Liv.	F. Liv. 1	F. Liv. 2	F. Liv. 3
Normal	170	70	90	10	0
		(6.93±1.17%)	(8.91±1.20%)	(0.99±1.01%)	(0.00±0.00%)
Overweight	440	170	90	80	100
		(16.83±0.95%)	(8.91±0.99%)	(7.92±1.21%)	(9.90±1.00%)
Obese	400	0	240	160	0
		(0.00±0.00%)	(23.76±0.76%)	(15.84±1.09%)	(0.00±0.00%)

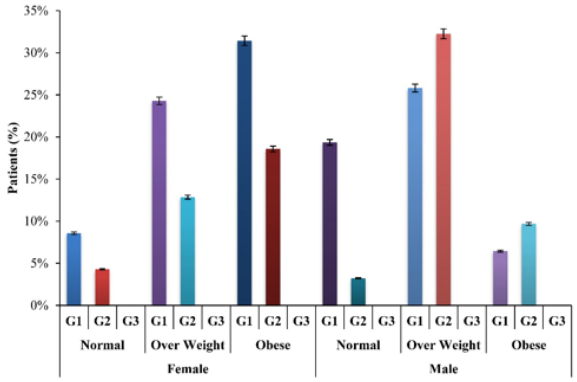

Figure No.1: Obesity and Nafdl

On USG, in the Normal weight category only 7% had nPEL, 9% had Grade 1 FL, 1% had Grade 2 Fatty liver and no person had Grade 3 FL. In overweight category17% had nPEL, 9% had Grade 1 FL, 8% had Grade 2 FL and 10% person had Grade 3 FL. In obese category no person had nPEL, 24% had Grade 1 FL, 16% had Grade 2 FL and no person had Grade 3 FL. Same is presented graphically in Graph A.

Two important trend needs to be noted, inspite of the body weight being in the normal range around 10% still had FL, on the other hand all in obese category had FL. The Grade 3 fatty changes were not seen in obese persons while 10% in overweight category had G3 FL.

As expected % of persons having FL follows the increase in weight both in G1 and G2, it was not seen in G3. Deposition of fat in liver is a multifactorial process, genetic background, sedentary lifestyle, fructose intake and pattern of fat storage reflected in Waist: Hip Ratios and Waist Circumference, both gender dependent, being the notable ones.

When BMI figures are combined for both gender, in the <25 BMI category 1% had nPEL, 12% had Grade 1FL, 4% had Grade 2 FL and none had Grade 3 FL. In 25-29.9 BMI category none had nPEL, 25% had Grade 1 FL, 19% had Grade 2 FL and none had Grade 3 FL. In 30-35 BMI category none had nPEL, 16% had Grade 1 FL, 8% had Grade 2 FL and none had Grade 3 FL. In >35 BMI category none had nPEL, 8% had Grade 1 FL, another 8% had Grade 2 FL and none had Grade 3 FL. Same is presented graphically in Graph B.

Table No.2: BMI and liver fat. All % calculated for total number of patients in the group. (N 1010)

BMI	Total Patients	Liver Fat			
		Nor. Liv.	F. Liv. 1	F. Liv. 2	F. Liv. 3
< 25	170	10	120	40	0
		(0.99±0.67%)	(11.88±0.63%)	(3.96±0.62%)	(0.00±0.00%)
25 – 29.9	440	0	250	190	0
		(0.00±0.00%)	(24.75±0.60%)	(18.81±0.58%)	(0.00±0.00%)
30 – 35	240	0	160	80	0
		(0.00±0.00%)	(15.84±0.71%)	(7.92±0.91%)	(0.00±0.00%)
> 35	160	0	80	80	0
		(0.00±0.00%)	(7.92±0.80%)	(7.92±0.76%)	(0.00±0.00%)

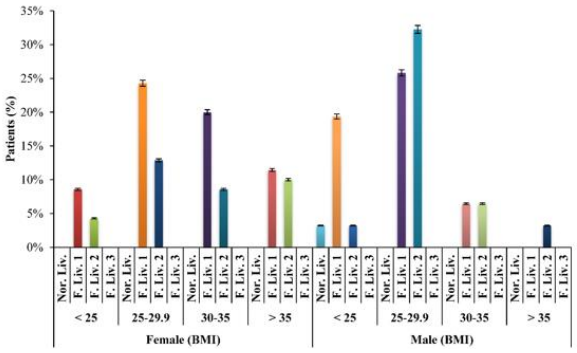

Figure No.2: BMI and NAFDL

DISCUSSION

Body mass index (BMI) is typically used to define overweight and obesity in epidemiological studies. Greater cardio-metabolic risk has also been associated with the localization of excess fat in the visceral adipose tissue and ectopic depots (such as muscle and liver), as well as in cases of increased fat to lean mass ratio (e.g. metabolically-obese normal-weight).[5] The age-standardized prevalence of being overweight or obese has increased almost 50% and 80% respectively over the past 35 years with female predominance. In low-income countries it's generally higher among middle-aged adults from wealthy and urban environments (especially women); whereas in high-income countries it affects both sexes and all ages, but is disproportionately greater in disadvantaged groups associated with adoption of an energy- and fat-rich diet and a sedentary lifestyle. It's one of the leading underlying causes of both NASH and NAFDL. Abdominal USG is the widely available, affordable, non-invasive tool to pick fatty infiltration of liver.[9]

Obesity andT2D both predispose to development of NAFLD. Early in the course, histologically, it's called steatosis or nonalcoholic fatty liver (NAFL). With hepatocytes degeneration and inflammation it's called nonalcoholic steatohepatitis (NASH). With advancement, fibrosis typical of cirrhosis sets in. All is clubbed together as NAFDL. Normally slowly progressing (on average 14 years to progress to next stage of fibrosis), in upto 20% of cases it progress rapidly to advanced fibrosis. Risk factors for rapid progression of fibrosis in NAFLD includes the existence of NASH on histology, advancing age, moribund obesity, excessive fructose intake, presence of insulin resistance and poorly controlled DM reflected as high HbA1c levels, post-menopause years and high ALT.[10]

Two important trend needs to be noted, inspite of the being in the <25 BMI category only 1% had normal liver but 12% had Grade 1 Fatty liver and 4% had Grade 2 Fatty liver. In 25 and above categories none had normal liver. The Grade 3 fatty changes were not seen in any of the BMI categories. In both 25-29.9 and 30-35 BMI categories maximum numbers had G1 and G2 changes as expected. This was not seen in >35 BMI group, this phenomenon is well explained on the basis of "Metabolically Healthy Obese Persons" who are not at risk of developing DM, HTN and Lipid abnormalities. Deposition of fat in liver is a multifactorial process, genetic background, sedentary lifestyle, fructose intake and pattern of fat storage reflected in Waist: Hip Ratios and Waist

Circumference, both gender dependent, being the notable ones. These results very loudly justify the need for similar studies. NAFDL is now an established entity with its significant role established as an underlying pathophysiological mechanism underlying the development of IR and its metabolic consequences leading to early and advanced atherosclerotic sequel.

In Men incidence of fatty liver remains stable from 30s through 60s but women catchup during 60s to match men.[10] Global burden of NAFLD related CLD is now estimated to be around 25%. The focus has now shifted from simply reflecting metabolic Syndrome (MetS) to the major underlying pathophysiologic mechanism of Insulin resistance in a bidirectional cause and effect mode for T2DM.[11]

The American Association of Liver Diseases predicts that NAFLD will surpass the chronic alcoholism as the as the leading cause for CLD and the indication for liver transplant due to the twin epidemics of obesity and DM. As Asians especially Indian populations are known to have more intra-abdominal adipose tissue for the same weight and height than white Caucasians (9-32% prevalence), almost half are reported to have clinical evidence of full-blown MetS. NAFLD precedes MetS starting from early childhood and keeps on increases with age[12]. The adult treatment panel III (ATP III) is considering to include NAFDL in the list of inclusion criteria for MetS. This alarming prevalence has led to a separate definition of MetS for children and adolescents. Recently NAFDL variant in lean individuals are being recognized increasingly.[13]

Ultrasonographic changes in liver and/or serum Alanine Aminotransferase (ALT) are used in all epidemiological studies of NAFDL inspite of the well-known limitations at both end of spectrum: US detects changes only when liver fat is more than 30% and ALT levels may be normal in advanced disease called "burned-out NASH".[11] The overall sensitivity and specificity of ultrasound in detection of moderate to severe fatty liver have been shown to be accurate and comparable to those of histology. [7,8] Liver biopsy is the gold standard for documenting and assessing the severity of NAFLD: The magnetic resonance (MR) techniques are very good non-invasive surrogate for initial assessment and for monitoring change over time and with interventions.[14] Quantitative assessment of liver fat by MRI-PDFF is now increasingly being recommended as an endpoint in NAFLD/NASH trials.[15,16].

CONCLUSION

After reviewing the literature and interpreting this study, it is very clear that HPE changes in the NAFLD is not only a simple reflexion of excess fat deposition like in other organs like subcutaneous tissue and around the abdominal viscera. USG is most cost-effective due to its wide availability, reliability in diagnosing and reproducibility in following changes both for better or worse, being cheap and non-invasive nature makes it ideal for early diagnosis of HPE in NAFDL cases in obese persons. Early detection of HPE changes and sensitization to its future implication as a risk factor for CLD and even HCC among both medical community and general public must be the priority in our professional circles. It shall be highlighted in all clinical conferences because early interventions in terms of lifestyle modifications targeted to not only weight reduction but more importantly weight maintenance have a great potential for reversal of all these changes.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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