Assessment of Non-Alcoholic Fatty Liver Disease in Adolescents with Malnutrition: A Cross-Sectional Study

Pawan Nimbhorkar[1], Dr. Akshai B.[2], Rakesh Thamke[3], Vijay Kamale[4]

[1]Junior Resident, Department of Family Medicine, MGM Medical College& Hospital, Navi Mumbai
Corresponding Author E-mail ID: *pawannimbhorkar95[at]gmail.com*
Contact No: 9561944606 / 8830908210

[2]Corresponding Author, Assistant Professor, Karuna Medical College, Vilayodi
E-mail ID: *akshaifreat[at]gmail.com*

[3]Associate Professor & Head, Department of Family Medicine, MGM Medical College& Hospital, Navi Mumbai
E-mail ID: *rthamke[at]yahoo.com*

[4]Professor & Head, Department of Pediatrics, MGM Medical College& Hospital, Navi Mumbai
E-mail ID: *drvijaynkamale[at]gmail.com*

Abstract: ***Introduction**: NAFLD is the most common liver disorder and its increased worldwide prevalence in adolescents is associated with the global obesity epidemic. NAFLD is strongly associated with malnutrition (under nutrition as well as obesity). The prevalence of lean NAFLD or non-obese NAFLD is also increasing. NAFLD has a close association with obesity, CV disease, diabetes mellitus and hepatocellular carcinoma, thus increasing occurrence of NAFLD is a matter of concern, as it is associated with increased morbidity and mortality. Indian data is scarce; therefore, the present study was undertaken to assess NAFLD in adolescents with malnutrition (under nutrition as well as obesity). **Objectives**: To assess NAFLD in adolescents with malnutrition (under nutrition as well as obesity). **Material & Methods**: A cross sectional study was conducted at MGM Medical College & Hospital, Navi Mumbai and MGM School, Nerul including 60 adolescents between age group of 12 to 19 years. Demographic details and anthropometric measurements were done for the children with necessary permission before the start of the study. Anthropometry was done using standard guidelines and WHO charts were used for classification of obese and underweight. USG abdomen and biochemical investigations were done for diagnosis of NAFLD. **Result**: We included 60 study subjects in our study. The average age of study subjects was 18.43±0.78 years ranged from 17 years to 19 years, among which 53.3% (n=32) were females. According to BMI for age, 50% (n=30) of subjects were obeseand50% (n=30) were underweight. Inpatients categorized according to BMI as an obese and underweight group, the SGOT and SGPT levels were significantly associated (p=0.04, p=0.04), whereas USG abdomen findings were not significantly associated (p=0.12). Similarly, in patients categorized according to WHR as normal, obese, and overweight, had a significant association with SGOT, SGPT levels and USG abdomen findings (p=0.02, p=0.02, p=0.034). **Conclusion**: BMI and WHR along with biochemical parameters can be used to predict the risk of NAFLD in adolescents in resource-poor setup.*

Keywords: Non-alcoholic fatty liver disease (NAFLD), obese adolescents, malnutrition, under nutrition, lean NAFLD.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is a broad term used to express a spectrum of conditions including hepatic steatosis without inflammation (non-alcoholic fatty liver), non-alcoholic steatohepatitis (NASH), and cirrhosis [1]. It is the most common liver disorder and its prevalence in western nations ranges from 20 to 30% and around 34% of children are followed in obesity clinics [2] [3]. NAFLD has a close association with obesity, CV disease, diabetes mellitus and hepatocellular carcinoma, thus increasing occurrence of NAFLD is a matter of concern, as it is associated with increased morbidity and mortality [4] [5].

NAFLD is characterized by the deposition of fat in more than 5% of hepatocytes in the absence of other causes of steatosis [6]. Currently, the increased occurrence of NAFLD is associated with the global obesity epidemic and is considered to be a hepatic manifestation of metabolic syndrome [7]. The prevalence of lean NAFLD or non-obese NAFLD is also increasing, such individuals may experience similar complications compared to obese NAFLD. Its occurrence in adolescents is ranging from 8% (in developed countries) to 16% (Asia Pacific region) [8] [9]. Moreover, urbanization, socioeconomic status and diet and physical activity are associated with the NAFLD [10].

Children with malnutrition are characterized by wasting, edema, hair discoloration, and hepatomegaly [11] and are known to have an electrolyte imbalance, increased oxidative stress, hepatic steatosis and decreased albumin synthesis [12] [13]. Compared to obese individuals, NAFLD is poorly characterized in adolescents with lean NAFLD and malnutrition. Therefore, the present study was undertaken to assess NAFLD in adolescents with malnutrition (under nutrition as well as obesity).

2. Literature Survey

NAFLD is defined as the accumulation of fat in >5% of hepatocytes in absence of secondary causes including alcohol or drugs. It incorporates a spectrum of diseases from NAFL to NASH, fibrosis, and cirrhosis. Currently, NAFLD is the leading cause of chronic liver diseases globally [14]. The overall global incidence of NAFLD is around 25%, ranging from 13%, 23%, and 27.4% in Africa, Europe and Asia respectively [15].

The two-hit hypothesis of pathogenesis of NAFLD has now been surpassed by a multi-hit model incorporating multiple interlocking processes such as lipotoxicity, innate immune activation, and microbiome on a background of genetic and environmental factors [16]. Most of the NAFLD subjects are always obese with association with pathogenic conditions [17]. Adoption of a sedentary lifestyle, less physical activity, availability of excess food calories is leading to the increasing prevalence of obesity. A higher risk of NAFLD is seen in children who gain weight during their school years than the weight gain in late adulthood [18].

It is reported that around 15-21% of Asian patients with NAFLD are non-obese ranging from 17% (Taiwan) to 75% (India). Moreover, the proportion of non-obesity can be high as 45% in adolescents with NAFLD [19] [20]. Lean NAFLD is associated with the heterogeneous spectrum of diseases resulting from various etiologies including dual alcoholic and non-alcoholic fatty liver disease, congenital and acquired lipodystrophy, genetic factors, congenital defect of metabolism, endocrine disorders, jejunoileal bypass, starvation or the receipt of total parental nutrition [21][22]. Metabolic disorders (Cystic fibrosis, Wilson's disease, α-1 antitrypsin deficiency, galactosemia, hereditary fructose intolerance), celiac disease, hepatitis C, diabetes mellitus, drug toxicity are less common causes of the steatosis [23]. Also, maternal overnutrition, gestational diabetes mellitus, intrauterine growth retardation and antibiotic use during pregnancy and infancy may be associated with an increased risk of NAFLD in children [24].

The diagnosis of NAFLD involves the identification of steatosis in the absence of a secondary cause followed by risk stratification for the presence of NASH and significant fibrosis [25]. For the diagnosis of 'Steatosis', Ultrasound is modality of choice and serological markers such as Fatty Liver Index (FLI), NAFLD Fat Score (NAFLD FS), and Hepatic Steatosis Index (HIS) can also be used [26] [27]. For diagnosis of 'Fibrosis', Fibroscan can be done along with scores like FIB-4 score, NFS (NALFD Fibrosis Score), etc [28].

Goyal P. et al conducted study in 2018 at Punjab to study correlation of NAFLD with BMI and biochemical markers. Goyal P. et al concluded that Z-BMI, mid arm circumference, waist circumference and ALT, AST, GGT, Triglycerides (TG), fasting blood glucose, HSCRP and uric acid were significantly higher in NAFLD and HDL-c was lower. They stated that the most significant associated risk factors with NAFLD were TG and Z-BMI. An early lifestyle interventional approach for the treatment of NAFLD can prevent NASH [29].

Anderson et al performed a systemic review and meta-analysis to estimate the prevalence of NAFLD in young people and to determine whether this varies by BMI category, gender, age. Anderson et al found that prevalence was generally higher in males compared with females and increased incrementally with greater BMI [30].

Alavian SM et al. performed a study on 966 children aged 7-18 years in Iran to investigate the prevalence of NAFLD in Iranian school-aged children and adolescents and to study association of NAFLD with biochemical and anthropometric measures. Alavian SM et al concluded that NAFLD was significantly associated with increasing age, waist circumference, ALT, fasting insulin and increased total cholesterol, LDL cholesterol and triglycerides [31].

Management of NAFLD consists of Life style modification, weight loss (if BMI>25 kg/m^2), decreased consumption of fats/ oils, daily exercise and controlled glycaemic levels (if diabetic) [32] [33].

3. Material & Methods

This observational cross-sectional study was conducted at MGM Medical College & Hospital, Kamothe, Navi Mumbai and MGM School, Nerul from July 2020 to October 2021 after Institutional Ethical & Scientific committee approval. Adolescents between age group of 12 to 19 years were taken into study after taking written informed consent from parents of children. Children with a previous history of chronic liver disease, having medication that can cause steatosis or altered liver function and other conditions that may affect the liver function such as pregnancy and substance abuse were excluded from the study.

Data collection was done by interviewing the mother/ father/ attending guardian using a case record which contained demographic variables and anthropometry. The demographic variables included were name, age, gender, address. Anthropometry included height, weight, waist circumference and hip circumference were measured using standard guidelines [34][35]. Further, BMI (Body Mass Index)and WHR (Waist-Hip Ratio) were calculated using this data. Based on the World health organisation (WHO) charts for 'BMI for age', children were classified as obese (BMI for age > +1 SD) and underweight (BMI for age < -1 to -2 SD) respectively.

Adolescents who were malnourished (obese, underweight) were selected with the help of purposive sampling technique by taking into consideration of their BMI. The sample size of 60 (30 obese and 30 underweight) was calculated by taking overall 10 % prevalence of malnutrition, 95% confidence level and 10 % margin of error.

Ultrasonography of Abdomen of all 60 patients was done. Five-point ultrasonographic criteria of diagnosis of fatty liver disease recommended by Dasharty's was used to diagnose NAFLD: (1) Increased hepatic brightness (hyper-echogenicity), (2) posterior attenuation of the right lobe, (3) increased contrast between the right kidney and liver, (4) loss of visualization of the right diaphragm and (5) diminished visibility of the intra hepatic vessels [36].Also, fasting venous blood samples were obtained from all 60 patients and used for the assessment of SGOT, SGPT, Lipid profile (total cholesterol, LDL, HDL, TG), FBSL (Fasting blood sugar levels) and HbA1c.

Statistical Analysis

Data were analysed using Stat V 13 software. Continuous variables were shown in Mean ± SD whereas, categorical variables were presented in percentage and frequency. The odds ratio was assessed to find the association between the exposure and outcome. The p-value is less than or equal to 5% considered as significant.

4. Results

Table 1: Distribution of subjects according to age

Age (Years)	Frequency (n)	Percentage (%)
17	11	18.3
18	12	20
19	37	61.7

Table 2: Frequency distribution of gender

Gender	Frequency (n)	Percentage (%)
Male	28	46.7
Female	32	53.3

Total 60 adolescents were included in our study.

From table no. 1, The average age of the children was 18.43±0.78 years ranged from 17 years to 19 years. From table no. 2, among the included subjects, 53.3% (n=32) were female and 46.7% (n=28) were male.

Table 3: BMI diagnosis of subjects

BMI diagnosis	Frequency (n)	Percentage (%)
Obese	30	50
Underweight	30	50

Table 4: Age wise distribution of BMI percentile

BMI Percentile	Age(Years)					
	17(n)		18(n)		19(n)	
	Obese	Underweight	Obese	Underweight	Obese	Underweight
<5th	0	8	0	2	0	12
<95th	2	0	6	0	12	0
>5th	0	0	0	1	0	2
85th – 95th	0	0	2	0	8	0
5th–10th	0	1	0	1	0	3
Total	2	9	8	4	20	17

Table 5: WHR (Waist Hip Ratio) diagnosis of subjects

WHR diagnosis	Frequency (n)	Percentage (%)
Normal	31	51.7
Obese	16	26.7
Overweight	13	21.6

According to BMI for age, 50% (n=30) of subjects were obese and 50% (n=30) were underweight (Table No. 3). Most of 17-year-old participants were under weight (n=9) whereas, in 18 and 19-year-old subjects majority were obese (n=8, n=20) (Table No. 4).

According to WHR (Waist Hip Ratio), 51.7% (n=31) of subjects were normal whereas, 26.7% (n=16) and 21.7% (n=13) were obese and overweight respectively (Table No. 5).

Table 6: Distribution of BMI categories according to USG abdomen findings

USG abdomen findings	Obese group, n (%)	Underweight group, n (%)
Mild hepatomegaly with grade1 fatty liver	5 (16.7)	1 (3.3)
Mild hepatomegaly with grade2 fatty liver	1 (3.3)	0
No abnormality	24 (80)	29 (96.7)

Paper ID: MR23329161839 DOI: https://dx.doi.org/10.21275/MR23329161839

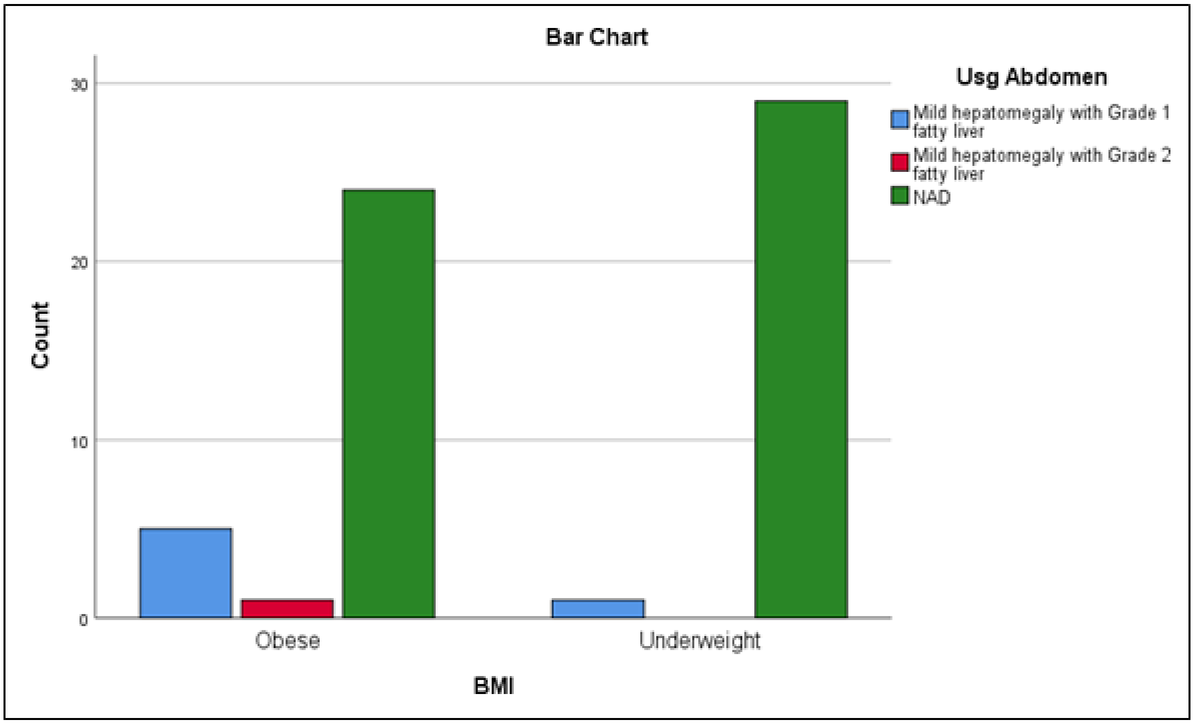

Figure 1: Distribution of BMI categories according to USG abdomen findings

Table 7: Distribution of WHR categories according to USG abdomen findings

USG abdomen Findings	Normal, n (%)	Obese, n (%)	Overweight, n (%)
Mild hepatomegaly withgrade1 fatty liver	1 (3.2)	1 (6.3)	4(30.8)
Mild hepatomegaly withgrade2 fatty liver	0	1 (6.3)	0
No abnormality	30 (96.8)	14 (87.5)	9(69.2)

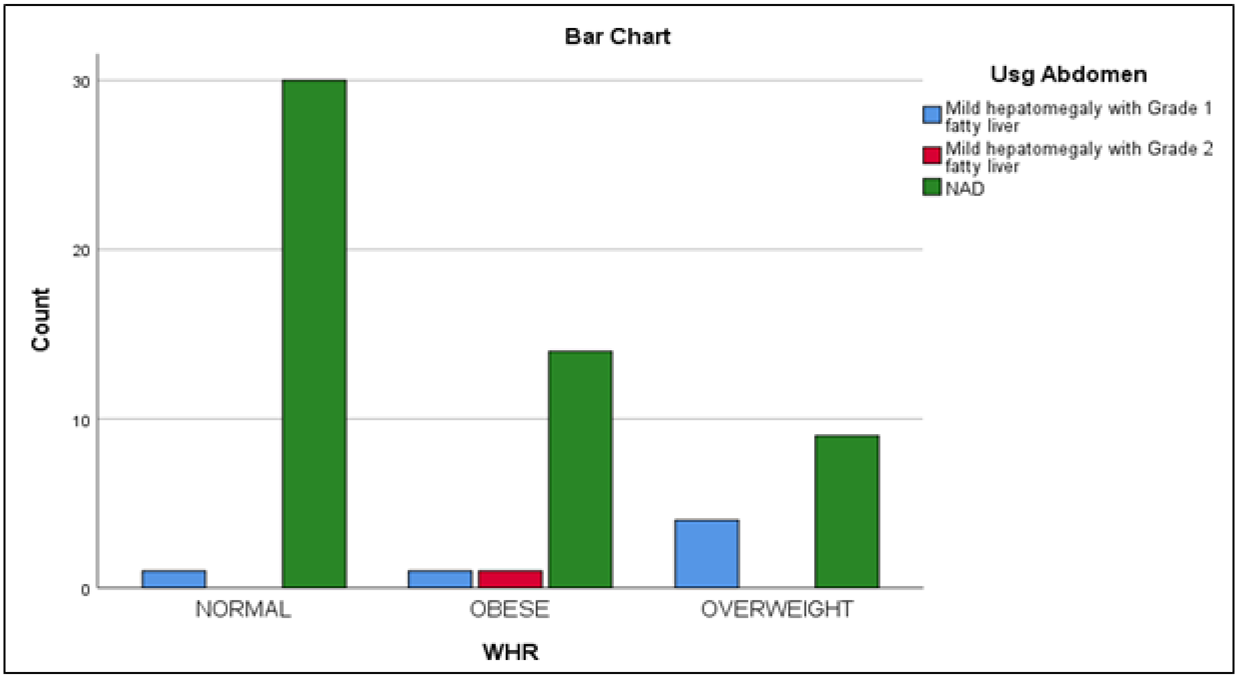

Figure 2: Distribution of WHR categories according to USG abdomen findings

From table no. 6, USG abdomen assessment in obese participants showed mild hepatomegaly with grade 1 fatty liver in 5 subjects (16.7%) and hepatomegaly with grade 2 fatty liver in 1subject(3.3%),whereas, in 24 subjects (80%) no abnormality was detected. In underweight patients, USG abdomen suggested mild hepatomegaly with grade 1 fatty liver in 1 subject (3.3%). No abnormality was detected in 29 subjects (96.7%).. Obesity and underweight were insignificantly associated with the USG abdomen findings (p=0.12).

From table no. 7, Participants who were categorized according to WHR as normal, obese, and overweight, the USG abdomen findings showed mild hepatomegaly with grade 1 fatty liver in 1 (3.2%), 1 (6.3%), and 4 (30.8%) subjects respectively. A significant association was found between WHR categories and USG findings (p=0.02).

Table 7: Distribution of BMI categories according to SGOT

SGOT	Obese group, n (%)	Underweight group, n (%)
Normal	24 (80)	29 (96.7)
Abnormal	6 (20)	1 (3.3)

Table 8: Distribution of BMI categories according to SGPT

SGPT	Obese group, n (%)	Underweight group, n (%)
Normal	24 (80)	29 (96.7)
Abnormal	6 (20)	1 (3.3)

In patients categorized according to BMI as an obese and underweight group, SGOT levels were abnormal in 6 (20%) and 1 (3.3%) patients respectively (Table no. 7).There is significant association observed between SGOT levels and patients who were obese and underweight (p=0.044). Whereas, the SGPT levels were normal in 24 (80%) and abnormal in 29 (96.7%) patients (Table no.8). There is significant association of obesity and underweight with SGPT levels (p=0.044).

Table 9: Distribution of WHR categories according to SGOT findings

WHR	SGOT	
	Normal, n (%)	Abnormal, n (%)
Normal	30(96.8)	1(3.2)
Obese	14(87.5)	2(12.5)
Overweight	9(69.2)	4(30.8)

Table 10: Distribution of WHR categories according to SGPT findings

WHR	SGPT	
	Normal, n (%)	Abnormal, n (%)
Normal	30 (96.8)	1 (3.2)
Obese	14 (87.5)	2 (12.5)
Overweight	9 (69.2)	4 (30.8)

For participants who were categorized according to WHR as normal, obese, and overweight, the SGOT was abnormal in 1 (3.2%), 2 (12.5%), and 4 (30.8%) subjects (Table no. 9), whereas SGPT was abnormal in 1 (3.2%), 2 (15.5%), and 4 (30.8%) subjects respectively (Table no. 10). There is significant association of WHR with SGOT (P=0.034) and SGPT (P=0.034).

Table 11: Distribution of participants according to blood parameters

Variable-Median	Obese	Underweight
SGOT	78	82
SGPT	85.5	85
TOTALCHOLESTEROL	185	179
HDL	50	38
LDL	119	113
TGL	139	140
RBS	176.5	157
HBA1C	5.2	4.4

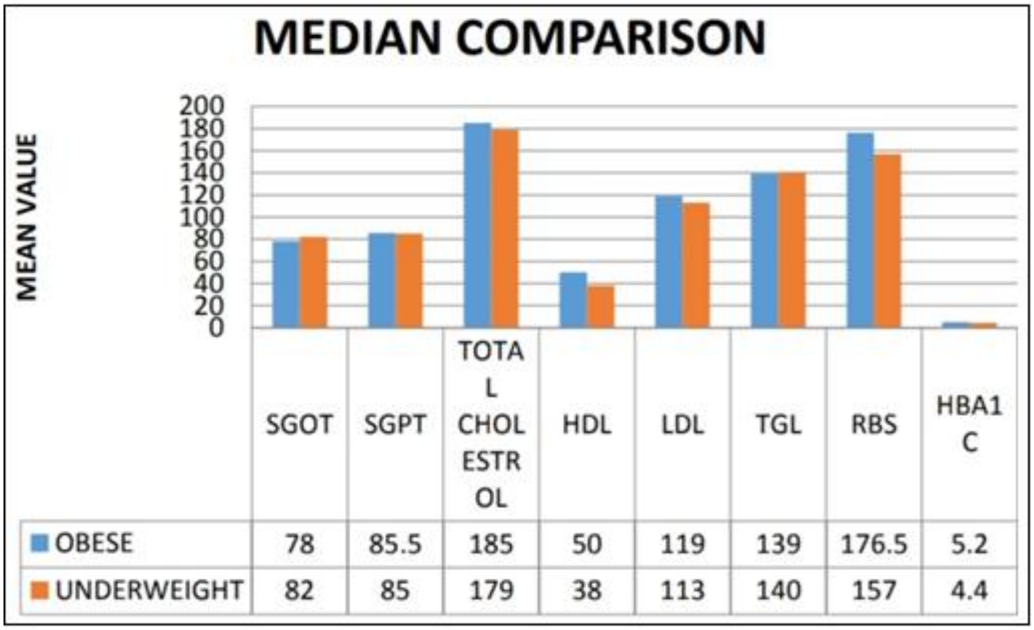

Figure 3: Distribution of participants according to blood parameters

In our study, SGPT, Total cholesterol, HDL, LDL, RBS and HbA1c levels were high in obese group whereas SGOT and Triglycerides were high in underweight group [Table no. 11 and Figure no. 3)

5. Discussion

Increased occurrence of NAFLD is associated with the global obesity pandemic. Prevalence of lean NAFLD or non-obese NAFLD is also increasing. NAFLD has a close association with obesity, CV disease, type 2 diabetes, and hepatocellular carcinoma which in turn causes increase in morbidity and mortality. The study was undertaken to assess the NAFLD in adolescents with malnutrition (obese and under nutrition). Total 60 adolescents were included in this study. The average age of study subjects was 18.43±0.78years ranged from 17 years to 19 years, among which 53.3% (n=32)were female and 46.7% (n=28) were male. Similar study was done by Lin MS et al in which average age of study subjects was 15.5±2.8 years, ranged from 10 to 19 years, 50.1% being male [37].

Assessment of risk factors of fatty liver suggested that BMI is among the most common epidemiological indexes used in the assessment of obesity [38] [39] [40] [41]. The risk of fatty liver is 4.1 to 14times more in subjects with higher BMI than normal BMI individuals [42] [43]. In our study, considering the International Obesity Task Force reference for BMI, subjects were divided into obese (≥25) and underweight (<18) [44] [45]. According to age, most of 17-year-old participants had underweight (n=9) whereas, in 18 and 19-year-old subjects majority were obese (n=8, n=20).Despite being commonly used for the prediction of NAFLD, BMI has its limitations including population-specific reference or change in body composition with growth and development. These limitations are overcome by using the WHR (Waist Hip Ratio). In our study, according to WHR, 51.7% of subjects were normal whereas, 26.7% and 21.7% were obese and overweight respectively. Al-Attas OS et al also suggested that WHR is more strongly associated with obesity than BMI [46].

In our study, we found that 'BMI for age' have no significant correlation with USG abdomen findings to diagnose NAFLD (p=0.12).These findings suggested that BMI is not a dependable modality in the assessment of NAFLD in adolescents.

On the other hand, significant association was found between WHR categories and USG findings (p=0.02). Similar results were concluded by the study of Ge W, Parvez F etal [47].

In patients' categorized according to BMI', a significant association was seen between SGOT and patients who were obese and underweight (p=0.044). Similar results were concluded by Piton A. et al [48] and Kim WR et al [49]. Also, significant association was seen between SGPT and patients who were obese and underweight (p=0.044). Similar results were concluded by Tunsaringkarn T et al [50]. The SGPT is a more specific and quite sensitive biomarker for liver disease, which had exhibited its association with the prediction of mortality in patients with liver disease as demonstrated in the underweight subjects [51] [52] [53] [54]. Moreover, Ramalh et al and Pulzi et al. suggested that greater the BMI, greater the degree of liver damage [55] [56]. In contrast with these findings the study of Das AK et al. suggested no association between BMI categories and liver enzymes level [57]. The difference in the results may be due to the variation in gender, age, and dietary habits, etc.

In patients 'categorized according to WHR', a significant association was seen between SGOT and patients who were normal, obese, and overweight (p=0.02). WHR categories also have significant association with SGPT levels (p=0.034). Kelishadi R et al also concluded similar results [58].

In our study SGPT, Total cholesterol, HDL, LDL, RBS and HbA1c levels were high in obese group, whereas SGOT and Triglycerides were high in underweight group. Similar results were concluded by Mansour-Ghanaei R et al [59]. Our study found that inpatients categorized according to BMI as an obese and underweight group, the SGOT and SGPT levels were significantly associated, whereas USG abdomen findings were not significantly associated. Similarly, in patients categorized according to WHR as normal, obese, and overweight, had a significant association with SGOT, SGPT levels and USG abdomen findings.

6. Conclusion

BMI categories were significantly associated with the SGOT, SGPT levels, but not with USG abdomen scans. WHR (Waist Hip Ratio) categories were significantly associated with the SGOT, SGPT and USG abdomen scans. BMI and WHR along with biochemical parameters can be used to predict the risk of NAFLD in adolescents in resource-poor setup.

7. Future Scope

The strength of the current study was the adequate sample size and uniform application of the protocol. The limitations of the study were the investigator was not blinded and the study was single centered, altogether could have led to some bias. Various other serological variables were not evaluated in this study. Moreover, intervention to reverse the risk factors of NAFLD was not included in the scope of the present study. Further, a well-designed study of a large sample size including all variables with intervention to reverse the risk factors could provide further evidence to confirm the present study findings.

Conflicts of Interest

The authors have no conflicts of interest.

References

[1] Sattar N, Forrest E, Preiss D. 'Non-alcoholic fatty liver disease'. BMJ, 2014 Jul29;349.

[2] Bellentani S, Scaglioni F, Marino M, Bedogni G. 'Epidemiology of non-alcoholic fatty liver disease'. Digestive Diseases, 2010; 28(1):155e61.
[3] Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. 'The prevalence of non-alcoholic fatty liver disease in children and adolescents: A systematic review and meta-analysis'. PLOS One2015; 10(10):1e14.
[4] Schwimmer JB, Pardee PE, Lavine JE, Blumkin AK, CookS. 'Cardiovascular risk factors and the metabolic syndrome in pediatric non alcoholic fatty liver disease'. Circulation, 2008 Jul 15; 119(3):277e83.
[5] Mellinger JL, Pencina KM, Massar HM, Hoffman U, Seshadri S, Fox CS, et al. 'Hepaticsteatosis and cardiovascular disease outcomes: An analysis of the Framingham Heart Study'. Journal of Hepatology, 2015 Aug; 63(2):470e6.
[6] Vos MB, Abrams SH, Barlow SE, et al. 'NASPGHAN clinical practice guidelinefor the diagnosis and treatment of nonalcoholic fatty liver disease in children: recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)'. Journal of Pediatric Gastroenterology and Nutrition, 2017; 64:319-34.
[7] Wang AY, Dhaliwal J, Mouzaki M. Lean non-alcoholic fatty liver disease. ClinicalNutrition,2019; 38:975-81.
[8] Conjeevaram Selvakumar PK, Kabbany MN, Lopez R, Rayas MS, Lynch JL,Alkhouri N. 'Prevalence of suspected non alcoholic fatty liver disease in lean adolescents in the United States'. Journal of Pediatric Gastroenterology and Nutrition, 2018; 67:75-9.
[9] Fu CC, Chen MC, Li YM, Liu TT, Wang LY. 'The risk factors for ultrasound-diagnosed non-alcoholic fatty liver disease among adolescents'. Annals of the Academy of Medicine ofSingapore,2009; 38:15-7.
[10] Liu CJ. 'Prevalence and risk factors for non-alcoholic fatty liver disease in Asian people who are not obese'. Journal of Gastroenterology and Hepatology,2012; 27:1555-60.
[11] Waterlow JC. 'Protein-energy malnutrition'. (London: Edward Arnold)1992.
[12] Leite HP, de Lima LF, de Oliveira Iglesias SB, Pacheco JC, de Carvalho WB. 'Malnutrition may worsen the prognosis of critically ill children with hyperglycemia and hypoglycemia'. Journal of Parenteral and Enteral Nutrition, 2013; 37:335-341.
[13] Manary MJ, Leeuwenburgh C, Heinecke JW. 'Increased oxidative stress in kwashiorkor'. The Journal of Pediatrics,2000; 137:421-424.
[14] Maurice J, ManousouP. 'Non-alcoholic fatty liver disease'. Clinical medicine. 2018; 18(3):245.
[15] Younossi ZM. Koenig AB. Abdelatif D, et al. 'Global epidemiology of non alcoholic fatty liver disease–Meta-analytic assessment of prevalence, incidence, and outcomes'. Hepatology. 2016; 64: 73–84.
[16] Maurice J, Manousou P. 'Non-alcoholic fatty liver disease'. Clinical medicine. 2018 Jun;18(3):245.
[17] [18] MitraS, DeA, ChowdhuryA. 'Epidemiology of non-alcoholic and alcoholic fatty liver diseases'. Translational gastroenterology and hepatology. 2020;5.
[19] Liu CJ. 'Prevalence and risk factors for non-alcoholic fatty liver disease in Asian people who are not obese'. Journal of gastroenterology and hepatology. 2012Oct;27(10):1555-60.
[20] Fu CC, Chen MC, Li YM, Liu TT, Wang LY. 'The risk factors for ultrasound-diagnosed non-alcoholic fatty liver disease among adolescents'. Annals of Academy of Medicine of Singapore,2009; 38: 15–17.
[21] Younossi ZM, Stepanova M, Negro F, Hallaji S, Younossi Y, LamB, Srishord M. 'Non alcoholic fatty liver disease in lean individuals in the United States'. Medicine,2012 Nov1;91(6): 319-27.
[22] Kumar R, Mohan S. 'Non-alcoholic fatty liver disease in lean subjects: characteristics and implications'. Journal of clinical and translational hepatology, 2017Sep 28; 5(3):216.
[23] Wang AY, Dhaliwal J, Mouzaki M. Lean non-alcoholic fatty liver disease. Clinical Nutrition,2019; 38:975-81.
[24] Wesolowski SR, Kasmi KC, Jonscher KR, Friedman JE. 'Developmental origins of NAFLD: A womb with a clue'. Nature Reviews Gastroenterology and Hepatology, 2017; 14:81-96.
[25] SinnDH.KangD.ChangY,etal. 'Non-alcoholic fatty liver disease and progression of coronary artery calcium score: a retrospective cohort study'. Gut,2017. pp. 323–9.
[26] Fedchuk L. Nascimbeni F. Pais R, et al. 'Performance and limitations of steatosis biomarkers in patients with non alcoholic fatty liver disease'. Alimentary Pharmacology and Therapeutics, 2014; 40:1209–22.
[27] Byrne CD. Targher G. EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Diabetologia,2016; 59:1141–4.
[28] Castera L. 'Noninvasive evaluation of nonalcoholic fatty liver disease'. Seminars in Liver Disease, 2015; 35:291–303.
[29] Goyal P, Thapa BR, Sharma NR, Menon J, Bhatia A. 'Nutritional Assessment in Obese Children with and without Non-Alcoholic Fatty Liver Disease (NAFLD)in an Urban Area of Punjab, India'. Indian Journal of Public Health Research &Development.2018 Dec1; 9(12).
[30] Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. 'Theprevalence of non-alcoholic fatty liver disease in children and adolescents: A systematic review and meta-analysis'.PlOS one. 2015 Oct 29; 10(10):e0140908.
[31] Alavian SM, Mohammad-Alizadeh AH, Esna-AshariF,ArdalanG,Hajarizadeh B. 'Non-alcoholic fatty liver disease prevalence among school-aged children and adolescents in Iran and its association with biochemical and anthropometric measures'. Liver international, 2009 Feb; 29(2):159-63.
[32] Leoni S, Tovoli F, Napoli L, Serio I, Ferri S, Bolondi L. 'Current guidelines for the management of non-alcoholic fatty liver disease: A systematic review with comparative

analysis'. World Journal of Gastroenterology. 2018 Aug 14.
[33] Arab JP, Candia R, Zapata R, Muñoz C, Arancibia JP, Poniachik J, Soza A, Fuster F, Brahm J, Sanhueza E, Contreras J, Cuellar MC, Arrese M, Riquelme A. 'Management of non alcoholic fatty liver disease: an evidence-based clinical practice review'. World Journal of Gastroenterology. 2014 Sep 14.
[34] Dasarathy S, Dasarathy J, Khiyami A, Joseph R, Lopez R, McCullough AJ. 'Validity of real time ultrasound in the diagnosis of hepatic steatosis: A prospective study'. Journal of Hepatology. 2009; 51:1061–7.
[35] Mansour-Ghanaei R, Mansour-Ghanaei F, Naghipour M, Joukar F. 'Biochemical markers and lipid profile in non alcoholic fatty liver disease patients in the PERSIAN Guilan cohort study (PGCS), Iran'. Journal of Family Medicine and Primary Care, 2019 Mar; 8(3):923-928.
[36] Dasarathy S, Dasarathy J, Khiyami A, Joseph R, Lopez R, McCullough AJ. 'Validity of real time ultrasound in the diagnosis of hepatic steatosis: A prospective study'. Journal of Hepatology. 2009; 51:1061–7.
[37] Lin MS, LinTH, GuoSE, Tsai MH, Chiang MS, Huang TJ, ChenMY. 'Waist-to-height ratio is a useful index for non alcoholic fatty liver disease in children and adolescents: a secondary data analysis'. BMC public health. 2017Dec; 17(1):1-8.
[38] Miyake T, Kumagi T, Hirooka M, Furukawa S, Koizumi M, Tokumoto Y, UedaT, Yamamoto S, Abe M, Kitai K, Hiasa Y. 'Body mass index is the most usefulpredictive factor for the onset of non alcoholic fatty liver disease: a community-based retrospective longitudinal cohort study'. Journal of gastroenterology. 2013Mar1; 48(3):413-22.
[39] Saida T, Fukushima W, Ohfuji S, Kondo K, Matsunaga I, Hirota Y. 'Effect modification of body mass index and body fat percentage on fatty liver disease in a Japanese population'. Journal of gastroenterology and hepatology, 2014 Jan; 29(1):128-36.
[40] Loomis AK, Kabadi S, Preiss D, Hyde C, Bonato V, St. Louis M, Desai J, GillJM, Welsh P, Water worth D, SattarN. 'Body mass index and risk of non alcoholic fatty liver disease: two electronic health record prospective studies'. The Journal of Clinical Endocrinology & Metabolism. 2016 Mar 1;101(3):945-52.
[41] WangL,GuoJ,LuJ. 'Risk factor compositions of non alcoholic fatty liver disease change with body mass index in males and females'.Oncotarget, 2016Jun14; 7(24):35632.
[42] Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. 'Establishing a standard definition for child overweight and obesity worldwide: international survey'.BMJ,2000; 320:1240-3.
[43] Cole TJ, Flegal KM, Nicholls D and Jackson AA. 'Body mass index cut offs to define thinness in children and adolescents: international survey'.BMJ,2007; 335:194.
[44] Stefan N, Fritsche A, Schick F, Häring H-U. 'Phenotypes of prediabetes and stratification of cardio metabolic risk'. The Lancet Diabetes & Endocrinology.2016; 4(9):789–98.
[45] Stefan N, Schick F, Häring H-U. 'Causes, characteristics, and consequences of metabolically unhealthy normal weight in humans'.Cellmetabolism,2017; 26(2):292–300.
[46] Al-Attas OS, Al-Daghri NM, Alokail MS, et al. 'Association of body mass index, sagittal abdominal diameter and waist-hip ratio with cardio- metabolic risk factors and adipocytokines in Arab children and adolescents'. BMC Pediatrics,2012; 12:119.
[47] Ge W, Parvez F, Wu F, Islam T, Ahmed A, Shaheen I, Sarwar G, Demmer RT, Desvarieux M, Ahsan H, ChenY. 'Association between anthropometric measures of obesity and subclinical atherosclerosis in Bangladesh'. Atherosclerosis, 2014Jan 1; 232(1):234-41.
[48] Piton A, Poynard T, Imbert-Bismut F, Khalil L, Delattre J, Pelissier E, et al. ' Factors associated with serum alanine transaminase activity in healthy subjects: consequences for the definition of normal values, for selection of blood donors, and for patients with chronic hepatitis C'. MULTIVIRC Group. Hepatology, 1998 May;27(5): 1213-9.
[49] Kim WR, Flamm SL, Di Bisceglie AM, Bodenheimer HC. 'Serum activity of alanine amino transferase (ALT) as an indicator of health and disease'. Hepatology, 2008 Apr; 47(4): 1363-70.
[50] [51] - Tunsaringkarn T, Zapuang K, Rungsiyothin A. 'Association between body mass index and liver function among gasoline station workers in Bangkok, Thailand'.Journalof Health Researchk, 2015; 29(1):55-61.
[52] Piton A, PoynardT,Imbert-Bismut F, Khalil L, Delattre J, Pelissier E, et al. ' Factors associated with serum alaninetransaminase activity in healthy subjects: consequences for the definition of normal values, for selection of blood donors, and for patients with chronic hepatitis C'. MULTIVIRC Group.Hepatology, 1998 May;27(5): 1213-9.
[53] Kim WR, Flamm SL, Di Bisceglie AM, Bodenheimer HC. 'Serum activity of alanine amino transferase (ALT) as an indicator of health and disease'. Hepatology, 2008 Apr; 47(4): 1363-70
[54] St George A, Bauman A, Johnston A, Farrell G, Chey T, George J. 'Independent effects of physical activity in patients with non alcoholic fatty liver disease'. Hepatology, 2009 Jul; 50(1): 68-76.
[55] RamalhoF. ' Hepatitis C virus infection and liver steatosis'. Antiviral Research, Oct;60(2):125-7.
[56] Pulzi FB, Cisternas R, Melo MR, Ribeiro CM, Malheiros CA, SallesJE. 'New clinical score to diagnose non-alcoholic steatohepatitis in obese patients'. Diabetologu and Metabolic Syndrome, 2011; 3(1): 3.
[57] DasAK,ChandraP,GuptaA,AhmadN. 'Obesity and the levels of liver enzymes (ALT, AST & GGT) in East Medinipur, India'. Asian Journal of Medical Sciences.2015; 6(1):40-2.

[58] KelishadiR,CookSR,AdibiA,FaghihimaniZ,Ghatrehsamanis,BeihaghiA,etal. 'Association of the components of the metabolic syndrome with non-alcoholic fatty liver disease among normal-weight, overweight and obese children and adolescents'. Diabetology and Metabolic Syndrome, 2009; 1:29.
[59] Mansour-Ghanaei R, Mansour-Ghanaei F, Naghipour M, Joukar F. 'Biochemical markers and lipid profile in nonalcoholic fatty liver disease patients in the PERSIAN Guilan cohort study (PGCS), Iran'. Journal of Family Medicine and Primary Care, 2019 Mar; 8(3):923-928.

Author Profile

Dr. Pawan M. Nimbhorkar, M.B.B.S. (Government Medical College, Nagpur, Maharashtra) 2018. M.D. Family Medicine (MGM Medical College & Hospital, Navi Mumbai, 3rd year Junior Resident). E-mail ID: pawannimbhorkar95@gmail.com. Contact No: 9561944606 / 8830908210. Correspondence Address: Dr. Pawan M. Nimbhorkar, Department of Family Medicine, MGM Medical College, Kamothe, Navi Mumbai – 410209 Maharashtra, India.

Dr. Akshai B., M.B.B.S., M.D. Pediatrics. Currently working as Assistant Professor, Karuna Medical College, Vilayodi. E-mail ID:akshaifreat@gmail.com

Dr. Rakesh Thamke, M.B.B.S., M.D. Pediatrics, currently working as Associate Professor & Head, Department of Family Medicine, MGM Medical College & Hospital, Navi Mumbai. E-mail ID: rthamke@yahoo.com

Dr. Vijay Kamale, M.B.B.S., M.D. Pediatrics. Currently working as Professor & Head, Department of Pediatrics, MGM Medical College & Hospital, Navi Mumbai. E-mail ID: drvijaynkamale@gmail.com