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NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE CHILDREN: FREQUENCY, METABOLIC PROFILES, AND ASSOCIATED RISK FACTORS

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ABSTRACT

Objective: To find out the metabolic profiles and risk factors for Non-alcoholic Fatty Liver Disease (NAFLD) in obese children.

Methodology: It was cross sectional study spanning from February 2022 to June 2023, involving the inclusion of children aged 5-18 years with BMI \geq 95th percentile, at the paediatric unit of combined military hospital, Rawalpindi. Thorough evaluations, encompassing anthropometric measurements, lipid profiles, thyroid levels, LFTs, FBS assessments, and blood pressure measurements, were systematically performed. The diagnosis of NAFLD was established through the use of ultrasonography by detecting fatty changes in the liver by evaluating the liver's echogenicity in comparison to the kidney, portal vein, and diaphragm.

Results: The study examined 82 children, having mean age of 10.46 ± 3.8 yrs with a mean Body mass index-Z score of 2.45 ± 0.45 . Notably, 63.4% of the obese children were identified with NAFLD. Among those with NAFLD, elevated alanine transaminase (ALT) levels were significantly elevated compared to their non-NAFLD counterparts (p -value < 0.05). Additionally, a significant association was found between NA- Fatty Liver Disease and waist circumference (p -value < 0.05). Conversely, no statistically significant associations were noted between NAFLD and lipid profile, fasting blood sugar levels, hypertension, sub-clinical hypothyroidism, acanthosis nigricans, and family history of obesity, hypertension, and diabetes mellitus (p -value > 0.05). However, daily screen time, daily playtime, and the type of daily food exhibited significant associations with NAFLD (p -value < 0.05).

Conclusion: NAFLD is notably prevalent among obese children. Timely diagnosis is crucial as untreated NAFLD can progress to chronic liver disease and contribute to significant morbidity in children.

Keywords: Metabolic Syndrome; Non-alcoholic Liver Disease; Non-alcoholic Steatohepatitis; Paediatric Obesity; Ultrasonography

INTRODUCTION

Non-Alcoholic Fatty Liver Disease (NAFLD) manifests as an abnormal accumulation of fat within the liver, exceeding 5%.¹ It presents diverse manifestations, spanning from a fundamental accumulation of fat in the liver to a more intricate scenario that involves a combination of fatty infiltration, inflammation, and fibrosis, identified as non-alcoholic steatohepatitis. In the paediatric context, NAFLD is frequently linked to obesity and exhibits associations with various metabolic risk factors, such as insulin resistance, dyslipidemia, and cardiovascular disease. Left unaddressed, NAFLD carries the risk of evolving into chronic liver disease, ultimately leading to liver failure. Therefore, it is important to be aware of this condition in obese children and steps should be taken to diagnose NAFLD in time.^{2,3} Paediatric NAFLD can be diagnosed in children as young as 2

years old, while NASH-related cirrhosis can manifest as early as 8 years old. However, the majority of diagnoses typically occur after the age of 10.^{4,5}

The prevalence of NAFLD in obese children exhibits a broad range, spanning from 1.7% to 85%.⁶ The occurrence of this condition is on the rise in developing nations. Given its potential for being asymptomatic over an extended period, emphasizing the crucial role of early detection and intervention becomes paramount to mitigate significant harm to the liver and other organs.⁷ It can be incidentally identified during a physical examination or through abnormal liver function test results, occurring in 7% to 11% of cases. Additionally, a substantial 74% of liver biopsies conducted on obese patients with metabolic risk factors may uncover the presence of underlying NAFLD.^{4,5} Timely diagnosis, the recognition of co-morbidities and risk factors, coupled

with preventive measures against potential complications, can halt the progression toward more severe forms of chronic liver disease. In resource-constrained countries like Pakistan, ultrasonography (USG) emerges as a cost-effective and pragmatic non-invasive alternative for detecting steatosis.^{5,6} While biopsy and histopathology stand as the most reliable means of detection, their invasive nature and limited availability pose challenges. Moreover, this approach can evaluate the extent and level of fatty infiltration within an outpatient department (OPD) setting.⁷

Limited data is available concerning the prevalence and correlated factors of NAFLD in children, particularly in developing countries like Pakistan.⁸ The research aimed to ascertain the prevalence of NAFLD among obese children in our geographical area. Timely diagnosis of the NAFLD and associated risk factors is important to prevent the long term morbidities in obese children.

METHODOLOGY

This cross sectional study was conducted from February 2022 to June 2023, at the paediatric unit of combined military hospital, Rawalpindi-Pakistan. Ethical approval (Serial No. 419) was secured from the IRB/Ethical Committee. Informed consent was required before enrolment in the study and was obtained from the parents of all participants after a thorough counselling them about the nature, methodology and importance of the study. The study encompassed children of any gender aged 5-18 years, with a BMI ≥ 95 th percentile, in accordance with the World Health Organization's 2017 guidelines for obesity.^{9,10} The study excluded children with conditions such as liver diseases other than NAFLD, familial hyperlipidemia, storage disorders, obesity attributed to genetic, metabolic syndrome, psychological disorders, viral hepatitis, other infectious diseases causing liver disease, and those on medications known to induce steatosis. Obese children

less than 5 years were also excluded from the study. Considering prevalence rate of childhood obesity in Pakistan of 5.6% using World Health Organization calculator, keeping 95% confidence level and 5% margin of error, sample size was calculated.⁹

Eighty-two (82) eligible cases who satisfied both the inclusion and exclusion criteria. Data was systematically recorded using a pre-designed form. Anthropometric measurements, including weight (in kg), height (in cm and m), BMI (in kg/m²), and waist circumference (in cm), were collected for each participant. These measurements were conducted using a digital weighing scale with a 100 g graduation and a height gauge with a 1 mm graduation, both manufactured by WS546 in Germany. BMI Z-scores were determined based on the 2017 W.H.O reference percentiles^{9,10} Obesity was defined in accordance with W.H.O guidelines as a body mass index (BMI) equal to or exceeding 30 kg/m², corresponding to the ≥ 95 th percentile.^{9,10} Waist circumference measurement was performed after complete exhalation, utilizing a non-retractable soft tape to measure at the navel with precision up to 0.1 cm. Abdominal obesity was determined if the measured waist circumference was ≥ 90 th percentile for an individual's age and gender.¹¹ The blood pressure of the children was evaluated while seated following a five-minute rest period. Using an electronic sphygmomanometer (Omron HEM 7143T1A), three measurements were conducted, and the mean value was calculated. Individuals with blood pressure ≥ 95 th percentile, as per Rutigliano et al, were categorized as hypertensive.¹²

Values for fasting blood glucose, lipid profile, liver function and thyroid profile were recorded. Elevated alanine transaminase (ALT) levels were defined as ≥ 45 U/L.¹³ Fasting blood sugar levels (FBS) ≥ 100 mg/dl were considered as elevated.¹⁴ Concerning the lipid profile, elevated levels in children

of both genders were characterized as Total cholesterol (TC) ≥ 200 mg/dl, triglycerides (TG) ≥ 150 mg/dl, low-density lipoprotein (LDL) ≥ 130 mg/dl, and very low-density lipoproteins (VLDL) ≥ 30 mg/dl. Furthermore, low levels of high-density lipoprotein (HDL) were identified if it measured ≤ 60 mg/dl.¹⁵ Thyroid hormone levels were assessed using pediatric reference intervals established by Ayub et al.¹⁶ A skilled sonologist performed abdominal ultrasounds on all children after a 12-hour overnight fast, utilizing a Siemens Acuson X300 machine equipped with a 2.5-5 MHz convex probe. The ultrasound aimed to detect fatty changes in the liver by evaluating the liver's echogenicity in comparison to the kidney, portal vein, and diaphragm. The examination also included measurements of the liver's size. Fatty liver severity was categorized on a scale of 0-3, where 0 indicated normal and 3 denoted the most severe condition. A grade of 1 represented mild fatty liver with increased echogenicity relative to the right renal cortex, while a grade of 2 was assigned when the echogenic liver obscured the walls of portal venous branches. Lastly, a grade of 3 was designated for a liver where the diaphragmatic outline was obscured due to fatty liver.¹⁷

The study also documented the family history of hypertension, obesity, and diabetes mellitus. Additionally, the patient's daily screen time, daily playtime, and dietary habits were systematically recorded to identify any associated risk factors.

Data was entered into SPSS V.20 for analysis purposes. Descriptive statistics, including percentages, means, and medians, were calculated. Mean and SD were employed for quantitative data with a normal distribution, while median with interquartile range was utilized for non-normally distributed quantitative data. Independent t-test was used for comparison of means between NAFLD and non-NAFLD groups, and the Chi-square test was used to evaluate the asso-

ciation of NAFLD with various risk factors. All factors showed p-value <0.05 was declared as significantly associated.

RESULTS

The present study included a cohort of 82 children, consisting of 35 males (42.7%) and 47 females (57.3%). The average age for males was 10.76 ± 4.03 years, whereas females had a mean age of 10.24 ± 3.59 years. The average body mass index for the all study cases was 31.23 ± 1.14 Kg/m², with a corresponding BMI Z-score of 2.45 ± 0.45 and an average BMI centile of 98.77 ± 1.37 . The mean body surface area was 1.44 ± 0.33 m² and the mean waist circumference was 74.06 ± 13.21 cm. Fasting hyperglycemia was present in 12 (14.6%), hypertension in 18 (22%), pre-existing acanthosis nigricans in 64 (74%), and subclinical hypothyroidism in 23 (28%). Table-I, presents the mean or median values of different parameters. In the study population, 63.4% of obese children were diagnosed with NAFLD, wherein 37 (45.1%) patients displayed mild fatty infiltration, 14 (17.1%) showed moderate infiltration, and 1 (1.2%) exhibited severe infiltration. A familial history of obesity, diabetes, and hypertension was identified in 34 (41.5%), 28 (34.1%), and 31 (37.8%) individuals, respectively (Table 1).

As shown in Table 2, a waist circumference ≥ 90 th centile revealed a notable association with NAFLD (p-value <0.001). However, factors such as age, gender, weight, height, body surface area (BSA), liver size, and BMI z-score exhibited no significant associations (p-value >0.05). Similarly, NAFLD demonstrated a significant association with serum ALT levels ≥ 45 IU/mL (p-value <0.001); however, levels of serum albumin, AST, and ALP had no statistically significant association with NAFLD (p-value >0.05). Additionally, no statistically significant differences were noted in the levels of fasting blood sugar, lipid profile, and thyroid function tests

Table 1: Features of the study population (n=82)

Features	Observed values, mean±SD, or n (%)	
Males	35 (42.7)	
Females	47 (57.3)	
Age (years) Mean±SD	10.46±3.8	
Weight (kg) Mean±SD	56.58±17.14	
height (cm) Mean±SD	133.26±21.32	
BMI (kg/m ²) Mean±SD	31.22±1.14	
BMI Z score, Mean±SD	2.45±0.45	
BMI percentiles, Mean±SD	98.77±1.37	
Waist circumference, Mean±SD	74.06±13.21	
Body surface area (m ²), Mean±SD	1.44±0.33	
Co-morbidities	Hyperglycaemia	12 (14.6)
	Pre-existing acanthosis nigricans	64 (78)
	Hypertension	18 (22)
	Subclinical hypothyroidism	23 (28)
Biochemical parameters	Total serum cholesterol (mg/dL), median (IQR)	141 (110.75-192)
	HDL (mg/dl) Median (IQR)	53 (39-67)
	LDL (mg/dl) Median (IQR)	60 (45-120)
	VLDL (mg/dl) Median (IQR)	23 (19-32.25)
	Triglycerides (mg/dl) Median (IQR)	84(59-180)
	AST (U/L) Median (IQR)	25.5 (18.75-34.25)
	ALT (U/L) Median (IQR)	63.5(21.75-107)
	ALP (U/L) Median (IQR)	214.5 (145-260)
	Fasting blood sugar (mg/dl) Mean±SD	84.80±14.79
	Albumin (g/dl) Mean±SD	4.38±0.65
	TSH (µIU/mL) Mean±SD	2.58±1.99
T3 (pg/ml) Mean±SD	2.73±0.54	
T4 (ng/ml) Mean±SD	1.44±0.47	
Liver size (cm), Mean±SD	9.87±2.17	
Grading of NAFLD using ultrasound (USG)	Normal	30 (36.6)
	Mild	37 (45.1)
	Moderate	14 (17.1)
	Severe	1 (1.2)
Family history	Hypertension present	31 (37.8)
	Diabetes mellitus present	28 (34.1)
	Obesity present	34 (41.5)
Playtime	1 hour a day	53(64.6)
	2 hours a day	29(35.4)
Screen time	Less than 2 hours a day	27(32.9)
	More than 2 hours a day	55 (67.1)
Junk food	1 junk food/day	36 (43.9)
	More than 2 foods/day	46(56.1)

Table 2: Clinical and Biochemical Characteristics of patients with and without NAFLD.n=82

Parameters		Children without NAFLD (n=52), n (%)	Children without NAFLD, (n=30), n(%)	p-value
Age (years) Mean±SD		9.79±3.55	11.63±3.40	0.032
Gender	Male	22 (69.9)	13 (37.1)	0.982
	Female	30 (63.8)	17 (36.2)	
Weight (kg) Mean±SD		53.36±15.89	62.15±18.06	0.008
Height (cm) Mean±SD		128.54±19.75	141.42±21.78	0.483
BMI Mean±SD		31.67±1.17	30.43±0.46	<0.001
BMI Z-score Mean±SD		2.55±0.41	2.30±0.47	0.011
BMI percentiles Mean±SD		99.05±1.15	98.28±1.59	0.013
BSA Mean±SD		1.38±0.31	1.56±0.35	0.017
Liver size Mean±SD		9.96±2.28	9.71±1.98	0.629
Waist circumference (cm)	Less than 90th centiles	9 (27.3)	24(72.7)	<0.001
	More than 90th centiles	43 (87.8)	6 (12.2)	
Albumin (g/dl)	Less than 5.5 g/dl	49 (64.5)	27 (35.5)	0.479
	More than 5.5 g/dl	3 (50)	3 (50)	
	Median (IQR)	4.3 (3.8-4.8)		
AST/SGOT (IU/L)	Less than 50 IU/L	47 (63.5)	27(36.5)	0.995
	More than 50 IU/L	5 (62.5)	3 (37.5)	
	Median (IQR)	25.50 (18.75-34.25)		
ALT/SGPT (IU/L)	Less than 40 IU/L	9 (31)	20 (69)	<0.001
	More than 40 IU/L	43(81.1)	10 (18.9)	
	Median (IQR)	63.5 (21.75-107)		
ALP (IU/L)	Less than 300 IU/L	49 (64.5)	27(35.5)	0.479
	More than 300 IU/L	3 (50)	3 (50)	
	Median (IQR)	21.5 (145-260)		
T3 (ng/ml) Mean±SD		2.72±0.51	2.74±0.59	0.855
T4 (ug/dl) Mean±SD		1.51±0.46	1.32±0.45	0.073
TSH (mIU/ml)	Less than 3mIU/ml	36 (61)	23(39)	0.470
	More than 3mIU/ml	16 (69.6)	7(30.4)	
	Mean±SD	2.58±1.99		
Serum cholesterol (mg/dl)	Less than 200mg/dl	36(57.1)	27 (42.9)	0.032
	More than 200mg/dl	16(84.2)	3 (15.8)	
	Median (IQR)	141 (110.75-192)		
HDL (mg/dl)	Less than 60mg/dl	31(62)	19(38)	0.740
	More than 60mg/dl	21(65.6)	11(34.4)	
	Median (IQR)	53 (39-67)		
LDL (mg/dl)	Less than 130mg/dl	38(58.5)	27(41.5)	0.069
	More than 130mg/dl	14(82.4)	3(17.6)	
	Median (IQR)	45 (60-120)		

between the two groups (p-values >0.05) (Table 2). No statistically significant associations (p-values >0.05) were identified between a family history of diabetes mellitus, hypertension, and obesity, as outlined in Table 3. Nevertheless, NAFLD demonstrated a noteworthy association with playtime of less than one hour per day, screen time exceeding two hours per day, and the consumption of more than two servings of junk foods daily (p-value < 0.05) (Table 3).

DISCUSSION

Childhood obesity is on the rise in developing nations, and Pakistan is no exception. It is crucial to comprehend the risk factors and related co-morbidities.¹⁸ NAFLD is a common complication associated with obesity in children, exhibiting a prevalence that spans from 1.7% to 85%.^{7,18,19} In our study, NAFLD was identified in 63.4% of obese children of the same age group, through ultrasound testing. A comparable prevalence of 62% in obese children was also reported in the study by Gupta et al. This study used Indian Academy of Paediatrics guidelines to define obesity while we followed WHO's guidelines²⁰. Our study aligned with the results reported by Pawar et al and Parry et al, both indicating a consistent prevalence of NAFLD at 62% and 61%, respectively, within the obese children. These studies however, included both obese and overweight children from 5 to 15 years in contrast to our study where we included only obese children from 5 to 18 years.^{21,22} Kodhelaj et al documented a higher occurrence of 68.7% in Europe, specifically among a cohort of 80 children aged 7-15 years in Albania.²³ In a study by Jimenez-Rivera et al, NAFLD was identified in a much higher 85% of the study participants.²⁴ Peng et al and Thiagarajan et al reported consistent findings, documenting a prevalence of NAFLD at 54.9% and 51.7%, respectively. These rates were established through the screening of obese and overweight children, employing a com-

VLDL (mg/dl)	Less than 30mg/dl	32 (62.7)	19 (37.3)	0.872
	More than 30mg/dl	20 (64.5)	11 (35.5)	
	Median (IQR)	23 (19-35.25)		
TGs (mg/dl)	More than 150mg/dl	37 (63.8)	21 (36.2)	0.912
	Less than 150mg/dl	15 (62.5)	9 (37.5)	
	Median (IQR)	84.5 (59-180)		
FBS (mg/dl)	Less than 100mg/dl	41 (58.6)	29 (41.4)	0.028
	More than 100mg/dl	11 (97.7)	1 (8.3)	
	Mean±SD	90.26±28.61		

Table 3: Comparison of risk factors and co-morbidities

Risk factors/co-morbidities		Children with NAFLD (n=52), n(%)	Children without NAFLD (n=30), n(%)	p-value
Family H/O HTN	Yes	20 (64.5)	11 (35.5)	0.872
	No	32 (62.7)	19 (37.3)	
Family H/O DM	Yes	16 (57.1)	12 (42.9)	0.396
	No	36 (66.7)	18 (33.3)	
Family H/O obesity	Yes	21 (61.8)	13 (38.2)	0.794
	No	31 (64.6)	17 (35.4)	
Play time	1 hour a day	42 (79.2)	11 (20.8)	<0.001
	2 hours a day	10 (34.5)	19 (65.5)	
Screen time	Less than 2 hours a day	10 (37)	17 (63)	0.001
	More than 2 hours a day	42 (76.4)	13 (23.6)	
Junk food	1 junk food/day	15 (41.7)	21 (58.3)	<0.001
	More than 2 food/day	37 (80.4)	9 (19.6)	
Hypertension	Yes	11 (61.1)	7 (38.9)	0.818
	No	41 (64.1)	23 (35.9)	
Pre-existing acanthosis nigricans	Yes	41 (64.1)	23 (35.9)	0.818
	No	11 (61.1)	7 (38.9)	
Sub-clinical hypothyroidism	Yes	16 (69.6)	7 (30.4)	0.470
	No	36 (61)	23 (39)	
Hyperglycaemia	Yes	41 (58.6)	29 (41.4)	0.028
	No	11 (91.7)	1 (8.3)	

combination of ultrasound examination and ALT levels.^{7,25} In contrast to our study a lower prevalence of 50.8% and 40% NAFLD has been reported in previous studies.^{19,26} These studies however included both overweight as well as obese children in contrast to our study which included only obese children.

Diverging from our study results, research conducted in Nairobi by Mburu et al, revealed a contrasting prevalence of 26.2% among children aged 6-18 years.²⁷ Similarly, Maleki et al conducted research in Iran, including both overweight and obese children. Their study revealed an overall prevalence

of NAFLD at 24.9% among obese children, with a specific prevalence of 22.3% in the age range of 6-11 years and an elevated prevalence of 35.5% in the age group of 12-19 years.²⁸ The prevalence rates of fatty liver across different populations may exhibit variations attributable to diverse factors, including genetic susceptibility and epigenetic mechanisms influencing hepatic fat changes. Furthermore, discrepancies in defining abnormal liver enzymes and variations in diagnostic criteria employed across studies contribute to the observed variability in prevalence rates. In our study, it was observed that 45.1% of patients exhibited mild fatty infiltration, 17.1% had moderate infiltration, and 1.2% displayed severe infiltration. These results closely mirror those of the study conducted by Kodhelaj et al, where 43.7%, 23.7%, and 1.3% of participants exhibited mild, moderate, and severe degrees of fatty liver, respectively.²³ In a meta-analysis conducted by Hassanipour et al, the prevalence of NAFLD was stratified by grade in obese children, revealing rates of 30%, 5.9%, and 0.6% for grades 1, 2, and 3, respectively. Correspondingly, Jimenez-Rivera et al, reported varying degrees of fatty infiltration, with 38% classified as mild, 20% as moderate, and 12% as severe.^{24,29} Our study identified a statistically significant elevation in ALT levels among children with NAFLD compared to those without NAFLD. This finding aligns consistently with observations from various previous studies.¹⁹⁻²⁴ In our study, we noted that ALT levels ≥ 45 IU/L were present in 81.1% of patients diagnosed with NAFLD, in contrast to a lower occurrence of 18.9% in patients without NAFLD. Correspondingly, Akhtar et al, reported a significant elevation in ALT levels among children with NAFLD (58.3%) compared to those without NAFLD (16.7%). Notably, they suggested utilizing ALT levels as a screening parameter for detecting NAFLD in obese children.¹⁷ As per Jimenez-Rivera et al, elevated alanine aminotransferase (ALT) levels were observed in 61% of individuals diagnosed with NAFLD.²⁴

In line with this, Gupta et al, reported a statistically significant correlation between elevated ALT levels and NAFLD in obese children. They further advocated that children exhibiting elevated liver enzymes should undergo sonography as a precautionary measure to exclude the presence of NAFLD.²⁰

In our study, akin to the results noted by Jain et al and Gupta et al, we did not identify statistically significant variations in lipid levels between children with and without NAFLD.^{30,20} Similarly, in their study, Thiagarajan et al reported analogous findings, noting no significant distinctions in the lipid profile between groups, except for a higher level of LDL cholesterol in the NAFLD group.²⁴

Imanzadeh et al documented a significant elevation in mean total cholesterol (TC) levels among patients with NAFLD compared to those without NAFLD.³¹ In a study by Kodhelaj et al a significant association was reported, demonstrating a significant correlation between TGs and TC with NAFLD.²³ Conversely, Jimenez-Rivera et al found no statistically significant distinctions between the two groups in terms of TC, HDL, LDL, and non-HDL cholesterol ($p = 0.63$, $p = 0.98$, $p = 0.72$, and $p = 0.37$, respectively).²⁴ In alignment with our results, Peng et al Gupta et al Altalebi et al and Parry et al all noted a significant association between waist circumference and NAFLD.^{7,19,20,22} In contrast, Thiagarajan et al reported disparate findings, suggesting no statistically significant difference in waist circumference between individuals with and without NAFLD.²⁵ Our study found no notable differences in the association of NAFLD with age and gender, consistent with earlier investigations.^{6,18,20,22,25,27} In contrast to our study and other existing research, Peng et al reported divergent results. Their research indicated a notably higher prevalence of NAFLD in males in comparison to females (14% vs. 2.4%), underscoring gender as a discernible risk factor for NAFLD.⁷ In a study conducted by Imanzadeh et

al it was observed that NAFLD affected 15 (27.3%) girls and 40 (72.7%) boys. Importantly, a statistically significant difference between the two genders was noted ($P = 0.02$).³¹

Although hypertension, subclinical hypothyroidism, and hyperglycemia were present in 22%, 28%, and 14.6%, respectively, none of these conditions exhibited statistical significance, in line with findings from prior studies.^{20,25,27} Contrary to our findings, Pawar et al observed in their study that systolic hypertension emerged as the sole independent factor significantly associated with NAFLD.²¹ Consistent with our study, the lack of significance in the presence of acanthosis nigricans aligned with the findings reported by Imanzadeh et al.³¹ Consistent with our study, findings from Gupta et al and Mburu et al and Imanzadeh et al collectively indicated that a family history of hypertension, diabetes mellitus, and obesity did not show a significant association with NAFLD.^{20,27,31} In contrast to our study, Gupta et al and Imanzadeh et al found that daily playtime of less than 1 hour and screen time exceeding 2 hours were not significant factors associated with NAFLD.^{20,31}

CONCLUSIONS

The rising prevalence of obesity in Pakistani children aged 5-18 years correlates with an increasing incidence of NAFLD. Timely identification of obesity-related conditions such as NAFLD is imperative to mitigate the development of chronic liver diseases and associated health complications. Raised levels of ALT and increased waist circumference are significant risk factors for NAFLD in children.

LIMITATIONS AND SUGGESTIONS

A relatively small sample size and the ab-

sence of documentation of fatty liver through liver biopsy were main limitations. The decision to forgo liver biopsy was influenced by the asymptomatic nature of a majority of the patients and the invasive nature of the procedure.

RECOMMENDATIONS

Due to the scarcity of localized research in this field, there is an urgent need for comprehensive investigations on a broader scale. These studies should explore the prevalence, accompanying risk factors, and concurrent health conditions linked with NAFLD among obese children within our geographic area. Such research studies hold promise in establishing a solid foundation for informed interventions, enabling timely and precise actions to alleviate the impact of the disease and its potential ramifications.

REFERENCES

1. Mahmood H, Abbas M, Azeem M, Younus I, Qadir A, Habib M. The risk factors associated with non-alcoholic fatty liver disease. *Pak J Med Health Sci.* 2023;17(4) 458-61.
2. Shah J, Okubote T, Alkhoury N. Overview of updated practice guidelines for pediatric nonalcoholic fatty liver disease. *Gastroenterol Hepatol* 2018;14(7):407-14.
3. Abbas Z, Zaheer R. Non-alcoholic fatty liver disease: A real threat in Pakistan. *J Pak Med Assoc.* 2020;70(12(B)):2437-40. DOI: 10.5455/jpma.95891.
4. Temple JL, Cordero P, Li J, Nguyen V, Oben JA. A guide to non-alcoholic fatty liver disease in childhood and adolescence. *Int J Mol Sci.* 2016;17(6):947. DOI: 10.3390/ijms17060947.
5. Berardis S, Sokal E. Pediatric non-alcoholic fatty liver disease: An increasing public health issue. *Eur J Pediatr.* 2014;173:131-39. DOI: 10.1007/s00431-013-2092-9.

6. Yu EL, Golshan S, Harlow KE, Angeles JE, Durelle J, Goyal NP, et al. Prevalence of nonalcoholic fatty liver disease in children with obesity. *J Pediatr*. 2019;207:64-70. DOI: 10.1016/j.jpeds.2018.11.029.
7. Peng L, Wu S, Zhou N, Zhu S, Liu Q, Li X. Clinical characteristics and risk factors of nonalcoholic fatty liver disease in children with obesity. *BMC Pediatr*. 2021;21:22. DOI: 10.1186/s12887-020-02458-5.
8. Zubair R, Mirza M, Iftikhar J, Saeed N. Frequency of incidental fatty liver on ultrasound and its association with diabetes mellitus and hypertension. *Pak J Med Sci*. 2018;34(5):1137-41. DOI: 10.12669/pjms.345.15606.
9. Tanveer M, Hohmann A, Roy N, Zeba A, Tanveer U, Siener M. The current prevalence of underweight, overweight, and obesity associated with demographic factors among Pakistan school-aged children and adolescents-An empirical cross-sectional study. *Int J Environ Res Public Health*. 2022;19(18):11619. DOI: 10.3390/ijerph191811619.
10. Monasor-Ortolá D, Quesada-Rico JA, Nso-Roca AP, Rizo-Baeza M, Cortés-Castell E, Martínez-Segura A, et al. Degree of accuracy of the BMI Z-Score to determine excess fat mass using DXA in children and adolescents. *Int J Environ Res Public Health*. 2021;18(22):12114. DOI: 10.3390/ijerph182212114.
11. Yamanaka AB, Davis JD, Wilkens LR, Hurwitz EL, Fialkowski MK, Deenik J, et al. Determination of child waist circumference cut points for metabolic risk based on acanthosis nigricans, the children's healthy living program. *Prev Chronic Dis*. 2021;18:210021. DOI: 10.5888/pcd18.210021.
12. Rutigliano I, De Filippo G, Pastore L, Messina G, Agostoni C, Campanozzi A. Obesity-related hypertension in pediatrics, the impact of American academy of pediatrics guidelines. *Nutrients*. 2021;13(8):2586. DOI: 10.3390/nu13082586.
13. Lu Y, Wang Q, Yu L, Yin X, Yang H, Xu X, et al. Revision of serum ALT upper limits of normal facilitates assessment of mild liver injury in obese children with non-alcoholic fatty liver disease. *J Clin Lab Anal*. 2020;34(7):e23285. DOI: 10.1002/jcla.23285.
14. Balkhiyarova Z, Luciano R, Kaakinen M, Ulrich A, Shmeliov A, Bianchi M, et al. Relationship between glucose homeostasis and obesity in early life-a study of Italian children and adolescents. *Human Molecular Genetics*. 2022;31(5):816-26. DOI: 10.1093/hmg/ddab202.
15. Cigri E, Inan FC, Er E, Yildiz E. The relationship between lipid profile and non-alcoholic fatty liver disease in children and adolescents with obesity. *J Coll Physicians Surg Pak*. 2022;32(05):591-95. DOI: 10.29271/jcsp.2022.05.591.
16. Ayub A, Irfan M, Nadeem A, Hayee S, Akhtar N, Nawaz F. Profiles of thyroid hormones in the overweight boys of district Rawalpindi, Punjab, Pakistan. *PJEST* 2023;4(3)1-8.
17. Kim PH, Cho YA, Yoon HM, Bak B, Lee JS, Jung AY, et al. Accuracy of attenuation imaging in the assessment of pediatric hepatic steatosis: correlation with the controlled attenuation parameter. *Ultrasonography*. 2022;41(4):761-69. DOI: 10.14366/usg.22031.
18. Altalebi RR, Al-Hussaniy HA, Al-Tameemi ZS, Al-Zobaidy MA, Albu-Rghaif AH, Alkuraishy HM, et al. Non-alcoholic fatty liver disease: relation to juvenile obesity, lipid profile, and hepatic enzymes. *J Med Life* 2023;16(1):42-7.
19. Akther R, Begum S, Alam F, Shymali KJ, Tithi BB, Rezaul Karim MR. Non-alcoholic fatty liver disease in obese and overweight children. *Int J Contemp Pediatr* 2021;8:976-80.
20. Gupta N, Jindal G, Nadda A, Bansal S, Gahukar S, Kumar A. Prevalence and risk factors for nonalcoholic fatty liver disease in obese children in rural Punjab, India. *J Family Community Med*. 2020;27(2):103-8. DOI: 10.4103/jfcm.JFCM_174_19.
21. Pawar SV, Zanwar VG, Choksey AS, Mohite AR, Jain SS, Surude RG, et al. Most overweight and obese Indian children have nonalcoholic fatty liver disease. *Ann Hepatol*. 2016;15(6):853-61. DOI: 10.5604/16652681.1226833.
22. Parry IA, Bhat RA, Khan I. The prevalence of non-alcoholic fatty liver disease and its association with metabolic syndrome and obesity in pediatric population of North India. *J Metabolic Syndr*. 2012;1:118.
23. Kodhelaj K, Resuli B, Petrela E, Malaj V, Jaze H. Non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in Albanian overweight children. *Minerva Pediatr*. 2014;66(1):23-30. DOI: 10.23736/S0026-4946.16.03721-4.
24. Jimenez-Rivera C, Hadjiyannakis S, Davila J, Hurteau J, Aglipay M, Barrowman N, et al. Prevalence and risk factors for non-alcoholic fatty liver in children and youth with obesity. *BMC Pediatr*. 2017;17(1):113. DOI: 10.1186/s12887-017-0851-8.
25. Thiagarajan S, Shrinuvasan S, Arun Babu T. Screening for non-alcoholic fatty liver disease among obese and overweight children: prevalence and predictors. *Indian J Gastroenterol*. 2022;41(1):63-8. DOI: 10.1007/s12664-021-01265-1.
26. Jallilian M, Rasad R, Rotbeh A. Fatty liver disease in overweight and obese Iranian children: comprehensive systematic review and meta-analysis. *Obesity Medicine*. 2022;35:2451-8476.
27. Mburu AN, Laving A, Macharia WM, Sande J. Prevalence of non-alcoholic fatty liver disease in overweight and obese children seeking ambulatory healthcare in Nairobi, Kenya. *BMJ Open*

- Gastroenterol. 2023;10(1):e001044. DOI: 10.1136/bmjgast-2022-001044
28. Maleki F, Hosseinpour M, Motlagh BM. OC49 Non-alcoholic fatty liver disease in obese and overweight Iranian children: a cross-sectional study. Arch Dis Child. 2019;1(04):A20-A21. DOI: 10.1136/archdischild-2019-epa.50.
29. Hassanipour S, Amini-Salehi E, Joukar F, Khosousi MJ, Pourtaghi, Ansar MM, et al. The prevalence of non-alcoholic fatty liver disease in Iranian children and adult population: A systematic review and meta-analysis. Iran J Public Health. 2023;52(8):1600-12. DOI: 10.18502/ijph.v52i8.6371.
30. Jain V, Jana M, Upadhyay B, Ahmad N, Jain O, Upadhyay AD, et al. Prevalence, clinical and biochemical correlates of nonalcoholic fatty liver disease in overweight adolescents. Indian J Med Res. 2018;148:291-301. DOI: 10.4103/ijmr.IJMR_1749_17.
31. Imanzadeh F, Olang B, Sayyari AA, Dara N, Khatami K, Hosseini A, et al. Prevalence and related factors for non-alcoholic fatty liver disease in obese students. J Compr Ped. 2023;14(3):e135095. DOI: 10.5812/compreped.135095.

Author's Contribution

IS conceived the idea, designed the study and performed data analysis. SN and FI helped in designing the study and performed data analysis. SI, HK and SK helped in data collection and write up of the manuscript. All authors made substantial intellectual contributions to the study.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.