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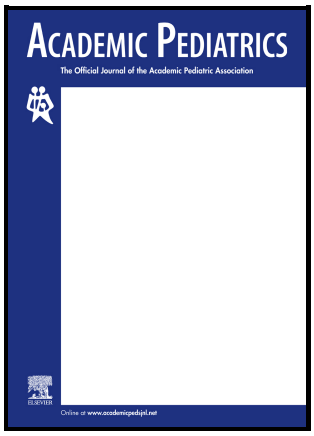

Missed Opportunities in Guideline-based Fatty Liver Screening among 3.5 million children.Short title: Fatty Liver Screening among 3.5 million children with obesity

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Missed Opportunities in Guideline-based Fatty Liver Screening among 3.5 million children.

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Short title: Fatty Liver Screening among 3.5 million children with obesity

Abbreviations:

MASLD: Metabolic dysfunction-associated steatotic liver disease

ALT: Alanine Aminotransferase

MASH: Metabolic dysfunction-associated steatohepatitis

CI: Confidence Interval

FQHC: Federally Qualified Health Centers

MACPAC: Medicaid and CHIP Payment and Access Commission

Contributors' Statement Page

Kabir Gulati, Dr. Gulati, and Dr. Kaelber conceptualized and designed the study, drafted the initial manuscript.

Kabir Gulati performed data search and analysis - using language in Explorys.

Dr Alkhouri and Dr. Durrani reviewed and revised the manuscript.

Drs. Sahni, Mhanna and Suri performed the statistical analyses.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Introduction:

NAFLD is a leading preventable cause of chronic liver disease in children.[1] As of June 2023, American Association for the study of liver disease has replaced NAFLD to MASLD (Metabolic

dysfunction-associated steatotic liver disease. Its prevalence ranges from 7% in the general population to 36.1% in children with obesity, with occurrence twice as common in males than females.[2] Even though MAFLD is often detected during puberty, metabolic dysfunction-associated steatohepatitis (MASH) is being increasingly described in prepubescent children with obesity.[3] Long-term data on pediatric MAFLD is limited but one retrospective study found that children with MAFLD had a 14 times higher risk of severe liver disease and death compared to children without MAFLD.[4] It is known that untreated fatty liver may progress to end-stage cirrhotic liver disease requiring liver transplantation for survival.[1,3,4] MAFLD is also correlated with metabolic diseases like insulin resistance, Type II diabetes, central adiposity, polycystic ovarian syndrome, Obstructive sleep apnea (OSA), dyslipidemia manifesting as elevated Triglyceride and low levels of high-density lipoprotein (HDL), which contributes to cardiovascular disease and hypertension.[1] MAFLD is an independent risk factor for cardiovascular disease, hepatocellular carcinoma and is the leading cause of cirrhosis in adults.[5,6]

Owing to potential serious consequences merely diagnosis of pediatric MAFLD is important, as studies have shown to arrest the course of early disease with simple measures such as lifestyle management consisting of weight reduction and physical activity.[1]

Because MAFLD is asymptomatic in most children, screening offers a valuable tool, as early detection provides an opportunity to prevent the chances of progression of liver fibrosis.

The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) recommend and the American Academy of Pediatrics (AAP) strongly endorsed MAFLD screening using alanine aminotransferase levels (ALT) begin between the ages of 9-11 for all children with obesity.[1,7] Various authors have highlighted issues of underdiagnosis of obesity and fatty liver in children.[8-12] However, there is a dearth of knowledge about adherence to

guidelines and socio-demographic trends in MAFLD screening in children at a population level. Enormous datasets with millions of pediatric patient's records, pulled from electronic health records (EHRs), offer a unique opportunity to gain such knowledge using real-world data in large populations of children.[13,14] The goals of this study were to use datasets derived from pooled EHR data to 1). Determine screening rates of MAFLD in a large population of children aged between 10-14 years with obesity and 2). Examine socio-demographic trends in MAFLD screening in children aged between 10-14 years with obesity.

Methods:

In our study, we used the IBM Watson Health Explorys tool which contains pooled, national level aggregated, de-identified, population-level EHR data from approximately 360 hospitals and 317,000 providers across 50 states in the United States. Types of data from contributing EHRs aggregated in Explorys include patient demographics (age, race/ethnicity, gender, current insurance type), diagnoses, findings, and procedures mapped to the SNOMED–CT codes, 8 prescription drug orders mapped to SNOMED (to represent the pharmacological class) and RxNorm (to represent the drug itself), and laboratory results are mapped to LOINC codes. All healthcare systems contributing EHR data have the contributing EHR as their primary medical record and so typically would include all of the data elements listed previously from all areas of the healthcare system (inpatient, outpatient, emergency department, etc.) across all specialties (primary care and subspecialties, etc.)[13,14]

Data was analyzed from the period 2021 to 2022. We included children aged 10-14 years because Explorys has fixed age categories for data search, and the age category of 10-14 years

overlapped most closely with the recommended age range of 9-11 years to begin screening for MAFLD in children with obesity.[1,7]

Obesity was determined based on 1) any BMI >=95% or 2) any encounter where an ICD obesity code was entered (ICD-10 E66, ICD-9 278). We examined the screening rate by calculating the percentage of children with obesity who had an ALT level checked. Among those who received an ALT test, we then calculated the percentage of children with an abnormal ALT result based on gender-specific pathological levels in children, see Table 1.

Further, to analyze socio-demographic trends in MAFLD screening in obese children, we looked at the following demographic variables in our patient population: - gender (male and female), race (white and non-white), and patient insurance type (Medicaid and non-Medicaid).

Statistical analysis:

Categorical variables are presented as percentages. Chi-square tests and odds ratio with 95% confidence intervals (CI) were calculated to compare screening rates by gender, race, and insurance. In a further analysis, we examined how gender, race, and Medicaid insurance status influenced the odds of receiving an MAFLD screening and an abnormal ALT test result in two separate multivariate logistic regressions. Statistical analyses were performed with Stata version 16.1 (StataCorp LLC, College Station, TX, USA.) Statistical significance was defined as a two tailed value of $p<0.05$.

Results:

Out of 3,558,420 children aged 10-14 years, 512,500 (14.4%) had obesity. A total of 47,830 with

obesity (9.3%) had ALT testing done. The socio-demographic characteristics of our study population included gender, race and insurance type presented in Table 1. The distribution of abnormal and normal ALT tests in the patient population is presented in Table 2.

In a logistic regression model, with screening as the dependent variable, and gender, race, and Medicaid insurance as the independent variables, female gender, white race and Medicaid insurance status were associated with a higher rate of ALT testing, see Table 3.

Further, among children who were screened, another logistic regression analysis was conducted with abnormal ALT as the dependent variable and gender, race and Medicaid insurance as independent variables. We found that female children and white children were less likely to have an abnormal ALT whereas children with Medicaid insurance were more likely to have an abnormal ALT test result, see Table 4.

Discussion:

Our study uniquely uses aggregated EHR data of millions of children to determine fatty liver disease screening rates in a large nationally representative sample within the United States. We found that the percentage of children with obesity receiving recommended MAFLD screening was very low (9.3%). This finding shows poor screening rates for MAFLD in a high-risk population. Under-screening leads to missed opportunities for early detection of fatty liver and potentially reversing disease progression from simple steatosis to advanced stages of NASH and cirrhosis. [1,5,6,8, 10, 12, 15]. A similar study based on a Canadian primary care setting by Morkem et al, 2022 reported low MAFLD screening rates in children.[34] This emphasizes MAFLD under screening at an international level.[34,35]

A significant contributing factor to low MAFLD screening rates may be the difference in the recognition of obesity by providers. Despite the increasing trend in obesity among children and adolescents, data suggest low rates of diagnosis and management of overweight and related comorbidities by healthcare providers. [8-12] In a study of 2256 outpatients, Riley et al. found that 2⁄3 of overweight children were not diagnosed and did not receive the recommended evaluations and screenings.[17]. Benson et al. looked at EHR data from 60,711 children from 1999-2007 at an extensive academic medical system and found that based on the BMI measurements, 19% of the children were overweight, and 23% were identified obese; however, among these, 90% of overweight patients and 46% of obese patients remained undiagnosed. They found a positive correlation between diagnoses and age, number of healthcare visits, and severity of obesity. The authors concluded that despite clear definitions of BMI, many overweight children remained undiagnosed. [17,18] We speculate that a child's health care team may not recognize the risk of MAFLD due to lack of a formal diagnosis.

Our study also revealed that non-white children were less likely to be screened for fatty liver than white children. Racial and ethnic disparities are pervasive in healthcare and adversely affect the quality of care and health outcomes in minorities. [19-21] In the 2021 National Healthcare Quality and Disparities Report, Black and Hispanic groups experienced worse quality of care, as compared to Whites, on 43% and 36% quality measures, respectively.[22] As compared to white children, minority children face disproportionately higher rates of unmet healthcare needs for myriad reasons. These include lower access to primary care providers (PCP) with race having a stronger association than income, low levels of health literacy and communication issues, perception of social class, greater frequency of missed preventive care appointments, etc. [19, 22]

We speculate that similar issues may be contributory to low levels of fatty liver screening in non-white children with obesity.

Another point is that the pediatric guidelines do not definitively recommend ALT measurement in obese patients; the guidelines state that providers should "consider screening" in this population. The AAP statement on screening in children does not provide further clarification and simply supports the NASPGHAN statement. The vagueness of the statements may be leading some providers to think that screening is not mandatory which may contribute to low screening rates.

Our study also found higher screening rates for MAFLD in females with obesity. This is interesting because numerous studies, including ours, have shown the prevalence of MAFLD is higher in obese males. While the exact reasons for gender disparity in screening for MAFLD are not known, there is evidence that not only do obese girls report higher levels of weight-related concerns, [23] but also parents are more concerned about their daughter's weight status as compared to their sons which could be a plausible explanation for higher rates of screening among girls. [24- 26] Most likely, these attitudes only partly explain the gender differences. Nevertheless, our finding highlights an important facet for future research in obesity, MAFLD, and other chronic diseases- gender disparities.

We found that Medicaid insurance was associated with higher MAFLD screening rates. This finding is interesting because Medicaid provides health coverage to low-income children and families, and overall, health disparities are more prevalent in socially disadvantaged children. There are a few plausible explanations for this association. Low-income patients are more likely to be obese, and hence more likely to be screened or have laboratory testing done. There is growing evidence that Medicaid coverage affords better access to care, such as increasing

insurance coverage for chronic diseases like Diabetes, higher screening rates for cancer, etc., compared to uninsured populations. [27-30] Cole et al., in their recent cohort study, conducted using 946 Federally Qualified Health Centers (FQHC), found that Medicaid expansion-state FQHC had improved blood pressure and glucose control over the last five years in Black and Hispanic patients compared to non-Medicaid expansion states. [30] With regards to the potential differences in preventive care (e.g., screening for MAFLD) between Medicaid enrollees versus private insurance holders, both the National Center of Health Statistics and the Medicaid and CHIP Payment and Access Commission (MACPAC) report that both groups fare comparably in access to and use of preventive care, and Medicaid adolescents may fare even better compared to those with private insurance because Medicaid provides greater financial protection than private insurance. 31 Because of the controversies around MAFLD screening in children and adults, including limited data on its cost-effectiveness, privately insured children and adolescents may face more significant financial barriers (out-of-pocket expenses) for screening for MAFLD.

Our study has some limitations. Firstly, we made an a priori assumption that an ALT checked in obese children must be for MAFLD screening, which is mainly true in children with obesity. Also, in Explorys, we couldn't differentiate between ALT tests done in primary care versus other settings like subspecialty or urgent care visits. While it is possible that a few ALTs could have been checked for different reasons, even if that is the case our study results would be an overestimate of actual screening rates, further emphasizing our findings of MAFLD under screening at the population level. Secondly, a patient could have had ALT checked in a healthcare system outside of Explorys so that specific data could have been missed. However, this would be a small proportion as we only looked at patients who had other healthcare data in

Explorys where, typically, their ALT and other tests would have occurred. Thirdly, a time window of 10-14 years could be a limitation. Since the recommendation is to “screen by 9- 11 years”, it is possible that some patients may be “just about to be screened” and would still “meet the guidelines.” However, in our opinion, including children in the age range of 10-14 years (3 years from the 11-year mark) should be enough time for providers who intend to screen the child for MAFLD. Thus, using the window should not significantly affect our findings.
Finally, a limitation of the Explorys platform is a relative lack of ethnicity data because ethnicity was not well captured in the contributing electronic health records. Up to 2/3rd of patients needed ethnicity data. Therefore, we choose not to include an ethnicity analysis in our results. However, this lack of ability to analyze our data based on ethnicity does not take away from our study's primary message, which is that routine screening for NAFLD occurs much less frequently than in a population that should be screened.

Our study findings bear important research, policy, and practice implications as MAFLD in children is a significant public health concern. Low NAFLD screening rates (9.3%) and disparities in MAFLD diagnosis and management will impede efforts to treat MAFLD effectively. Reporting MAFLD screening as a health quality measure and incentivizing screening using value-based payment models may help reduce implementation gaps in screening for MAFLD in children with obesity. [32,33]

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Table 1: Demographics of 10–14-year-olds with obesity by ALT test checked.

Children with Obesity	ALT checked (N=47,830)	No ALT checked (N=464,670)
Gender:		
Female	22,960 (48.0%)	212,820 (45.8%)
Male	24,870 (52.0%)	251,850 (54.2%)
Race:		
White	32,180 (67.3%)	296,300 (63.8%)
Non-White	15,650 (32.7%)	168,370 (36.2%)
Insurance:		
Medicaid	17,280 (36.1%)	139,630 (30.0%)
Non-Medicaid	30,550 (63.9%)	325,040 (70.0%)

The analysis revealed statistically significant differences in socio-demographic characteristics—gender, race, and medical insurance status—between individuals who underwent the ALT test and those who did not ($p < 0.001$)

Table 2: Demographics of 10–14-year-olds with obesity by ALT test results.

ALT Levels	Abnormal (N=7,920)	Normal (N=40,750)
Gender:		
Female	3,380 (42.7%)	19,920 (48.9%)
Male	4,540 (57.3%)	20,830 (51.1%)
Race:		
White	5,200 (65.7%)	27,280 (66.9%)
Non-White	2,720 (34.3%)	13,470 (33.1%)
Insurance:		
Medicaid	3,010 (38.0%)	14,830 (36.4%)
Non-Medicaid	4,910 (62.9%)	25,920 (63.6%)

Table 3: Multivariate Logistic Regression Analysis for ALT checked.

Variable	ALT Checked	
	OR	95% CI
Female vs. Male	1.09	1.07-1.11
White vs. Non-White	1.21	1.18-1.23

Medicaid vs. non-Medicaid	1.34	1.32-1.37

Note: OR, odds ratio; CI, confidence interval.

Table 4: Multivariate Logistic Regression Analysis for Abnormal ALT.

Variable	Abnormal ALT	
	OR	95% CI
Female vs. Male	0.78	0.74-0.82
White vs. Non-White	0.95	0.90-1.00
Medicaid vs. Non-Medicaid	1.07	1.01-1.12

Note: OR, odds ratio; CI, confidence interval.

Conflict of Interest Disclosures:

The authors have no example conflicts of interest to disclose.

What's new in this study?

Our study adds knowledge about screening rates and sociodemographic characteristics of MAFLD screening among children.