

Elevated alpha-fetoprotein levels in children with metabolic dysfunction-associated steatotic liver disease (MASLD)



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Background

- Metabolic dysfunction-associated steatotic liver disease (MASLD) can progress to end-stage liver disease (ESLD) and hepatocellular carcinoma (HCC) in adults and less frequently, in children
- Elevated alpha-fetoprotein (AFP) may indicate ESLD, hepatic malignancies, or germ cell tumors
- There is an increased incidence of HCC in patients with MASLD and advanced fibrosis

Objective

- Investigate the prevalence of elevated AFP in children with advanced fibrosis in the context of MASLD
- Ascertain whether pediatric MASLD is associated with AFP elevations in the absence of advanced disease

Methods

- Retrospective cohort study at the Steatohepatitis Center of CCHMC
- Inclusion Criteria:**
 - Jan 2000 - 2024
 - ≤ 18 years at time of establishing care
 - ≥ 1 AFP level
 - No known liver disease or malignancy
- Data Collected:**
 - Demographics
 - BMI, BMI z-score
 - Additional labs
 - Histology
 - Radiology

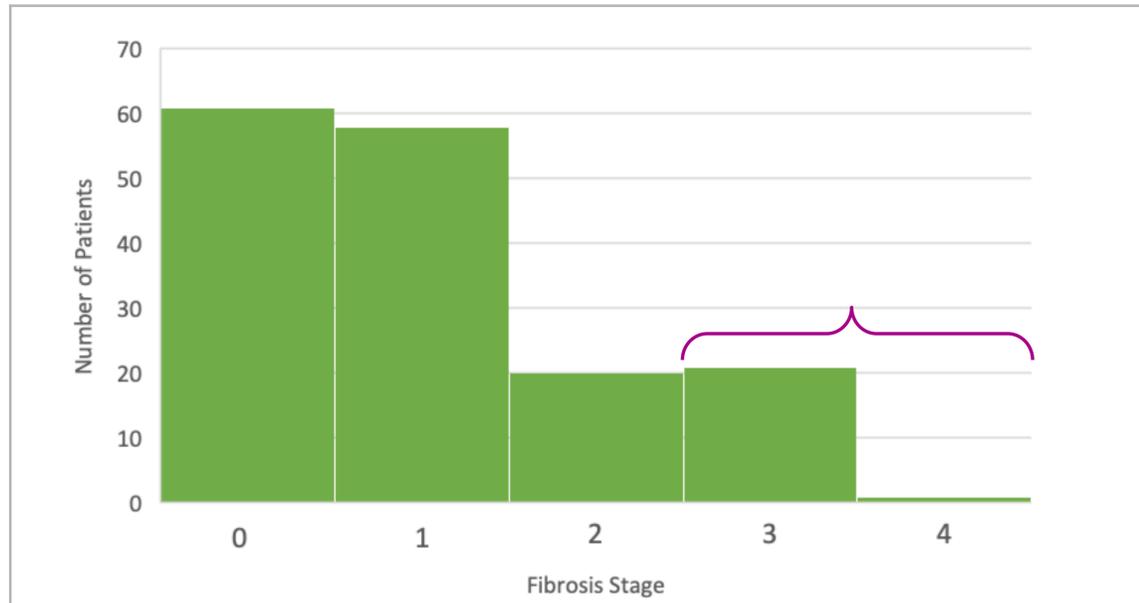
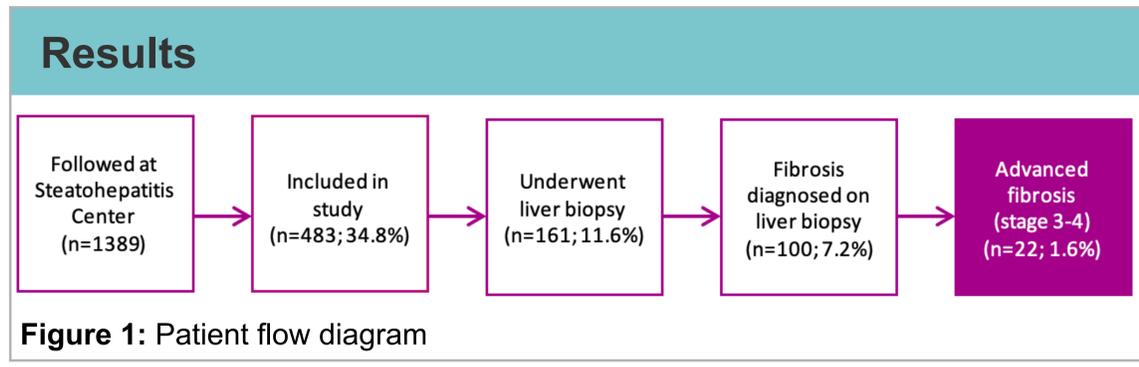


Figure 2: Distribution of fibrosis stages among patients who had a liver biopsy

	Imaging				Other tumor markers	AFP trend	Outcome and findings
	Liver U/S	Liver MRI	Scrotal U/S	Other imaging			
Patient 1	✓	✓				6 mo later: remained elevated	Cholecystitis
Patient 2		✓	✓	CT head		6 mo later: normalized	Normal
Patient 3		✓				No repeat	Normal
Patient 4	✓	✓	✓	CT chest, MRI head	β-HCG	18 mo later: remained elevated	Normal
Patient 5		✓	✓		AFP L3/total	29 mo later: normalized	Epididymal cysts, hydrocele
Patient 6		✓			β-HCG	2 mo later: normalized	Normal
Patient 7	✓				AFP L3/total	28 mo later: remained elevated	Normal
Patient 8	✓				AFP L3/total	No repeat	Cholecystitis
Patient 9						13 mo later: Remained elevated	Normal

Table 1: Work up of patients with elevated AFP

Results

Of the 22 patients with advanced fibrosis:

- Age 11 years; 10-18 (median; IQR)
- 82% male
- 55% non-Hispanic
- All had severe obesity
 - BMI z-score 2.56; 2.33-2.75 (median; IQR)

None had an elevated AFP

Of the 9 patients with elevated AFP:

- Peak AFP 11.1 ng/mL; 10.4-14.3 (median; IQR)
- Age 16 years; 13-18 (median; IQR)
- 78% male
- 67% non-Hispanic
- All had severe obesity
 - BMI z-score 2.56; 2.07-2.71 (median; IQR)

Outcomes summarized in Table 1

Discussion

- None** of the patients with advanced fibrosis had elevated AFP or malignancy
- AFP was elevated in a small proportion of the general MASLD population, and **not** associated with malignancy

Conclusion

- AFP is an imperfect screening tool for HCC due to low sensitivity and specificity
- Risk factors for progression to ESLD and HCC in children with MASLD have not been entirely elucidated
- These results suggest that the risk of HCC in pediatric MASLD cohorts is exceedingly low