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MASS SPECTROMETRY TO ASSESS MULTI-PLATFORM BIOMARKERS OF LIVER FIBROSIS IN BILIARY ATRESIA: A SYSTEMATIC REVIEW

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PURPOSE

- Biliary Atresia (BA) is a dreadful disease with an unpredictable outcome.
- Various biomarkers have been investigated to predict the prognosis in BA.
- Recent advances in high-throughput mass spectrometry (MS) have enabled detailed profiling of circulating and excretory biomarkers, offering a non-invasive window into hepatic fibrogenesis.
- This study synthesises evidence on the application of MS —particularly liquid chromatography–tandem MS (LC-MS/MS) and data-independent acquisition MS (DIA-MS)—in assessing fibrosis severity and prognosis in BA.

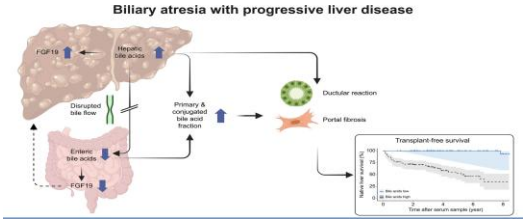


Fig. Graphical abstract from Ref [3]

METHOD

- A PubMed search done on 18 June 2025, using search words “biliary atresia mass spectroscopy liver fibrosis”, yielded 9 articles.
- The manuscripts were studied to explore the transformative role of MS in understanding and diagnosing liver fibrosis in biliary atresia and patient care.

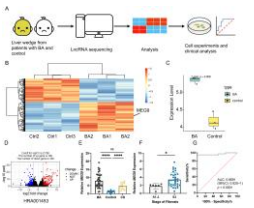


Fig. 1 Upregulated expression of lncRNA MEG9 in BA liver tissues.[2]

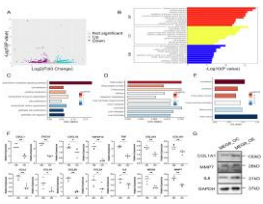
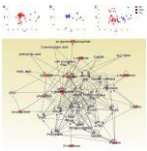
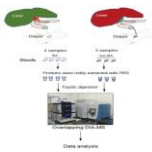


Fig.2 Downstream pathways activated by MEG9 [2]





RESULTS

- LC-MS/MS-based bile acid profiling revealed significantly elevated total and conjugated bile acids in patients with portal hypertension and progressive disease following KPE.
- Serum levels of fibroblast growth factor 19 (FGF19), quantified alongside bile acids, were reported as a strong predictor of liver fibrosis and transplant-free survival, with FGF19 >109 pg/mL associated with a hazard ratio of 4.31 for poor outcomes.
- Reduced levels of 7α-hydroxy-4-cholesten-3-one (C4), a surrogate marker of bile acid synthesis, correlated with advanced fibrosis, suggesting suppressed hepatic bile acid production.
- Fecal proteomic studies using DIA-MS identified over 100 proteins differentially expressed in BA versus non-BA controls, providing a stool-based diagnostic signature with high discriminatory power (AUC >0.90).
- Urinary bile acid screening via tandem mass spectrometry has been effective in detecting inborn errors of bile acid synthesis, though overlap with BA necessitates confirmatory testing.
- Targeted metabolomic approaches further differentiated BA from neonatal hepatitis syndrome using plasma biomarkers such as N-acetyl-D-mannosamine. lncRNA MEG9 was shown to enhance cholangiocyte inflammatory signaling via S100A9 interaction, while ^13C-phenylalanine breath testing correlated well with fibrosis grades.
- Integration of microbiome sequencing with MS-derived bile acid profiles uncovered dysbiosis in patients with cholangitis post-Kasai portoenterostomy.

CONCLUSION

- MS has revolutionised biomarker discovery, enabling multi-platform, high-resolution profiling of bile acids, metabolites, and proteins, facilitating early diagnosis, monitoring, and mechanistic understanding of fibrosis in BA.
- These tools offer a future role for clinical translation and personalised patient care

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