Diagnostic delay in inherited metabolic diseases: Implications for newborn screening from the U-IMD registry

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Introduction and Aim

Early diagnosis is essential to prevent irreversible morbidity and mortality in inherited metabolic diseases (IMDs). However, comprehensive data on the diagnostic process in IMDs are scarce. This study aimed to systematically characterize diagnostic delay across a large European IMD cohort and to assess differences between individuals diagnosed via newborn screening and after onset of symptoms.

Methods

We analyzed data from the Unified European registry for Inherited Metabolic Diseases (U-IMD), the patient registry of the European Reference Network (MetabERN). Age at symptom onset, mode of diagnosis, age at diagnosis, and diagnostic delay were assessed across IMDs. Diagnostic delay was defined as the time between symptom onset and diagnosis.

Results

Data from 3,747 individuals with confirmed diagnoses of 345 IMDs were included. Median age at onset of symptoms was 120 days. Most individuals were diagnosed following clinical presentation and faced substantial diagnostic delays, with 47.6% experiencing a delay of at least one year. Diagnostic delay varied widely between disorders and disease groups and showed no relevant improvement over recent decades in this group. In contrast, individuals diagnosed through newborn screening had a markedly lower age at diagnosis (median 9 days vs. 1095 days, $p < 0.001$) and 53.2% remained asymptomatic at last follow-up.

Conclusion

Diagnostic delay remains a major challenge in IMDs and persists across many disorders despite advances in diagnostics. Newborn screening, however, enables substantially earlier diagnosis and prevention of symptom manifestation. These findings underscore the importance of continued expansion and optimization of newborn screening programs and complementary early diagnostic strategies to reduce diagnostic delay and improve outcomes.

References

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