ESPED Erhebungseinheit für Seltene Pädiatrische Erkrankungen in Deutschland

UNIVERSITÄTSmedizin. MAINZ

Forschungsstelle für Pädiatrische Epidemiologie mit Unterstützung der Deutschen Gesellschaft für Kinder- und Jugendmedizin e.V. (DGKJ)

The Yellow Infant – Neonatal and Infantile Cholestasis

In cooperation with the German Society for Paediatric Gastroenterology and Nutrition (GPGE) and the German Society for Neonatology and Paediatric Intensive Care (GNPI)

Objectives and Research Questions

Aims

The aims of this study are:

1. To provide an updated assessment of the incidence of neonatal and infantile cholestasis, as well as its etiology.
2. To establish a data-validated, step-by-step diagnostic pathway and optimize its timeline (Diagnostic Algorithm).
3. To evaluate adherence to current clinical guidelines [1].

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Start of study: July 2026

Expected Case Numbers: Approximately 300 cases per year across Germany

Background

The term "neonatal cholestasis" or, more accurately, "infantile cholestasis" describes a conjugated hyperbilirubinaemia in infants up to a corrected age of approximately 4 months [1]. This condition is suspected in cases of prolonged jaundice (icterus prolongatus) lasting beyond the 14th day of life (or beyond the 21st day in exclusively breastfed infants) or when other symptoms such as acholic (pale) stools are present. In such cases, total bilirubin as well as direct (conjugated) bilirubin levels should be measured [1]. A conjugated bilirubin value of > 1 mg/dl (equivalent to > 17 µmol/l) is considered pathological.

The differential diagnosis comprises numerous etiological entities. Globally, the most common cause of infantile cholestasis is extrahepatic biliary atresia, accounting for 20% to 41% of cases [1,2]. Reaching a diagnosis requires a comprehensive and rapid workup, as surgical intervention (the Kasai hepatic portoenterostomy [3]) is highly time-sensitive in these patients.

Relevance to Health Services Research and Clinical Science

According to published study data [1,2], the etiology remains unexplained in up to 24% of neonatal and infantile cholestasis cases. A systematic recording of the diagnostic workups performed, and their respective outcomes is highly warranted; the existing database is over 10 years old, and significant new diagnostic modalities - such as low-threshold molecular genetic testing - have emerged in recent years. These advances may help reduce the percentage of cases classified as idiopathic.
Additionally, this study will allow researchers to evaluate and potentially optimize both the timeline and the substance of the diagnostic algorithm and guideline adherence in neonatal and infantile cholestasis. This addresses key aspects of health services research. Furthermore, this data will provide a valuable foundation for the update of the S2k guideline on neonatal cholestasis [1], which has recently expired and is scheduled for revision in the coming years.

Case definition

Inclusion criteria

Infants aged 14 to 90 days admitted due to a conjugated hyperbilirubinaemia > 1 mg/dl (17 µmol/l).

Literature:

[1] Grothues D, Engelhardt H, Genzel-Boroviczeny O, Gnädig M, Harm M et al. S2k-Leitlinie: Cholestase im Neugeborenenalter [S2k Guideline: Cholestasis in the Newborn Period], AWMF Registry No. 068/015; 2021

[2] Hoerning A et al. Diversity of disorders causing neonatal cholestasis - the experience of a tertiary pediatric center in Germany. Front Pediatr 2: 65, 2014

[3] Kasai M, Suzuki S (1959) A new operation for, 'non-correctable' biliary atresia: hepatic portoenterostomy. Shuiyutsu13:733–739