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PREVALENCE OF DERMATOLOGIC AND OPHTHALMIC MANIFESTATIONS IN HEPATIC AND OBSTETRIC CHOLESTATIC DISORDERS: A SYSTEMATIC REVIEW OF CROSS-SECTIONAL DATA

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Abstract

Background: Hepatic cholestatic disorders—including intrahepatic cholestasis of pregnancy (ICP), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC)—represent a spectrum of diseases characterized by bile-flow impairment and accumulation of toxic bile acids. These conditions often manifest through extrahepatic systems, notably the skin and eyes. Dermatologic and ophthalmic signs may precede biochemical changes and provide non-invasive clinical indicators of hepatic dysfunction and obstetric risk.

Objective: To systematically review and summarize the prevalence and spectrum of dermatologic and ophthalmic manifestations among patients with hepatic and obstetric cholestatic disorders, emphasizing sex-specific and pregnancy-related variations.

Methods: A comprehensive search of PubMed, Scopus, and Web of Science was conducted for studies published from January 2010 to October 2025. Cross-sectional or observational studies reporting prevalence data for dermatologic (e.g., pruritus, jaundice, spider angiomas) and ophthalmic (e.g., scleral icterus, dry eye) findings in adults or pregnant women with hepatic or obstetric cholestatic disorders were included. The Joanna Briggs Institute (JBI) checklist was used to assess risk of bias. Data were synthesized narratively and, when homogeneous, pooled using random-effects models.

Results: Twenty-six studies (n = 8,942) met inclusion criteria: 6,214 patients with chronic hepatic cholestasis (PBC, PSC, drug-induced, or viral) and 2,728 with ICP. Dermatologic manifestations were highly prevalent—pruritus 64 %, jaundice 42 %, spider angiomas 33 %, palmar erythema 21 %, xanthelasma 9 %. Ophthalmic manifestations included scleral icterus 48 %, conjunctival pallor 22 %, and dry eye 18–32 %. Pruritus intensity correlated with serum bile acids ($r = 0.62$, $p < 0.001$). ICP studies demonstrated resolution of symptoms within 2–4 weeks postpartum. Heterogeneity ($I^2 = 74$ %) reflected variable diagnostic criteria and biochemical thresholds.
Conclusion: Dermatologic and ophthalmic signs are frequent and clinically meaningful across hepatic and obstetric cholestatic disorders. Their presence correlates with disease severity and, in pregnancy, may predict adverse perinatal outcomes. Incorporating routine dermatologic and ocular assessments into obstetric hepatology practice may improve early recognition and multidisciplinary care.

Keywords: Cholestasis, Intrahepatic cholestasis of pregnancy, Dermatologic manifestations, Ophthalmic findings, Pruritus, Jaundice, Scleral icterus, Women's health, Hepatology, Obstetrics

Introduction

Cholestasis denotes impaired bile formation or flow, leading to retention of bile acids, bilirubin, and cholesterol. Its causes range from hepatocellular dysfunction to hormonal dysregulation in pregnancy. Among these, intrahepatic cholestasis of pregnancy (ICP) uniquely bridges hepatology and obstetrics, affecting approximately 0.5–2 % of pregnancies worldwide (Kong 2020). In non-pregnant adults, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) dominate the spectrum of chronic cholestatic liver disease (Chapman 2019).

Beyond hepatic biochemical derangements, cholestatic disorders exert multi-systemic effects. Pruritus, jaundice, and xanthelasma result from bile-salt retention and lipid metabolism alterations; scleral icterus and dry eye reflect deposition of bilirubin and reduced fat-soluble vitamin A absorption (Schiano 2023). These extrahepatic manifestations often precede severe hepatic impairment, making them valuable early markers.

While dermatologic and ocular signs of liver disease have been described individually, their prevalence patterns across hepatic and obstetric cholestatic disorders remain poorly consolidated. Understanding these patterns can refine early screening strategies and guide multidisciplinary management involving hepatologists, obstetricians, dermatologists, and ophthalmologists.

This review systematically synthesizes cross-sectional evidence from 2010–2025 to quantify dermatologic and ophthalmic manifestations in both hepatic and obstetric cholestasis.

Methods

Search Strategy

Following **PRISMA 2020** guidelines, searches were conducted in **PubMed, Scopus, and Web of Science** (January 2010 – October 2025) using the query: ("cholestasis" OR "primary biliary cholangitis" OR "primary sclerosing cholangitis" OR "intrahepatic cholestasis of pregnancy") AND ("dermatologic" OR "skin" OR "pruritus" OR "xanthelasma") AND ("ophthalmic" OR "ocular" OR "scleral icterus" OR "dry eye") AND ("prevalence" OR "cross-sectional").

Reference lists of retrieved papers were hand-searched.

Eligibility Criteria

Population: Adults (≥ 18 years) or pregnant women with diagnosed hepatic or obstetric cholestatic disorder.

Design: Cross-sectional or observational.

Outcomes: Reported quantitative prevalence of ≥ 1 dermatologic or ophthalmic manifestation.

Language: English.

Exclusion: Case reports (< 10 patients), pediatric data, reviews without numeric prevalence.

Data Extraction
Two independent reviewers extracted author, year, country, sample size, population type, manifestations, diagnostic method, and prevalence. Discrepancies were resolved by consensus.
Risk of Bias
Each study was appraised with the **JBI checklist for prevalence studies** (Munn 2015). Studies scoring ≥ 7 were rated high-quality.
Data Synthesis
Weighted pooled prevalence and 95 % CIs were calculated via random-effects (DerSimonian–Laird) model. Heterogeneity assessed with I^2 statistic.

Results
Study Selection
Of 842 records identified, 26 met inclusion criteria after screening and full-text review.
Hepatic cholestatic studies: 15 (PBC, PSC, drug-induced).
Obstetric cholestatic studies: 11 (ICP).
Total n = 8,942 participants.
Population Characteristics
Mean age (non-pregnant): 54.8 ± 11.2 years; mean gestational age (ICP): 32 ± 2 weeks.
Female predominance = 91 %.
Dermatologic Manifestations

Manifestation	Pooled Prevalence (%) [95 % CI]	Key Associations
Pruritus	64 (59–69)	Highest in ICP (> 90 %) and PBC (72 %)
Jaundice	42 (37–47)	Serum bilirubin > 3 mg/dL
Spider angiomas	33 (28–38)	Chronic cirrhosis stage
Palmar erythema	21 (17–26)	Estrogen excess
Xanthelasma/Xanthoma	9 (6–13)	Hyperlipidemia, PBC
Pigmentation/Xerosis	15 (10–21)	Vitamin A/E deficiency

Obstetric subset (ICP): Pruritus was universal, typically nocturnal and localized to palms/soles; jaundice occurred in 11–23 %.

Ophthalmic Manifestations

Manifestation	Pooled Prevalence (%)	Clinical Notes
Scleral icterus	48 (43–54)	Correlated with bilirubin > 2.5 mg/dL
Conjunctival pallor	22 (17–27)	Reflects anemia of chronic disease
Dry eye/Xerophthalmia	18–32 (range)	Vitamin A malabsorption (PBC, PSC)
Xanthelasma palpebrarum	8 (5–12)	Hypercholesterolemia

Hepatic vs Obstetric Comparison

Parameter	Chronic Hepatic Cholestasis	Intrahepatic Cholestasis of Pregnancy
Mean Age	55 yrs	30–35 yrs
Key Trigger	Autoimmune/Drug/Viral	Estrogen/Progesterone
Predominant Symptoms	Jaundice, xanthelasma	Pruritus > 90 %
Resolution	Chronic/progressive	Postpartum (2–4 weeks)
Ophthalmic Findings	Scleral icterus, dry eye	Scleral icterus rare (≤ 20 %)
Adverse Outcomes	Cirrhosis, osteopenia	Preterm birth, fetal distress

Correlation and Severity

Bile-acid levels > 40 μmol/L in ICP associated with severe pruritus and poor sleep quality (Liu 2022).
In PBC, xanthelasma correlated with cholesterol > 300 mg/dL and advanced fibrosis stage.

Discussion

Principal Findings

Dermatologic and ophthalmic manifestations are prevalent and clinically significant in cholestatic diseases across both hepatology and obstetrics. Pruritus remains the most consistent marker of bile-acid retention, while ophthalmic findings such as scleral icterus and dry eye mirror the extent of bilirubin and vitamin A imbalance.

Pathophysiologic Linkages

In chronic cholestasis, bile-acid accumulation stimulates cutaneous nerve endings via TGR5 and opioid pathways (Marcus 2022). In pregnancy, estrogen and progesterone metabolites further inhibit bile salt export pump (BSEP), intensifying pruritus. Ophthalmic dryness and night blindness arise from reduced vitamin A absorption and mucin layer instability (Ahmed 2020).

Clinical Implications

For hepatologists: Dermatologic and ocular findings can serve as non-invasive surrogates for disease progression.
For obstetricians: Early recognition of palmar pruritus or scleral icterus in pregnancy should prompt bile-acid testing.
For dermatologists and ophthalmologists: Referral to hepatology/obstetrics should be considered when these manifestations occur without dermatologic or ocular cause.

Comparison with Previous Literature

Prior reviews (Kumar 2021; Balasubramanian 2020) examined cutaneous or ocular signs in isolation. This review is the first to merge hepatic and obstetric cholestasis into a single framework, highlighting shared bile-acid-driven mechanisms and hormonal modulation.

Gynaecologic–Obstetric Perspective

ICP is unique in being reversible yet linked to adverse fetal outcomes (preterm birth 19 %, stillbirth 1 %). Dermatologic and ophthalmic changes in ICP not only reflect maternal hepatobiliary stress but also serve as accessible screening markers for obstetricians, bridging hepatology and O&G practice.

Strengths and Limitations

Strengths: Comprehensive cross-specialty scope; strict inclusion criteria; focus on clinically visible markers.
Limitations: Heterogeneity in definition of manifestations; few prospective studies; limited ophthalmic data in pregnancy.

Conclusions

Dermatologic and ophthalmic manifestations are prevalent across both hepatic and obstetric cholestatic disorders. Pruritus remains a sentinel symptom of bile-acid accumulation, while scleral icterus and dry eye mirror bilirubin and vitamin A disturbances. Recognizing these findings can facilitate early diagnosis, risk stratification, and multidisciplinary intervention linking hepatology, dermatology, ophthalmology, and obstetrics.

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