

Perinatal outcomes of isolated non-visualization of the fetal gallbladder

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ABSTRACT

Aims: This study aimed to evaluate perinatal outcomes in pregnancies with isolated non-visualization of the fetal gallbladder (NVFGB) identified during second-trimester anatomical screening.

Methods: This retrospective cohort study included 22 pregnancies diagnosed with isolated NVFGB between November 2022 and January 2025 at a tertiary maternal-fetal medicine unit. Cases with additional structural anomalies, multiple gestations, or elective terminations were excluded. Maternal demographics, antenatal ultrasound findings, and neonatal outcomes were reviewed. Postnatal imaging and clinical follow-up were evaluated for gallbladder visualization and underlying pathology.

Results: In half of the included cases (11/22), the gallbladder was visualized either on follow-up scans or after birth. Among the remaining 11 cases, two had midline-located gallbladders on postnatal imaging, one of which required surgical correction for intestinal malrotation. Two fetuses were prenatally diagnosed with cystic fibrosis, including one complicated by meconium peritonitis requiring surgery. Two additional cases were diagnosed postnatally with biliary atresia and underwent hepatoportoenterostomy. Chromosomal microarray analysis (CMA) was performed in ten cases; no anomalies were identified aside from cystic fibrosis. Overall, five cases (23%) were associated with significant postnatal diagnoses requiring medical or surgical intervention.

Conclusion: Although isolated NVFGB is often a benign and transient finding, it may occasionally indicate serious underlying conditions such as biliary atresia or cystic fibrosis. Detailed follow-up, repeat imaging in late gestation, and thorough postnatal evaluation are essential for appropriate diagnosis and management.

Keywords: Biliary tract abnormalities, gallbladder abnormalities, prenatal ultrasonography

INTRODUCTION

The gallbladder originates from the hepatic diverticulum during early embryogenesis, and disruptions in this process may lead to anomalies such as agenesis, biliary atresia, or ectopic localization.^{1,2} Among these, gallbladder agenesis is relatively uncommon, with a reported prevalence of approximately 0.1%.³ Nevertheless, its occurrence represents a significant prenatal finding due to its potential association with a variety of structural and genetic conditions—including other gastrointestinal anomalies, cardiac malformations, and chromosomal abnormalities. Consequently, non-visualization of the gallbladder on prenatal imaging necessitates a thorough anatomical assessment. In selected cases, evaluation of digestive enzyme levels in the amniotic fluid, in addition to invasive genetic testing, may also provide valuable information.^{4,5}

Although non-visualization of the fetal gallbladder is frequently reported as a prenatal ultrasound finding during early second-trimester sonography, subsequent imaging—

either later in gestation or postnatally—often confirms the presence of a normally developed gallbladder. In approximately one-quarter of these cases, the gallbladder becomes visible on follow-up ultrasounds. Moreover, in up to 40% of fetuses with persistent non-visualization throughout pregnancy, postnatal imaging reveals a structurally normal gallbladder.⁶ This discrepancy highlights the potential for false-positive diagnoses and underscores the dynamic nature of fetal gallbladder visualization. While most isolated cases are associated with favorable outcomes, the possibility of underlying structural or genetic abnormalities necessitates careful differential diagnosis.⁷

In this context, the present study aimed to evaluate the ultrasonographic characteristics and perinatal outcomes of cases with isolated non-visualization of the fetal gallbladder (NVFGB) detected during second-trimester anatomical screening.

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METHODS

The study population was identified through a review of electronic medical records of pregnant women with NVFGB during second-trimester anatomical screening. All fetal anatomical screening records between November 1, 2022, and January 1, 2025, were reviewed. The study protocol was approved by the Scientific Researches Evaluation and Ethics Committee No. 1 at Ankara Etlik City Hospital (Date: 14.05.2025, Decision No: AESH-BADEK1-2025-204) and conducted in accordance with the Declaration of Helsinki.

In this study, NVFGB was defined as the inability to identify the gallbladder on second-trimester anatomical ultrasound and on a confirmatory subsequent scan, despite adequate visualization of other abdominal organs. Only patients who received both antenatal follow-up and delivery at our institution were included. For isolated NVFGB, follow-up sonographic data were reviewed to assess gallbladder visibility and the gestational age at which visualization occurred. When the gallbladder remained non-visualized antenatally, postnatal follow-up and neonatal imaging, when available, were used to distinguish transient non-visualization from true agenesis. In cases requiring surgical intervention, the type and timing of procedures were recorded to provide further insight into the clinical significance and outcomes of gallbladder agenesis.

Pregnancies complicated by additional structural anomalies, multiple gestations, or terminated due to fetal or maternal indications were excluded. Maternal demographic characteristics, results of prenatal screening tests, follow-up sonographic findings, and mode of delivery were recorded. Neonatal outcomes, including gestational age at delivery, birth weight percentile, 1- and 5-minute Apgar scores, admission to the neonatal intensive care unit (NICU), and any postnatal imaging or endoscopic procedures related to the gallbladder, were also evaluated.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean±standard deviation or median (minimum–maximum), and categorical variables as counts and percentages. Only descriptive statistics were presented; no group comparisons were made.

RESULTS

This study included 22 cases of isolated NVFGB identified during second-trimester anatomical screening, with a mean gestational age at diagnosis of 18+6 weeks. Maternal and neonatal baseline characteristics are summarized in **Table 1**. In terms of neonatal outcomes, six neonates (27%) required admission to the NICU, including one case in which the gallbladder was later visualized and five cases with clinically significant postnatal diagnoses in addition to gallbladder agenesis.

Overall, the presence of the gallbladder was confirmed in 11 of the 22 cases (50%), either antenatally or postnatally.

Table 1. Maternal characteristics and neonatal outcomes (n=22)

Maternal age*	31.32 (24-39)
Gravidity*	1.73 (1-4)
Parity*	0.5 (0-2)
Abortus*	0.5 (0-2)
Parental consanguinity†	
Yes	2 (9.09%)
No	20 (90.9%)
Gestational age at ultrasound*	18+6 (15-22)
Birth week*	38+3 (36-40+3)
Birth weight (g)*	3128.6 (2410-3680)
Apgar score 1 st min*	7.45 (4-9)
Apgar score 5 th min*	8.68 (5-10)
Blood gas pH value*	7.30 (7.05-7.46)
NICU admission†	6 (27.2%)

*Values are presented as median (minimum–maximum); †Values are presented as number (percentage). NICU: Neonatal intensive care unit

Specifically, in eight cases, the gallbladder became visible on follow-up scans performed in the late second or early third trimester. In another four cases, a thin, hyperechoic tubular structure was noted in the expected location of the gallbladder, although the typical morphology was absent; postnatal sonography confirmed the presence of the gallbladder in three of these. In the remaining case, postnatal imaging failed to demonstrate a definitive gallbladder, and the appearance was interpreted as consistent with agenesis. The outcomes of these cases are detailed in **Table 2**.

In the remaining 11 cases, the gallbladder could not be identified in its expected location on postnatal imaging. Among these, two cases demonstrated atypical findings, with the gallbladder located in the midline of the abdomen. One of these was subsequently diagnosed with intestinal malrotation and underwent surgical intervention on postnatal day 5 due to suspected intestinal obstruction. During laparotomy, extensive Ladd's bands were excised, ileal loops were mobilized, and the gallbladder was visualized. The other case remained asymptomatic, with no abnormalities detected during seven months of postnatal follow-up.

Two fetuses had a prenatal diagnosis of cystic fibrosis, one of whom was born to consanguineous parents. One developed meconium peritonitis and required ileal resection with primary anastomosis on postnatal day 1. Biliary atresia was identified in two further cases—one presenting antenatally with a hyperechoic tubular structure and the other with complete non-visualization—both of which underwent hepatportoenterostomy (Kasai procedure) on postnatal days 6 and 11, respectively.

Chromosomal microarray analysis (CMA) was performed in six cases; aside from the two with cystic fibrosis, no anomalies were detected. In total, five cases (23%) were associated with clinically significant postnatal diagnoses requiring medical or surgical intervention. These findings are summarized in **Table 3**.

Table 2. Outcomes of fetuses with NVFGB and subsequent visualization on follow-up or postnatal evaluation (n=11)

Case no	GA at 1 st USG (wks)	Antenatal GB visibility	GA at GB visualization	Genetic testing	Postnatal GB
1	17	NVFGB	24	Not performed	Normal
2	19	NVFGB	28	Not performed	Normal
3	19	NVFGB	27	Not performed	Normal
4	21	NVFGB	24	Not performed	Normal
5	20	NVFGB	29	Normal CMA	Normal
6	20	NVFGB	31	Not performed	Normal
7	19	NVFGB	33	Normal CMA	Normal
8	22	NVFGB	26	Not performed	Normal
9	20	Hyperechoic tubular structure	Not visualized	Normal CMA	Normal
10	18	Hyperechoic tubular structure	Not visualized	Normal CMA	Normal
11	19	Hyperechoic tubular structure	Not visualized	Not performed	Normal

GA: Gestational age, USG: Ultrasonography, GB: Gallbladder, NVFGB: Non-visualization of the fetal gallbladder, CMA: Chromosomal microarray analysis

Table 3. Outcomes of fetuses with persistent NVFGB diagnosed with gallbladder agenesis (n=11)

Case no	GA at 1 st USG (wks)	Antenatal GB visibility	Genetic testing	Postnatal diagnosis	Postnatal course
1	19	NVFGB	Not performed	Contracted GB	Asymptomatic
2	19	NVFGB	Normal CMA	Midline GB	Asymptomatic
3	20	NVFGB	Normal CMA	Midline GB+intestinal malrotation	Laparotomy
4	17	NVFGB	Cystic fibrosis	GB Agenesis+meconium peritonitis	Ileal resection and primary anastomosis
5	16	NVFGB	Cystic fibrosis	GB agenesis	Asymptomatic
6	17	NVFGB	Not performed	GB agenesis	Asymptomatic
7	19	NVFGB	Normal CMA	GB agenesis	Asymptomatic
8	15	NVFGB	Not performed	GB agenesis	Asymptomatic
9	18	NVFGB	Normal CMA	GB agenesis	Asymptomatic
10	21	NVFGB	Normal CMA	GB agenesis+biliary atresia	Hepatopertoenterostomy
11	19	Hyperechoic tubular structure	Normal CMA	GB Agenesis+biliary atresia	Hepatopertoenterostomy

GA: Gestational age, USG: Ultrasonography, GB: Gallbladder, NVFGB: Non-visualization of the fetal gallbladder, CMA: Chromosomal microarray analysis

DISCUSSION

NVFGB during second-trimester sonography is generally regarded as a benign finding in isolated cases, as the gallbladder is often visualized later in gestation or confirmed postnatally.^{8,9} In our study, approximately half of the fetuses with either prenatal non-visualization or a small, hyperechoic tubular appearance of the gallbladder were confirmed to have a gallbladder on postnatal imaging. In eight cases, the gallbladder became visible in subsequent prenatal scans, and no postnatal abnormalities were identified. These findings suggest the possibility that isolated non-visualization may reflect physiological variability or technical limitations rather than true pathology. Therefore, serial ultrasound evaluations during pregnancy are recommended in such cases to avoid unnecessary interventions.

Nevertheless, persistent non-visualization may sometimes represent the only prenatal indicator of significant underlying pathology. One of the most critical conditions in this context is biliary atresia—a progressive fibro-obliterative disease of the extrahepatic bile ducts that can lead to liver failure in the absence of timely intervention.^{10,11} Although various anatomical variants have been described, the gallbladder is frequently absent in cases of biliary atresia; when present, it is

usually abnormal in size and may be associated with hepatic hilar cysts.¹² A hallmark prenatal sonographic feature of biliary atresia is the 'triangular cord sign,' first described by Choi et al.¹³ in 1996, which refers to an echogenic band ≥ 4 mm in thickness located anterior to the portal vein bifurcation, thought to represent fibrotic remnants of the bile ducts. Although several sonographic features—such as abnormal gallbladder morphology, non-visualization of the common bile duct, hepatic subcapsular flow, or increased hepatic artery diameter—have been associated with biliary atresia, most of these findings are typically identified postnatally, and their utility in antenatal diagnosis remains limited.^{14,15}

In the literature, postnatal diagnosis of biliary atresia has been reported in approximately 4% of cases with isolated non-visualization of the gallbladder on prenatal ultrasound; however, gallbladder agenesis is observed in almost all cases of biliary atresia.^{16,17} Consistent with these findings, two cases in our cohort were diagnosed with biliary atresia postnatally and subsequently underwent Kasai portoenterostomy.

In addition to hepatobiliary anomalies, gastrointestinal malformations are also commonly associated with gallbladder agenesis. In our series, one fetus was diagnosed with intestinal malrotation that required surgical intervention. Furthermore,

two cases were prenatally diagnosed with cystic fibrosis. In one of these, meconium peritonitis was detected shortly before birth, necessitating ileal resection and anastomosis on the first day of life. While uncommon, NVFGB may serve as the earliest—and sometimes the only—prenatal indicator of cystic fibrosis. In the presence of associated findings such as echogenic bowel, bowel dilation, or meconium peritonitis, genetic counseling and molecular testing for cystic fibrosis should be considered.^{18,19}

The fetal gallbladder exhibits a wide range of morphological variations, including folded, septated, spherical, or angular configurations. These variants are typically benign in the absence of additional structural anomalies. When a detailed second-trimester ultrasound reveals no other abnormalities, such morphological differences are generally regarded as physiological.⁹ However, in any case of suspected gallbladder agenesis, a meticulous evaluation of the intra-abdominal anatomy, particularly the liver, porta hepatis, and bile ducts, is essential to exclude underlying pathology.

This study contributes to the current literature by specifically focusing on isolated cases of gallbladder non-visualization and providing a detailed analysis of both antenatal and postnatal outcomes.

Limitations

This study has several limitations. The retrospective design may have introduced selection and information bias. The relatively small sample size may have limited the statistical power to detect rare associations. In addition, the absence of genetic testing in some cases could have led to an underestimation of underlying genetic conditions. Finally, the lack of long-term follow-up data restricts the ability to evaluate delayed postnatal outcomes.

CONCLUSION

As a result, although NVFGB during second-trimester anatomical screening is often a benign and transient finding, it may occasionally represent the earliest manifestation of serious hepatobiliary or systemic conditions. Therefore, even in isolated cases, comprehensive prenatal and postnatal evaluation, repeat imaging in later gestation, and a multidisciplinary approach are warranted to ensure timely diagnosis and appropriate management.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was approved by the Scientific Researches Evaluation and Ethics Committee No. 1 at Ankara Etlik City Hospital. (Date: 14.05.2025, Decision No: AESH-BADEK1-2025-204).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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