

Received: 2020.07.16  
Accepted: 2020.10.02  
Available online: 2020.11.02  
Published: 2021.01.05

# Utility of Magnetic Resonance Imaging in Diagnosis of Prenatal Non-Visualization of the Fetal Gallbladder: A Case-Series Study

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**Source of support:** Departmental sources

**Background:** This study aimed to assess the utility of magnetic resonance imaging (MRI) in the diagnosis of prenatal non-visualization of the fetal gallbladder (PNVGB).


**Material/Methods:** The clinical data of 32 pregnant women with PNVGB who underwent MRI examination during the second and third trimester of pregnancy were collected and their outcomes were analyzed.

**Results:** MRI showed that 26 patients (81.3%) had isolated PNVGB and 6 (18.8%) had additional malformations. In 26 patients with isolated PNVGB, 7 were found in the gallbladder on MRI and 4 were found on subsequent ultrasonography. One patient had termination of pregnancy (TOP) and 1 patient was lost to follow-up; the remaining 24 patients were known to deliver a healthy child. Among the 6 patients with additional malformations, 3 terminated their pregnancies due to combined severe abnormalities: 1 patient with horseshoe kidney and 1 with fetal echogenic bowel both had a healthy child, while 1 with fetal growth restriction (FGR) delivered a child who walked on tiptoe.

**Conclusions:** MRI contributes to identifying PNVGB detected or suspected by ultrasonography.

**MeSH Keywords:** **Gallbladder Diseases • Magnetic Resonance Imaging • Prenatal Diagnosis**

**Full-text PDF:** <https://www.medscimonit.com/abstract/index/idArt/927474>

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## Background

Prenatal non-visualization of the fetal gallbladder (PNVGB) is uncommon in clinical practice, accounting for only about 0.10–0.15% of pregnancies [1,2]. Bile is formed by the fetal hepatic cells at 12 gestational weeks and enters the duodenum through the bile duct after 13 gestational weeks. The length, anteroposterior diameter, and transverse diameter of the fetal gallbladder have a linear relationship with gestational age between 15 weeks and 30 weeks, after which a plateau is observed [3,4]. The fetal gallbladder can be observed by transvaginal ultrasound at 14–16 weeks of gestation in 99.9% of pregnancies [1,2]. In 95% of pregnancies, it can be observed at 24–32 weeks of gestation by transabdominal ultrasound [5]. However, after 35 weeks, the gallbladder may not be visualized at the complete contraction due to the enhanced contraction function. Additionally, other factors like fetal positions and operating methods may also lead to PNVGB.

PNVGB is reported to have a correlation with benign conditions, including isolated gallbladder agenesis or several severe disorders such as cystic fibrosis, aneuploidies, and biliary atresia [6]. Gallbladder agenesis is a benign condition, with an incidence rate of 1/6300 [7], while biliary atresia is a severe disease associated with liver transplantation and death [8]. Typically, the gallbladder is very small or not seen by ultrasonography in cases of biliary atresia, and biliary atresia, which is characterized by intra- and extrahepatic bile duct obliteration, can progress rapidly to liver fibrosis and cirrhosis, and can even result in death if untreated [9–11]. Therefore, correct differential diagnosis is crucial due to the poor prognosis of some of these entities.

Prenatal diagnosis plays a crucial role in the identification of PNVGB [12,13]. Recently, fetal magnetic resonance imaging (MRI) has been used as a supplementary imaging method for fetuses at risk [14,15]. Through fetal MRI, the gallbladder can be visualized, mainly depending on the signal properties of gallbladder bile. Until now, the gallbladder MRI appearance has been described in fetuses without gastrointestinal abnormalities [16], but there are few data regarding the use of MRI in the diagnosis of PNVGB diagnosed by ultrasonography. Therefore, the present study was performed to assess the utility of MRI in the diagnosis of PNVGB by ultrasonography.

## Material and Methods

### Study population

In this retrospective study, 32 pregnant women with PNVGB diagnosed by ultrasonography were enrolled. Between September 2013 and December 2017, they all underwent MRI examinations

during the second and third trimester of pregnancy at Women's Hospital, School of Medicine, Zhejiang University. Based on MRI findings, we excluded the pregnant women with non-visualization of gallbladders due to intracranial abnormalities, foci in the liver, masses in the sacrococcygeal region, and unilateral renal agenesis of the fetuses, as well as those with gallbladders visible on ultrasonography but non-visualization on MRI. All the pregnant women voluntarily participated in this study and provided informed consent.

### MRI techniques

MRI was performed using a 1.5T and an 8 cardiac coil MRI system (General Electric Company, Signa HDxt, USA.), without maternal sedation. The subjects in a supine position were scanned through the single-shot fast spin echo (SSFSE) sequence on T2-weighted images (TR/TE, 2400/130 ms; field of view, 360×360 mm; slice thickness, 3 mm; acquisition time, 15–20 s). MRI findings were analyzed by a junior radiologist and a senior radiologist.

### Follow-up visit

All the patients were followed up postnatally, and the follow-up deadline was June 2019. The outcomes of children were ascertained by telephone call with their parents, including presence or absence of recurrent respiratory tract infection and jaundice, digestive and nutritional status, color of stool, growth and development, presence or absence of hepatobiliary ultrasonic B, and its results.

## Results

### Characteristics of study population

The average age of the 32 pregnant women was (31.3±4.6) years old. MRI examination was performed at (31.3±3.2) gestational weeks (GW), and the mean follow-up duration was (22.7±13.1) months. Among 32 patients, PNVGB was detected at the second trimester (n=6) and third trimester (n=26) of pregnancy. MRI examination found that 26 patients (81.3%) had isolated PNVGB (Table 1), while 6 patients (18.8%) had additional malformations (Table 2).

### Outcomes of 32 patients with PNVGB

The outcomes of 32 patients with PNVGB are summarized in Figure 1. In 26 patients with isolated PNVGB, 7 cases were found in the gallbladder on MRI and 4 on subsequent ultrasonography. There was 1 patient with termination of pregnancy (TOP) and 1 was lost to follow-up. Of the remaining 24 patients, all had a healthy child, among whom 10 did not receive

**Table 1.** Characteristics of 26 cases of isolated PNVGB.

Case	MRI (WG)	MRI appearance	Follow-up ultrasonography	Visualized time of gallbladder	Gender of baby	Postnatal ultrasonography	Final diagnosis	Outcome	Follow-up duration
1	30+	PNVGB	PNVGB	–	Male	Non-visualization of gallbladder	Gallbladder agenesis	Healthy	26 months
2	27	PNVGB	1.3×0.3 cm	27+	Female	Normal	Transient PNVGB	Healthy	25 months
3	32+	Visible, small, 0.7–1.2 cm	PNVGB	32+	Male	Not performed	Unknown	Healthy	25 months
4	32	PNVGB	1.1×0.3×0.4 cm	33+	Female	Not performed	Unknown	Healthy	25 months
5	29	PNVGB	PNVGB	2 days after birth	Male	Normal	Transient PNVGB	Healthy	20 months
6	31	PNVGB	PNVGB	–	Female	–	Unknown	TOP	–
7	34	Visible, small, 0.6×0.3 cm	PNVGB	34	Female	Not performed	Unknown	Healthy	21 months
8	32	Visible, small, 0.5×1.0 cm	PNVGB	32	Female	Not performed	Unknown	Healthy	21 months
9	32	PNVGB	PNVGB	–	Male	Not performed	Unknown	Healthy	19 months
10	33	PNVGB	PNVGB	–	Male	Not performed	Unknown	Healthy	40 months
11	36	Visible, small	PNVGB	1 month after birth	Male	Normal	Transient PNVGB	Healthy	28 months
12	37	PNVGB	PNVGB	2 days after birth	Female	Normal	Transient PNVGB	Healthy	52 months
13	33	Visible, small	PNVGB	33	Male	Non-visualization of gallbladder	Gallbladder agenesis	Healthy	51 months
14	26	Visible, 0.5×0.9 cm	PNVGB	26	–	–	–	–	Lost
15	31	PNVGB	PNVGB	6 months after birth	Female	Normal	Transient PNVGB	Healthy	57 months
16	36	Visible, small	PNVGB	36	Male	Not performed	Unknown	Healthy	18 months
17	27	PNVGB	PNVGB	–	Male	Not performed	Unknown	Healthy	15 months
18	32	PNVGB	PNVGB	15 months after birth	Female	Normal	Transient PNVGB	Healthy	15 months
19	33	PNVGB	Visible	33 weeks-birth	Female	Not performed	Unknown	Healthy	17 months
20	34	PNVGB	PNVGB	–	Male	Non-visualization of gallbladder	Gallbladder agenesis	Healthy	18 months
21	29	PNVGB	PNVGB	3 days after birth	Female	Normal	Transient PNVGB	Healthy	15 months
22	29	PNVGB	PNVGB	3 days after birth	Male	Small and left position	Gallbladder agenesis	Healthy	12 months
23	26	PNVGB	PNVGB	7days after birth	Male	Small	Gallbladder agenesis	Healthy	10 months

**Table 1 continued.** Characteristics of 26 cases of isolated PNVGB.

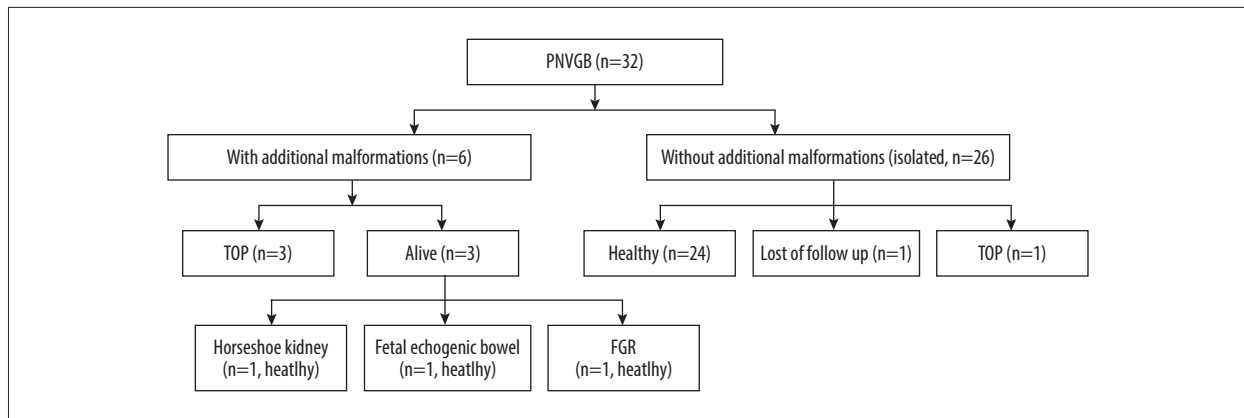
Case	MRI (WG)	MRI appearance	Follow-up ultrasonography	Visualized time of gallbladder	Gender of baby	Postnatal ultrasonography	Final diagnosis	Outcome	Follow-up duration
24	37	PNVGB	PNVG	3 months after birth	Female	Normal	Transient PNVGB	Healthy	11 months
25	32	PNVGB	PNVGB	–	Male	Not performed	Unknown	Healthy	11 months
26	25	PNVGB	Visible	29	Male	Normal	Transient PNVGB	Healthy	6 months

MRI – magnetic resonance imaging; WG – gestational weeks; PNVGB – prenatal non-visualization of the fetal gallbladder; TOP – termination of pregnancy.

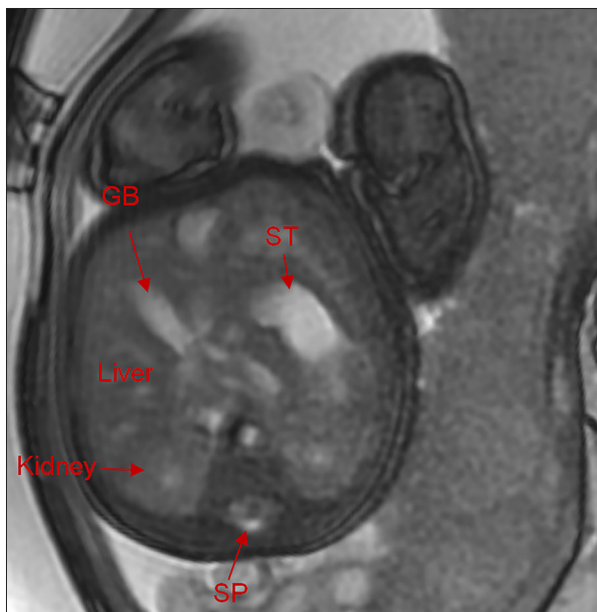
**Table 2.** Characteristics of 6 cases of additional fetal malformations.

Case	MRI (WG)	MRI appearance	Follow-up ultrasonography	Visualized time of gallbladder	Gender of baby	Postnatal ultrasonography	Final diagnosis	Outcome	Follow-up duration
1	32	Thickened subcutaneous fat all over the body, slightly thickened rectum and PNVGB	Fetal multiple abnormalities, the whole thickened skin and PNVGB	–	Male	–	Unknown	TOP (no autopsy)	–
2	28	Fetal left renal pelvis dilatation and PNVGB	Bilateral mild dilation of fetal renal pelvis, a strong spot in the left ventricle and PNVGB	–	Male	–	Unknown	TOP (no autopsy)	–
3	31	Horseshoe kidney, hydramnios and PNVGB	Horseshoe kidney, hydramnios and visible of gallbladder (1.1×0.2 cm)	31+	Male	Normal	Transient PNVGB	Healthy	21 months
4	31+	Rough edge of bilateral ventricles and echo intensity, PNVGB	Ventricular dilation with the rough edge, gyrus backward development, a cyst in the left ventricular occipital horn and PNVGB	-	Female	–	Unknown	TOP (no autopsy)	–
5	28	PNVGB	Visible gallbladder and fetal echogenic bowel	29	Male	Not performed	Transient PNVGB	Healthy	13 months
6	35	FGR and PNVGB	FGR and PNVGB	–	Male	Not performed	Unknown	Walk on tiptoe	19 months

MRI – magnetic resonance imaging; WG – gestational weeks; PNVGB – prenatal non-visualization of the fetal gallbladder; TOP – termination of pregnancy; FGR – fetal growth restriction.



**Figure 1.** Outcomes of 32 cases of PNVGB. PNVGB – prenatal non-visualization of gallbladder; TOP – termination of pregnancy; FGR – fetal growth restriction.



**Figure 2.** The MRI in 1 patient with PNVGB at 33 gestational weeks showed a normal gallbladder (3.2×1.2×1.2 cm). GB – gallbladder; ST – stomach; SP – spleen.

ultrasonography, 9 had normal gallbladders, 3 showed non-visualization of gallbladders, 1 had a small gallbladder, and 1 had a left small gallbladder.

Among 6 patients with additional malformations, 3 terminated their pregnancies due to combined severe malformations; 1 patient with horseshoe kidney showed a visible gallbladder on the following ultrasonography and had a healthy child with normal gallbladder; 1 patient with fetal growth restriction (FGR) did not receive ultrasonography postnatally and had a child who walked on tiptoe; 1 patient with fetal echogenic bowel was found to have a visible gallbladder on subsequent ultrasonography, but the postnatal ultrasonography was not performed, and the child was healthy.

### MRI in the diagnosis of PNVGB

Among 32 patients, 7 patients (21.9%) with isolated PNVGB had visible gallbladders on MRI (Figure 2), in which 1 was lost to follow-up and the others all had a healthy child during 18–51 months of follow-up (Table 1). In 25 patients (78.1%) with non-visualized gallbladders on MRI, normal gallbladder and gallbladder agenesis found in 9 patients and 4 patients, respectively, postnatal ultrasonography was not performed in 8 patients, and TOP occurred in 4 patients, without an autopsy (due to parent refusal) (Tables 1, 2).

One patient was lost to follow-up. Twenty-seven children survived, and examination by a neonatologist revealed no jaundice, digestive tract symptoms, biliary atresia, or apparent aneuploidy. The children were healthy and well-developed at the age of 6–57 months, except for 1 child who walked on tiptoe, and this information was confirmed by telephone with the parents.

### Discussion

Ultrasonography is an optimal imaging technique in prenatal diagnosis due to its non-invasiveness, no use of radiation, and real-time imaging and repeated examinations. It is usually performed several times during pregnancy. However, complicated pathological conditions or abnormalities are extremely difficult to show clearly due to the limited visual field [17]. MRI, a highly sensitive imaging method without ionizing radiation, can show the delicate fetal anatomy, such as the brain, chest, abdomen, and vasculature, and can repeatedly display obviously suspicious lesions to improve the diagnostic ability [18]. For complex fetal malformations and rare cases, MRI can provide additional information that ultrasonography is unable to show [19,20]. In the present study, 32 patients with PNVGB diagnosed by ultrasonography underwent MRI examination during the second and third trimester of pregnancy.

Through MRI examination, 26 cases were found to be isolated PNVGB, among whom 7 patients presented visible gallbladders; 6 patients had additional malformations, suggesting that MRI may be valuable in identification of the fetal gallbladder.

Isolated PNVGB is reported to be related to biliary atresia in only 2 case reports [21,22]. One patient terminated the pregnancy at approximately 18 gestational weeks and the diagnosis was made based on the results of autopsy. The other had biliary atresia with an uncommon postnatal course, which might have been caused by peritonitis and ileal necrosis. In this study, 26 out of 32 cases were suggested to be isolated PNVGB, but none had biliary atresia. Among these cases, 24 patients delivered a healthy child except for 1 case of TOP and 1 patient lost to follow-up, indicating that the prognosis of patients with isolated PNVGB was favorable. Additionally, among 6 patients with additional malformations, 3 chose TOP due to combined severe abnormalities. It was thus clear that MRI can offer more information about the fetus and is superior to ultrasonography in the identification of fetal malformations.

The MRI appearance of the fetal gallbladder is alterable, and the fetal bile changes in an age-dependent manner with the signal intensity, especially after 30 GW, which may result in non-visualization of the gallbladder [16]. Additionally, there is a significant gallbladder contractility in fetuses, and the contractility cycle is about 3 hours during pregnancy [23]. It was reported that the phase of the fetal gallbladder contraction can cause non-visualization when the signal intensity of the remaining gallbladder bile is the same as that of the liver on either T2- or T1-weighted sequences [16]. In the present study, the pregnant women with visualization of gallbladder on ultrasonography underwent MRI because of some other factors, such as abnormal fetal head and fetal growth, but not PNVGB on ultrasonography; the gallbladder was found in 6 patients on subsequent prenatal ultrasonography and in 9 patients by the postnatal ultrasonography. The reason why the gallbladder was not indicated on MRI might be associated with the gallbladder contraction at each time of examination.

In this study, 5 patients with non-visualization of the gallbladder or small gallbladders through the prenatal and postnatal ultrasonography were diagnosed as having gallbladder agenesis. Among these 5 patients, a small gallbladder on MRI was visible in 1, which suggested that MRI has potential for fetal gallbladder screening. One patient with non-visualized gallbladder on both MRI and subsequent ultrasonography terminated the pregnancy at 32 gestational weeks because the risk of gallbladder atresia could not be completely ruled out, and the autopsy was not performed due to patient refusal.

This study has some limitations. First, this was a case-series study, so statistical analysis was not performed. Second, cystic fibrosis (CF) was not identified in 32 patients. CF, an autosomal recessive disease, is reported to be associated with PNVGB [13,24]. Moreover, chromosome examination was not conducted in the fetuses who were aborted, although the surviving children undergoing chromosome examination showed no signs of chromosomal abnormalities.

The findings from this retrospective study are supported by a recent systematic review of the literature [25].

## Conclusions

Additional information on fetuses is crucial for prenatal diagnosis and neonatal care. MRI should be considered as an important supplementary technique when PNVGB is detected or suspected by ultrasonography.

## Conflict of interest

None.

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