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Undetectable gall bladder in fetus: what to do?

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Abstract

Objective: This study aims to evaluate the rate of undetectable gall bladder in fetus during antenatal examinations and accompanying characteristics.

Methods: A total of 2704 fetuses examined in the second trimester were separated into two groups according to the presence or lack of their gall bladders during the imaging. The differences among the groups were compared. Those failed to image were examined second time. If it was failed to image in the second examination, more advanced examinations were performed and the prognosis was evaluated.

Results: Gall bladder was found in situ in 96.9% of the cases in the first examination and in 99.1% of the cases cumulatively in the second examination. The majority (90.5%) of the cases of whose gall bladder cannot be detected were between 15 and 18 weeks of their gestation. While imaging success was increasing as week of gestation increases, gall bladder was displayed in all cases which had no fetal anomaly after 22 weeks of gestation. While gall bladder could not be detected in 19.6% of the cases with fetal anomaly, a higher rate of fetal anomaly (22.6%) was observed in cases whose gall bladder could not be detected which was statistically significant ($p<0.001$). The lack of isolated gall bladder was determined in one of 3 cases who delivered and whose gall bladder could not be detected.

Conclusion: Gall bladder should be seen during fetal examination until 22 weeks of gestation. Imaging is ensured usually by consecutive evaluations. The cases in the contrary condition should be evaluated in terms of fetal anomaly, if necessary, cystic fibrosis, biliary atresia and karyotype anomalies should be investigated.

Keywords: Biliary atresia, cystic fibrosis, fetal anomaly, gall bladder, ultrasonography.

Özet: Fetüste görüntülenemeyen safra kesesi: Ne yapmalı?

Amaç: Çalışmanın amacı antenatal muayenelerde fetüste görüntülenemeyen safra kesesi oranı ve buna eşlik eden özelliklerin değerlendirilmesidir.

Yöntem: Gebeliğin ikinci trimesterinde incelenen 2704 fetüste safra kesesi, görüntülenme özelliğine göre var veya yok şeklinde iki grupta incelendi. Gruplar arası farklar karşılaştırıldı. Görüntülemede başarısız olanlar ikinci incelemeye tabi tutuldu. İkinci incelemede de görüntüleme başarısız olursa daha ileri tetkiklere geçildi ve prognoz değerlendirildi.

Bulgular: İlk muayenede olguların %96.9'unda, ikinci muayenede ise kümülatif olarak olguların %99.1'inde safra kesesi yerinde bulundu. Safra kesesinin görüntülenemediği olguların büyük çoğunluğu (%90.5) gebeliğin 15–18. haftalarında yer almakta idi. Gebelik haftası ilerledikçe görüntüleme başarısı artarken, 22 haftadan sonra fetal anomali saptanmayan olguların hepsinde safra kesesi görüldü. Fetal anomali olgularının %19.6'sında safra kesesi görülemezken, safra kesesi görülemeyen olgularda istatistiksel anlamlı olarak daha yüksek oranda (%22.6) fetal anomali saptandı ($p<0.001$). Safra kesesinin görülemediği ve doğum yapan 3 olgudan birinde izole safra kesesi yokluğu belirlendi.

Sonuç: Fetal muayene sırasında safra kesesi 22 gebelik haftasına kadar görülmelidir. Genellikle ardışık incelemelerde görüntüleme sağlanır. Aksi durumdaki olgular fetal anomali yönünden değerlendirilmeli, gerekiyorsa kistik fibroz, bilier atrezi ve karyotip anomalileri araştırılmalıdır.

Anahtar sözcükler: Ultrasonografi, safra kesesi, fetal anomali, kistik fibroz, bilier atrezi.

Introduction

The most of the problems detected regarding to fetal gall bladder during prenatal period are benign.[1] Being unable to observe fetal gall bladder in the ultrasonography is a rare condition, and it should be investigated.[2] Most likely, the gall bladder which cannot be displayed in the first examination is seen in the second examination right after or during the last trimester or after deliv-

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ery, and newborn has no problem in this case.[3,4] Second and third possibilities are the lack of isolated gall bladder with good prognosis and biliary atresia with poor prognosis.[2,5,6]

If gall bladder cannot be observed during antenatal period, the examination should be repeated within 10–15 days, and if it cannot be seen again, morphological examination of fetus should be detailed, and pathologies that may accompany should be investigated. In the series reviewed, additional anomaly possibilities up to 24% were reported.[7] In the presence of these additional findings, karyotyping analysis is recommended.[7]

On the other hand, lack of gall bladder is found in 75% of the cases with cystic fibrosis.[8] Investigating digestive enzymes as well as cystic fibrosis mutation analysis in the amniotic fluid of fetuses whose gall bladder were not observed helps the diagnosis of this disease.[7] Carrying out specific genetic research in parents for cystic fibrosis in families who do not approve invasive procedure may also help diagnosis.[9] Although the lack of isolated gall bladder is a benign finding, the prognosis is poor together with biliary channel atresia. In such cases, it is recommended to investigate digestive enzyme in amniotic fluid before 22 weeks of gestation although it is controversial.[7,9]

In this study, the success of imaging fetal gall bladder via ultrasonography was investigated retrospectively, and clinical, sonographic and laboratory characteristics were evaluated in cases whose gall bladder could not be detected.

Methods

In this study conducted retrospectively, it was investigated if gall bladder of 2704 fetuses were in situ in routine or targeted ultrasonographic examinations in 15–30 weeks of gestations between January 2008 and November 2015. The examinations were carried out by a single operator using General Electric Voluson 730 and E8 devices (GE Healthcare, Little Chalfont, UK).

Gall bladder was noted as the presence or lack of cystic, long tubular structure with echogenic walls and having blunt concave end on one side and drop-like end on the other side on right upper quadrant under the liver and on the right to the intrahepatic umbilical vein with an angle of 30–45 degree to the midline[10] (**Figs. 1** and **2**).

In cases with undetectable gall bladder, week of gestation, characteristics in fetus, sonography and other imaging methods (if any), and additional findings of genetic analyses were also noted. Mean and standard deviation values of age and week of gestation were calculated, and the groups were compared with t-test, chi-square and Fisher tests. Statistical significance level was defined as $p<0.05$.

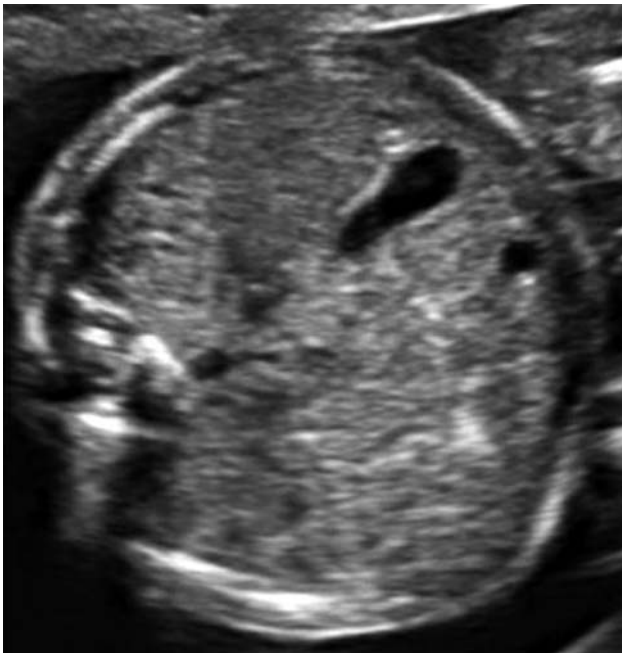

Fig. 1. Gall bladder on transverse section.

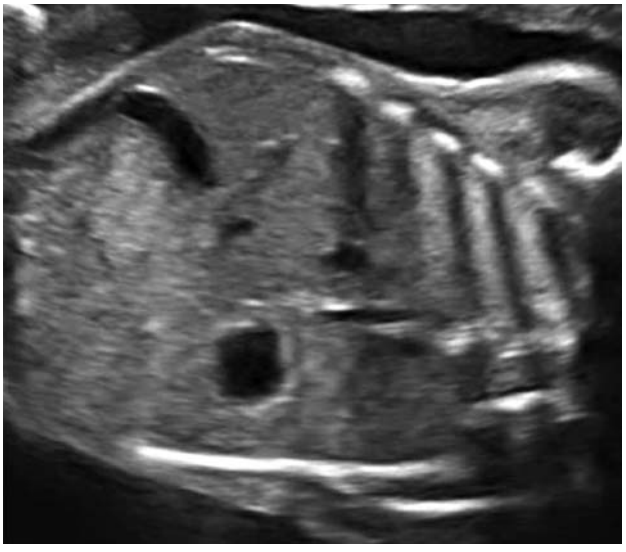

Fig. 2. Gall bladder and stomach on parasagittal section.

Table 1. The success for imaging gall bladder and the distribution by weeks of gestation.

N	15–16 weeks 185	17–18 weeks 483	19–20 weeks 662	21–22 weeks 852	23–30 weeks 522	Total 2704
Gall bladder (+) n (%)	145 (78.4%)	447 (92.65%)	657 (99.24%)	849 (99.65%)	522 (100%)	2620 (96.89%)
Gall bladder (-) n (%)	40 (21.6%)	36 (7.45%)	5 (0.76%)	3 (0.35%)	0 (0%)	84 (3.11%)
Medical evacuation-Fetal loss (n)	7	8	1	1	0	17
Follow up (-) (n)	1	2	0	1	0	4
Gall bladder detected late n (%)	31 (96.87%)	25 (96.15%)	3 (75%)	1 (100%)	0	60 (95.23%)
Follow up (+) (n)	1	1	1	0	0	3

Results

Mean age of the pregnant women who were examined was 33.2±3.6, and mean week of gestation was 20.4±2.6. In the first examination, gall bladder could not be seen in the expected anatomic region in 84 fetuses (3.1%). Considering the success of imaging by years, cumulative success was 95% in the first years of the review while it was over 99% in recent years.

When the relationship between imaging and week of gestation was evaluated, it was found that the possibility of imaging gall bladder was increasing as week of gestation progressed: The imaging success in the first evaluation was 78.4% in 15–16 weeks of gestation, 92.7% in 17–18 weeks of gestation, 99.2% in 19–20 weeks of gestation, 99.7% in 21–22 weeks of gestation and 100% in further weeks (**Table 1**). Mean week of gestation in the group with undetectable gall bladder was 16.5±1.5 weeks and it was 20.5±2.5 in the group with detectable gall bladder (p<0.001). 90.5% of the cases whose gall bladder could not be displayed were in 15, 16, 17 and 18 weeks of their gestation.

Four cases did not come to their follow-up examinations, and therefore their examinations could not be continued. In 17 cases with undetectable gall bladder had a condition requiring medical evacuation or resulting with a fetal loss, and it was not possible to carry out a second examination for most of the cases in this group. When these 21 cases who could not be followed up were excluded from the examination group, it was seen that the gall bladder was in its original region in 95.2% (60/63) of the cases who underwent re-examination, and general imaging success was determined as 99.1%.

The success of imaging gall bladder was lower in case groups with multiple anomalies, non-immune hydrops, chromosomal anomaly, genitourinary anomaly and cardiac anomaly compared to the other group with normal findings (**Table 2**). In the first evaluation in this group, the rate for not observing gall bladder was 19.6% and it was significantly different than the group with undetectable gall bladder which was found to have no anomaly (p<0.001). The anomaly rate was 17.9% in the group with undetectable gall bladder and 4.8% in fetus karyotyping (22.6% in total) (p<0.001) (**Table 3**).

Table 2. Fetal anomalies and undetectable gall bladder.

Anomaly type	n	Gall bladder (+)	Gall bladder (-)	The rate of undetectable gall bladder
Chromosomopathy	23	19	4	17.39%
CNS - NTD	17	16	1	5.88%
Cardiac	15	12	3	20.00%
Genitourinary	14	10	4	28.57%
Multiple	8	5	3	37.50%
Hydrops fetalis	6	3	3	50.00%
Skeletal	4	3	1	25.00%
Gastrointestinal	3	3	0	0%
Diaphragma	3	3	0	0%
Minor	4	4	0	0%
Total	97	78	19	19.58%

CNS: Central nervous system; **NTD:** Neural tube defect

Table 3. Success of imaging gall bladder and the presence of fetal anomaly

	Anomaly (+)	Anomaly (-)	Total
Gall bladder (+)	78 (2.98%)	2542 (97.02%)	2620
Gall bladder (-)	19 (22.61%)	65 (77.38%)	84
Total	97	2607	2704

p<0.001

Karyotyping analysis and cystic fibrosis investigation were offered to three cases who continued their follow-up visits except the group who were terminated or resulted with spontaneous loss. Only one of them accepted the offer, and no pathological finding was found after both evaluations. Fetal magnetic resonance imaging (MR) was also applied to this case, but the gall bladder and its tracts could not be seen. As a result of the clinical and laboratory examinations conducted until the end of postpartum third month, gall bladder could not be detected again, but no additional pathological finding was observed, neither. Other two cases did not come for their follow-up visits; only one of them was contacted via phone and it was learnt that the newborn was healthy.

Cystic fibrosis was found in a case whose gall bladder was detectable but had other gastrointestinal findings, and the pregnancy was terminated. The presence of gall bladder was confirmed in retrospective sonographic images of this case.

Discussion

Biliary tract and liver start to develop from hepatic bulge on 4–6 weeks of gestation in the embryo. On the eighth week, extrahepatic ways develop from hepatoblasts with hepatocyte precursors, and join with intrahepatic arms. The lumens of them are all open from the beginning and they take shape as tubular structures in 12 weeks.[11,12] As of this period, bile production can be detected and gall bladder becomes detectable in the duodenum.[1,13] Ductal layer malformation may occur when epithelium and mesenchyme interaction is irregular.[13]

Gall bladder growing curves were created between the second trimester and term, and it was shown that the gall bladder was growing linearly between 15 and 30 weeks of gestation.[1,14] Goldstein et al.[15] stated the length and diameter of gall bladder as 10×3 mm in 15–19 weeks of gestation, 15×4 mm in 20–22 weeks of gestation, 19×6 mm in 23–24 weeks of gestation, 21×7 mm in 25–30 weeks of gestation, and 26×7 mm after 31 weeks of gestation. The dimension of the gall bladder grows in proportional to the week of gestation, and it is considered that it is not affected by fetal gender.[16] Chan et al.[1] and Hata et al.[14] showed that the dimensions of the gall bladder stay stable after 30 weeks of gestation. Goldstein et al. reported that there is also discharge to the duodenum in addition to the bile production, and therefore there may be slight changes in gall bladder volume.[15]

Biliary contractility in adults is regulated by cholecystokinin secreted by duodenum mucosa. It was claimed that a similar condition may be also in fetus.[17] No change occurs in the dimensions of fetal gall bladder up to 3 hours after the maternal nourishment.[15,18] Yet, the volume of gall bladder remains stable but it displays a sinusoidal increase-decrease; since this may vary in each fetus, the gall bladder should not be characterized as "extremely full" or "empty" just with a single imaging, and the examination should be repeated in following weeks.[17]

In the sonographic examinations during prenatal period, various benign findings may be observed in the fetal gall bladder such as isolated lack, malformation, duplication, being ectopic, or containing gallstone or biliary sludge.[1] However, the biliary atresia which is the most severe form of this condition affects general prognosis negatively. Depending on the inflammation and destruction, biliary atresia which is the fibrous obliteration of extra- and intrahepatic biliary tracts causes obstructive jaundice in newborn. This may begin during antenatal period: Either the channel never develops or the bile flowing into interstitium causes hepatic inflammation, or primitive biliary tracts continue proliferation around porta hepatis and causes obliteration.[12] It is though that the loss of Hes 1, which is a factor related with transcription, during embryonic period causes the underdevelopment of extrahepatic channels and the lack of gall bladder during intrauterine period.[19]

It is not obligatory to image gall bladder in basic examinations,[20,21] but the centers carrying out detailed imaging are required to detect gall bladder.[22] Not detecting fetal gall bladder during second trimester is a rare and usually a temporary finding, and it show itself in following examinations or after birth.[1,3] Undetectable gall bladder is seen in one out of 875 cases.[4] In actual absence of isolated gall bladder has been reported in 1 out of 6300 cases.[23] Biliary atresia is even more rare and it has been reported in 1 out of 16,000 cases.[24] Bronstein et al.[5] and Goldstein et al.[15] could be able to detect gall bladder in 99% of the cases examined transvaginally in 14–16 weeks of gestation. In the transabdominal examinations carried out during second and third trimesters, this rate was reported as 65–82% during 24–27 weeks of gestation by Hata et al.,[14] and as 82–94% during 15–40 weeks of gestation by Hertzberg et al.[3] In our series, we

could not detect fetal gall bladder in situ in 3.1% of the cases during the first examination in 15–22 weeks of gestation. The imaging success increased to 99% from 97% in those who underwent second examination. When affecting factors and the cases who could not be followed up were excluded, the gall bladder was detected in the second examination while it was undetectable in the first transabdominal examination in 60 out of 63 fetuses. When terminated morphological and chromosomal anomalies and fetal loss cases and also the cases which could not be followed up were excluded from the series, the rate of undetectable gall bladder after two consecutive examinations was found as 0.11% (3/2683). When we reviewed the reasons for being unable to detect, especially in the first 4 years between 2008 and 2011, we noticed that the failure of imaging in 1014 cases which was more than 5% regressed to 2% in 1690 cases in the last 4 years. Also, the sooner the week of gestation, the more we failed to image the gall bladder. We reached findings which made us consider that there may be other factors affecting the imaging success other than experience and advancing week of gestation such as fetal malformations and concurrent chromosomal anomalies. Hence, Shen et al.[9] in 2011 and Dreux et al.[7] in 2012 recommended checking for other systems and organs certainly with a detailed examination in cases where fetal gall bladder cannot be detected. Dreux et al.[7] found severe anomalies in 24% of their series. In this retrospective study, we also found morphological or genetic anomalies in fetuses in 22.6% of the cases whose gall bladders were undetectable ($p<0.001$). Among the anomalies found in all groups, we found that 22.6% of the cases had undetectable gall bladder ($p<0.001$). However, we could not distinguish if it was caused by carrying out only one examination or by gall bladder accompanying systemic malformation. Because, the gall bladders that were undetectable during the first examination in the group which terminated their pregnancies relatively in the early weeks would have been detectable more easily in the following weeks if the pregnancies had not been terminated. Taking this affecting factor into consideration, we believe that it would be more reasonable to approach cautiously to fetal anomalies where gall bladder cannot be detected until further postpartum and postmortem studies are carried out in wider series.

Another issue in our cases with anomaly is that the gall bladder which is relatively small possibly due to mechanical effects in case of fluid increases in body and organs cannot be observed in the sonography. Hydrops, acid, megacystis and hydronephrosis cases are more than the one third of the cases whose gall bladders cannot be detected.

It is known that the lack of isolated gall bladder may progress with cystic fibrosis.[25] In a study performed in France between 2002 and 2009, cystic fibrosis was found in 13.5% of the cases with undetectable gall bladder.[26] It was claimed that relative risk is 11 times higher if also hyperechogenic intestine is present. In another series of 60 cases with cystic fibrosis risk, gall bladder could not be detected in 12 cases (20%) but there was no such finding for those who had low risk for cystic fibrosis. Gall bladder could not be seen in 17–19 weeks of gestation in 75% of the cases who were found to have cystic fibrosis.[8] In our series, we investigated cystic fibrosis in two cases: While we did not see the disease in one case with undetectable gall bladder, we found cystic fibrosis in other case who had detectable gall bladder, and we terminated the pregnancy.

If any anomaly related with biliary tracts is suspected during sonographic examination, ruling out biliary atresia is claimed to be the first step to do.[27] Biliary atresia is a rare disease with unknown etiology which is seen in 5 out of 100,000 live births in Europe and in 1 out of 30 cases in Pacific countries. Perinatal viral infections, inflammatory and immune disorders, genetic predisposition, abnormal embryogenesis and toxins may be responsible for its development.[28] There are two types, who are syndromic (15%) and nonsyndromic (85%). Polysplenia, lack of inferior vena cava, azygos continuation of infrahepatic vena cava, preduodenal portal vein, intestinal malrotation, heterotaxia, situs inversus and cardiac defects may accompany to syndromic type.[27] Both types are considered to start during antenatal period. In biliary atresia cases, atretic gall bladder is seen frequently during postnatal period and neonatal cholestasis, fibrosis and cirrhosis follow each other. The loss is inevitable if hepatoportoenterostomy operation or hepatic transplantation is not carried out.[27] In our series, we did not find any biliary atresia.

During 13–20 weeks of gestation, enzyme insufficiency in the amniotic fluid or identifying a cystic formation together with the lack of gall bladder in the liver may have a role in the early diagnosis of biliary atresia.[29–32] In study carried out on a wide series for that purpose, it was found that gamma-glutamyl-transferase which is a hepatobiliary enzyme could be isolated

between 16 and 22 weeks of gestation and that its levels were associated with the week of gestation.[33] From this point of view, it was asserted that biliary atresia cases could be detected by checking for digestive enzymes before 22 weeks of gestation in amniotic fluid following a cystic fibrosis investigation which resulted normal in a mother-to-be with undetectable gall bladder in consecutive examinations. This examination may be guiding also for cystic fibrosis.[7,32] Dreux et al.[7] reported the sensitivity as 90% and specificity as 80% for detecting cystic fibrosis or biliary atresia by abnormal enzyme finding in amniotic fluid before 22 weeks of gestation. If the week of gestation is higher than 22, the sensitivity rate decreases to 53%. While enzymes were in the normal range in 82% of the cases in case of undetectable gall bladder, incorrect results are obtained in 9% of the cases who have detectable gall bladder.[7]

On the other hand, Shen et al.[9] carried out literature review and reported that only one case out of 268 cases with isolated undetectable gall bladder had biliary atresia, and claimed that this may be a coincidental finding. The same team also suspects the amniotic enzyme studies. Hence, considering that biliary atresia diagnosis during postnatal period can only be established with advanced examinations such as acholic gaita, abnormal blood biochemistry, radionuclide scanning in liver, endoscopic retrograde cholangiopancreatography and magnetic resonance imaging, it seems that relying only one enzyme may be a fault.[34]

While chromosomal anomaly risk increases if lack of gall bladder is together with additional anomalies, the indication of karyotyping analysis to be performed in isolated case is controversial.[4,6,34] One XXY and one trisomy 21 cases were reported in the literature.[34] Rarely, lack of gall bladder can be seen within the syndrome accompanied by multiple anomalies depending on gene mutation such as Holt-Oram syndrome.[35] In our case, we found trisomy in 3 cases and triploidy in 1 case; while we could not detect gall bladder in any of them, they also had additional anomalies and their pregnancies were terminated upon the requests of the families. Since we had no autopsy finding, we did not consider appropriate to evaluate or discuss the actual absence of gall bladder in this study. Blazer et al.[4] carried out a study on a transvaginal ultrasonography series of 29,749 cases and they could not found gall bladder in two examinations with one-week interval during 14–16 weeks of gestation, and they qualified as "undetectable gall bladder", and repeated the review transabdominally at 22–26 weeks of gestation. After first two examinations, the number of cases with undetectable gall bladder was 34 with a rate of 1/875. While prognosis was good in all cases (n=20, 59%) with the lack of isolated gall bladder, they terminated 9 (41%) out of other 14 cases found to have additional anomaly. Karyotype anomalies were also found in five of them. Remaining 5 cases were continued to be examined and it was found that gall bladder was in situ in 4 of them. Yet, the number of healthy case is only 1. It was shown that gall bladder was actually absent only in 5 of isolated cases during neonatal period.

In their series of 20 cases, Gündoğmuş et al.[6] found cystic fibrosis, karyotype anomaly (47,XXX) and multiple anomaly in one case each, respectively (18% in total). Amniotic enzyme level was abnormal in 18% of the cases, but only one of them was identified to have cystic fibrosis. Prognosis was good in other 2 cases although gall bladder was absent. Dreux et al.[7] could not detect gall bladder in 102 cases, and they found cystic fibrosis in 10 of them, biliary atresia in 8 of them, digestive system anomalies in 6 of them, chromosomal anomaly in one of them and the lack of isolated gall bladder in 22 of them. Gall bladder could be seen in the second examinations in remaining 55 cases. In our study, we found fetal anomaly in 17.8% of the cases with undetectable gall bladder and chromosomal anomaly in 4.8% of them. Among them who were followed up, no cystic fibrosis and biliary atresia were found.

Shen et al.[34] carried out a prospective and consecutive examination on cases with undetectable gall bladder between 2004 and 2009 and investigated cystic fibrosis, karyotyping and digestive enzymes. They qualified 16 out of 21 cases as isolated and they found no problem in 15 of them for 4–30 months after delivery. Cystic fibrosis was found only in one case during prenatal period and it was terminated. In other 5 cases, the pregnancy was terminated in 3 cases due to karyotype anomaly (two trisomy 18 and 1 triploidy cases) and one case due to multiple anomaly. The last case had a good prognosis despite having venous return anomaly.[34] This researcher group found no biliary atresia case in their series. This team claims that the prenatal diagnosis of isolated biliary atresia is not possible and this approach has no practicality due to the low number of enzyme studies. In our series consisting of 20 cases with undetectable gall bladder, we found that pregnancy was terminated due other reasons

(karyotype anomaly in 23.5%) in 17 fetuses. First of the fetuses being followed up was born with a complex anomaly associated with gastrointestinal and urinary systems, but no information about prognosis could be obtained from the parent. The second fetus was followed up for a short time with the diagnoses of ureterocele, hydroureter, hydronephrosis and accessory ectopic kidney, but postnatal follow-up could not be carried out since the baby was born in another country. Third fetus was followed up until birth, and the diagnosis of the lack of isolated gall bladder was confirmed during postnatal period.

Cyst or cysts to be seen in the liver in the antenatal sonographic examinations were reported 20 years ago that they could be the first signs of biliary atresia; however, it was also reported that it is difficult to distinguish atresia type.[36] When antenatal sonography reports (which were known to be abnormal) of 13 newborns known to have biliary problem were reviewed (averagely 20 weeks), the accuracy of pre-diagnosis was confirmed only in 15% of them.[37] Others were followed up until the last day of pregnancy with inaccurate pre-diagnoses of abdominal cyst, ovarian cyst and duodenum atresia.[37]

"False gall bladder indication" during postnatal period can be defined as cystic structure filled with fluid and shorter than 15 mm, which has walls more irregular than expected in the region that gall bladder should locate.[38] This finding may be guiding in antenatal examinations and also in differential diagnosis. Hypoechogenic small cystic structure(s) in liver hilus may be the sign of biliary atresia while wider echoic cysts may indicate ductus choledochus and echogenic small cysts may indicate uncongested ductus choledochus.[39]

While magnetic resonance (MR) imaging may provide information about gall bladder and its tracts,[40] displaying the presence of meconium in the intestine by MR signal may indicate the presence of bile acids.[10]

The steps to follow when gall bladder cannot be detected in the antenatal examinations can be seen in the algorithm provided in **Fig. 3**.

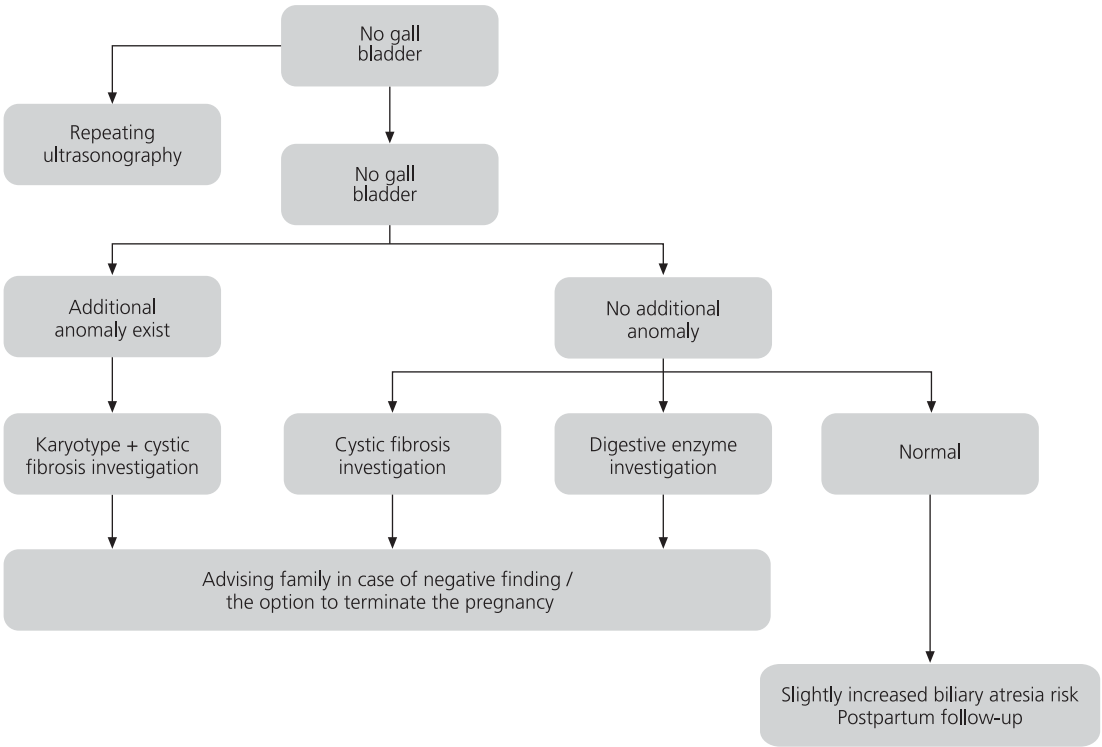

Fig. 3. The steps to follow if gall bladder cannot be detected in antenatal examinations.

Conclusion

If gall bladder cannot be detected in the antenatal examinations, multiple anomaly, cystic fibrosis, aneuploidy, biliary atresia and the lack of isolated gall bladder should be suspected. Ultrasonographic examination should be repeated within 1–2 weeks and if it is still undetectable, the examinations for related diseases should be carried out rapidly. General prognosis is positive in isolated cases during postnatal period. The data are insufficient for now to utilize sonographic information also during antenatal period which are obtained during postnatal period by MR imaging and the evidence level of enzyme investigations.

We failed to detect gall bladder in about 1% of the cases among the fetuses that we examined during 15–30 weeks of gestation. Isolated absence is even rarer and it is one per thousand. The possibility for being unable to detect the gall bladder is higher in the early weeks of gestation. The success for imaging in the second examination increases. Fetal anomalies were more frequent in cases with undetectable gall bladder. The success for imaging gall bladder in fetuses with anomaly is also low. We could not distinguish clearly if our findings were caused by the early period terminations or systemic recurrence, and therefore we planned a wider study for this issue.

Conflicts of Interest: No conflicts declared.

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