ESPR
European Society of Paediatric Radiology

ESPR 2022- Marseille

« Anomalies » of the fetal gallbladder: pre- and postnatal correlations

Fred AVNI Stéphanie FRANCHI-ABELLA Catherine GAREL

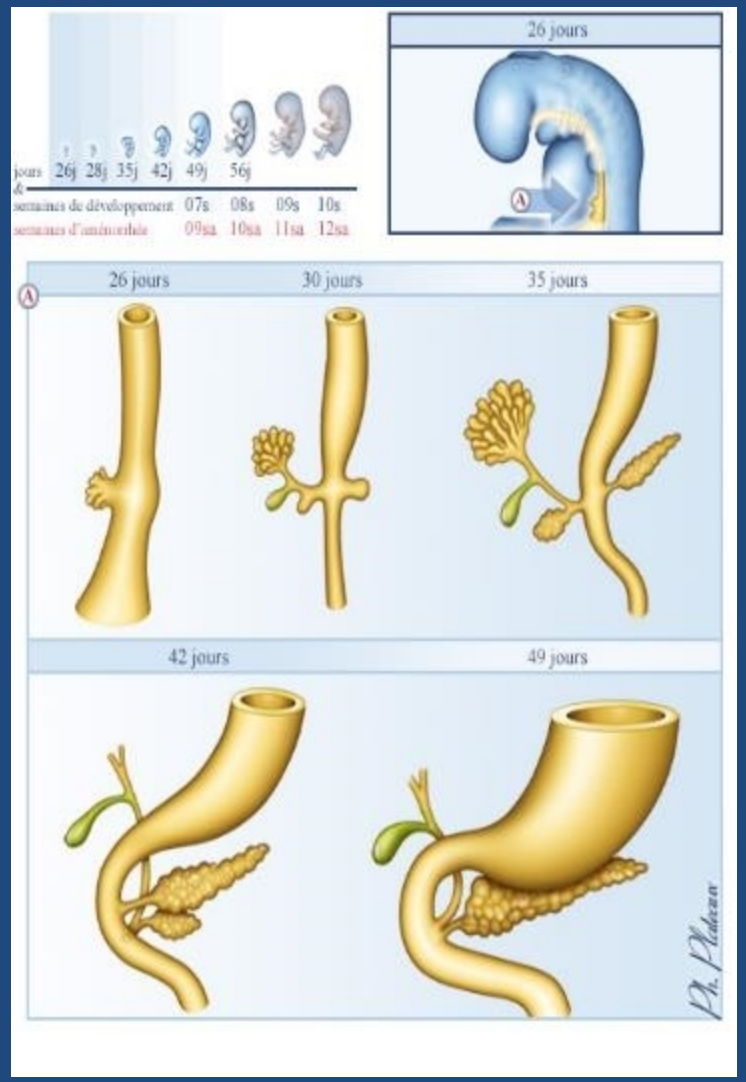
Brussels (B) and Paris (F) *members of the GRRIF*

The authors declare no conflict of interest

The Fetal GB (fGB)

- The ***fetal GB*** (fGB) does not constitue a « **to-be-seen** » landmark during 2nd(3rd) trimester obstetrical US examinations
- Still, among others, non-visualization of the fGB raises concern especially regarding potential diagnosis of ***biliary atresia***
- ***This course is about <u>all you could want to know about the fGB</u> , when to expect significant (perinatal) complications and how to manage them ?***

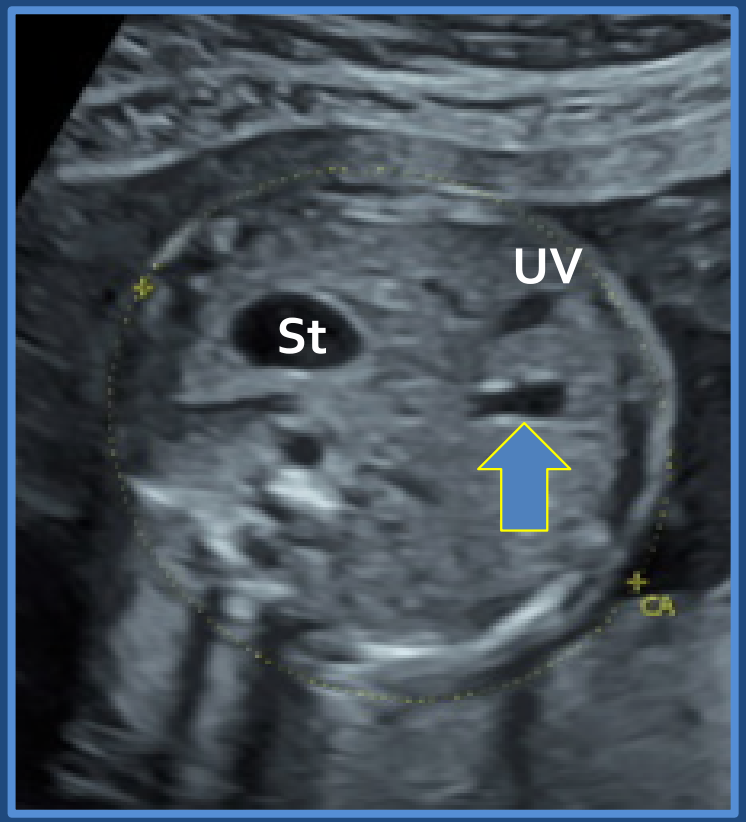
fGB: Embryo-fetal development



- The fGB shares a common embryological origin with the liver and ventral pancreas
- 4th week: liver buds arise from the foregut endoderm; they are precursors to the intra-hepatic bile ducts as well
- 5th week: development of the fGB and cystic duct in parallel with the extrahepatic bile ducts, common bile duct and dorsal pancreas
- 6-7th week: fusion with the ventral pancreas, the biliary ducts become permeable
- Around the 12th week, bile production begins and reaches the duodenum through the common bile duct

fGB: US anatomy

- The fGB is a tiny but easily accessible pear-shaped cystic pouch, best seen during the 2nd trimester on a transverse scan of the fetal abdomen



Surg Clin N Am 2014; 94 : 203–217
Korean J Radiol 2008;9 : 54-58

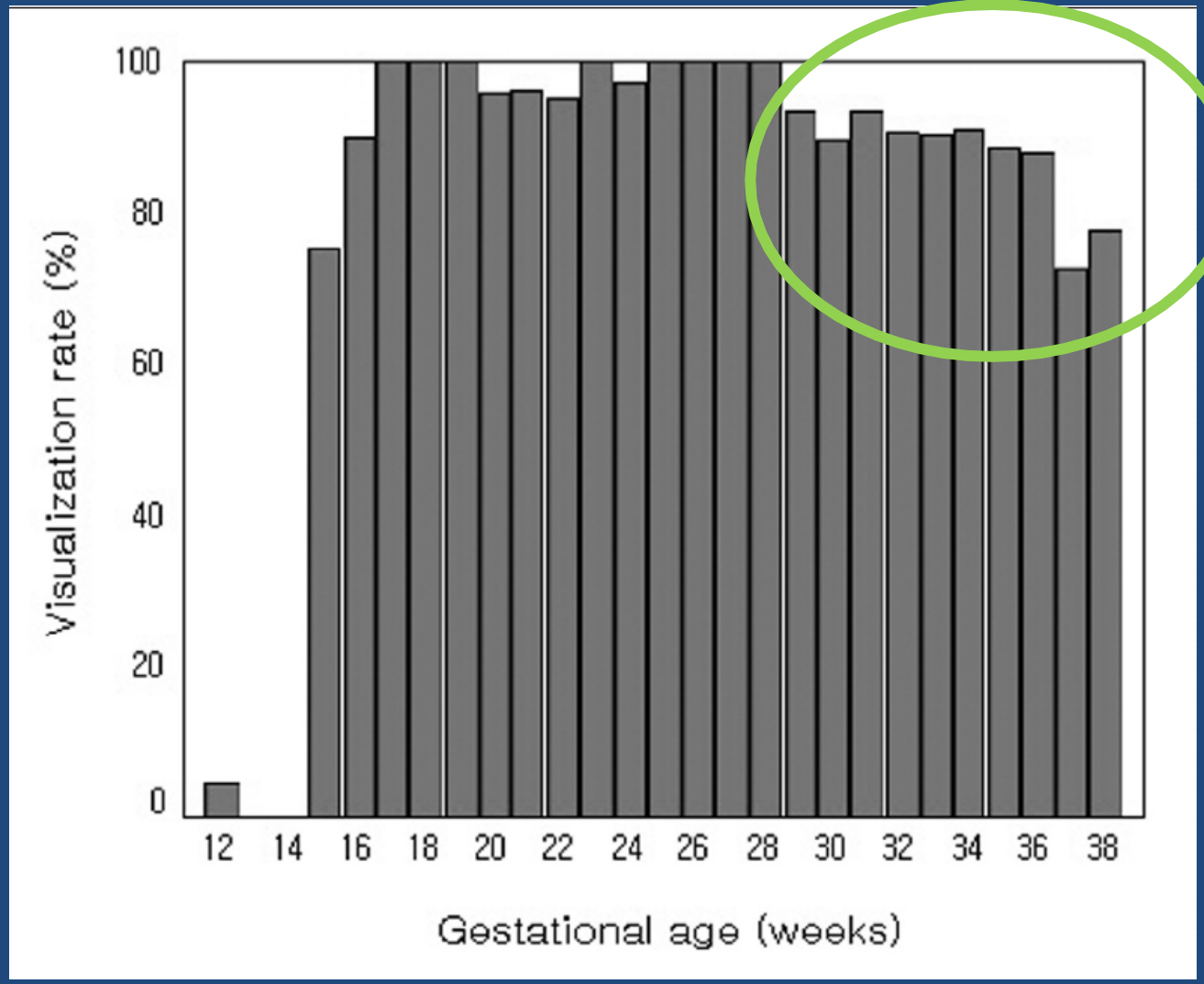
fGB size:
The fGB grows with advancing GA

Table 1. Fetal Gall Bladder Length, Height, Width, Area and Volume according to Gestational Age

Gestational Age (weeks)	n	Length (mm)	Height (mm)	Width (mm)	Area (mm^2)	Volume (mm^3)
12 – 14	4	3.7 ± 1.5	0.8 ± 0.1	0.9 ± 0.3	17.5 ± 9.0	1.3 ± 0.4
15 – 19	46	11.5 ± 3.7	2.9 ± 0.9	3.6 ± 1.5	192.5 ± 114.0	73.3 ± 72.3
20 – 22	333	15.0 ± 3.4	3.8 ± 1.0	4.2 ± 1.1	301.4 ± 124.7	137.3 ± 85.9
23 – 24	73	18.1 ± 4.2	4.4 ± 1.1	4.9 ± 1.3	435.8 ± 191.3	226.7 ± 153.7
25 – 26	37	18.8 ± 3.6	4.7 ± 1.1	5.0 ± 1.1	456.1 ± 159.7	249.4 ± 131.5
27 – 30	101	23.1 ± 4.6	5.3 ± 1.4	5.6 ± 1.5	672.8 ± 252.5	396.8 ± 254.6
31 – 34	478	26.5 ± 5.8	5.8 ± 1.4	6.3 ± 1.7	878.0 ± 346.2	556.2 ± 339.5
35 – 40	220	26.5 ± 5.7	5.8 ± 1.6	6.1 ± 1.7	866.1 ± 339.5	538.5 ± 334.5

Note.— Data are mean ± standard deviation.

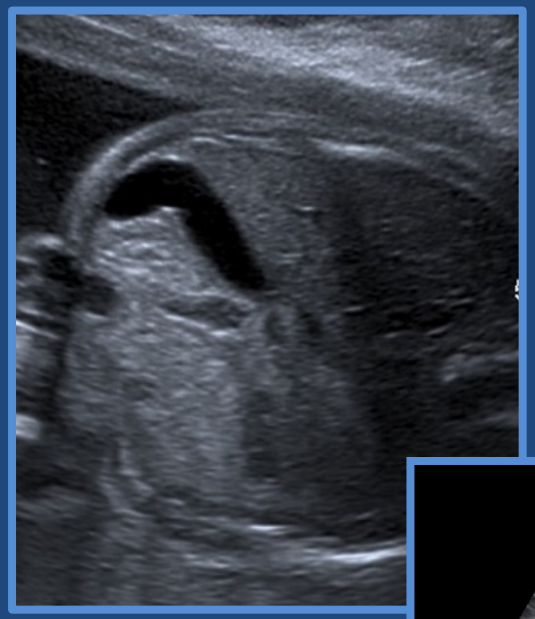
fGB: Rate of visualization during obstetrical US

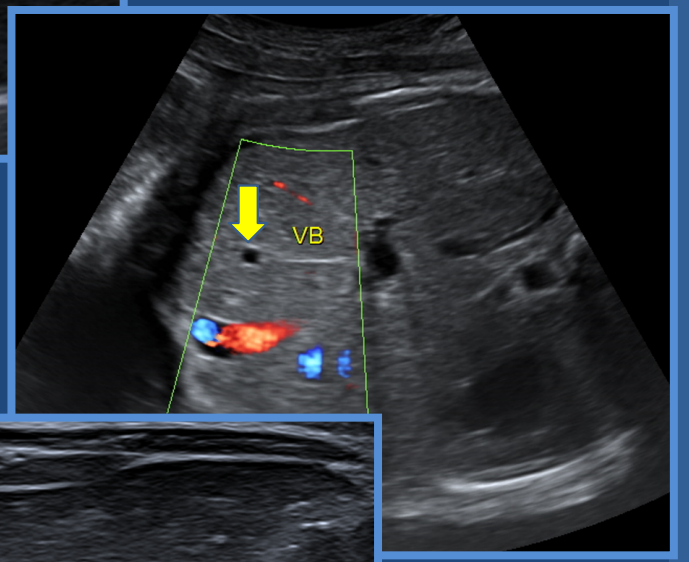


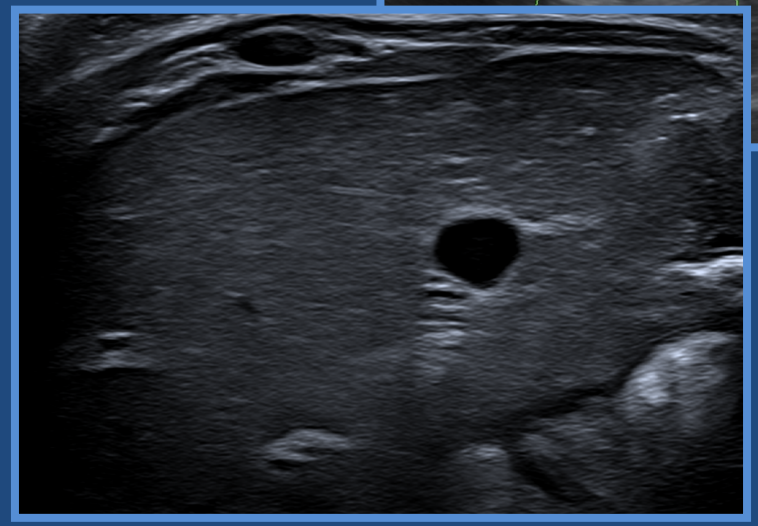
The rate of visulization of the fGB is lower during the 3d trimester

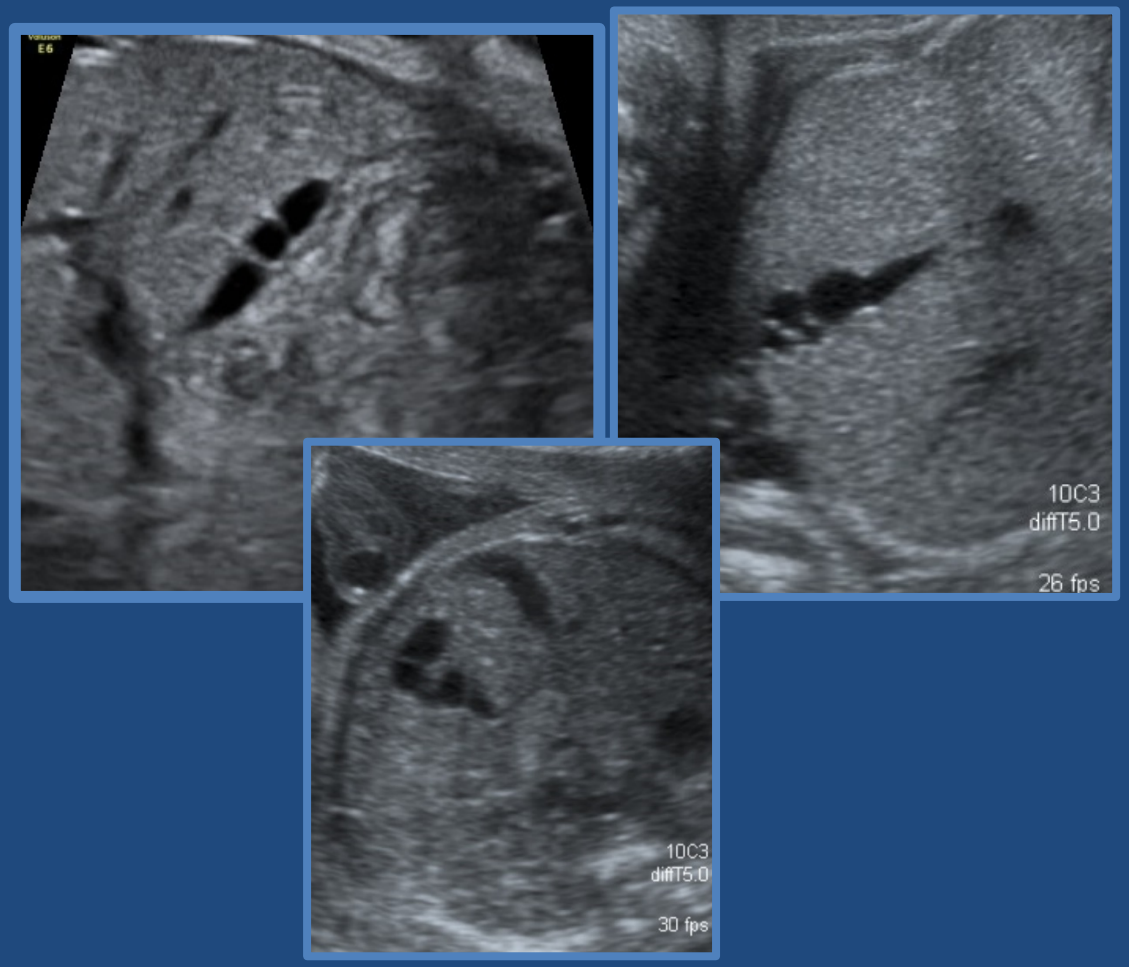
Normal fGB: Shape and size

- (Too) Big/ small
- Septated
- Convoluted/ tortuous
- Short/ Round

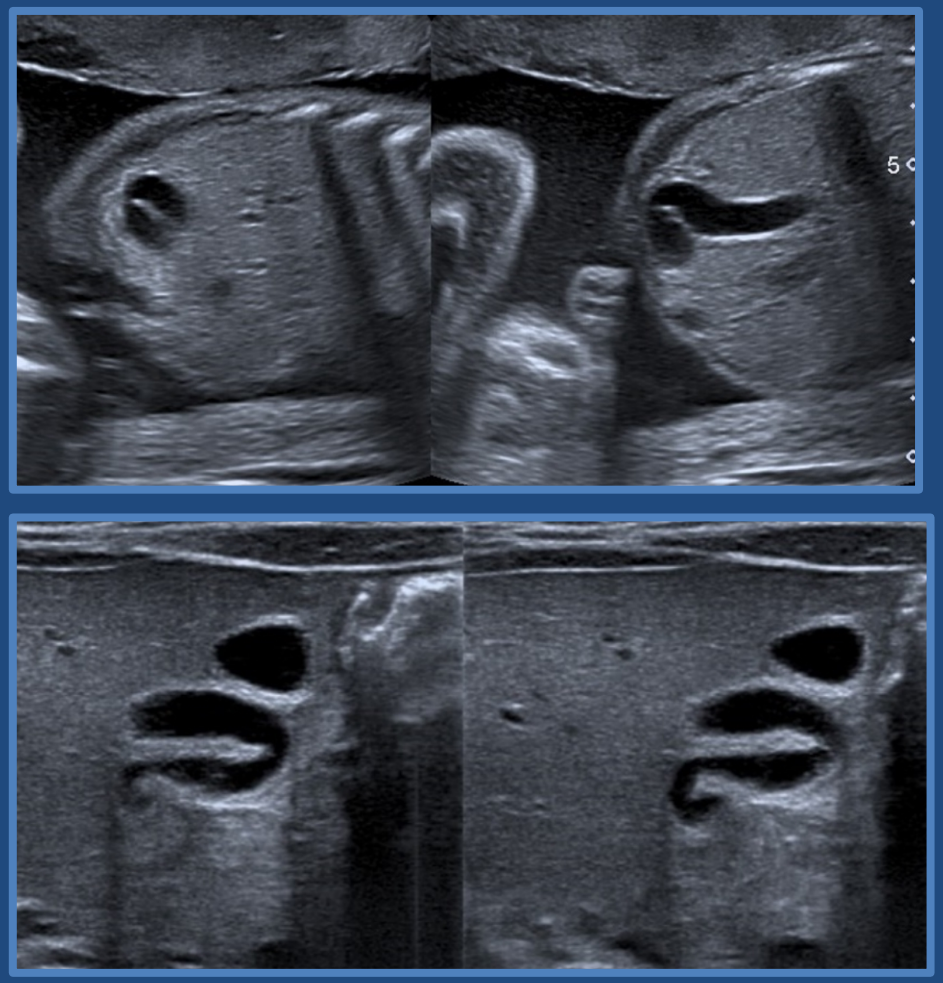






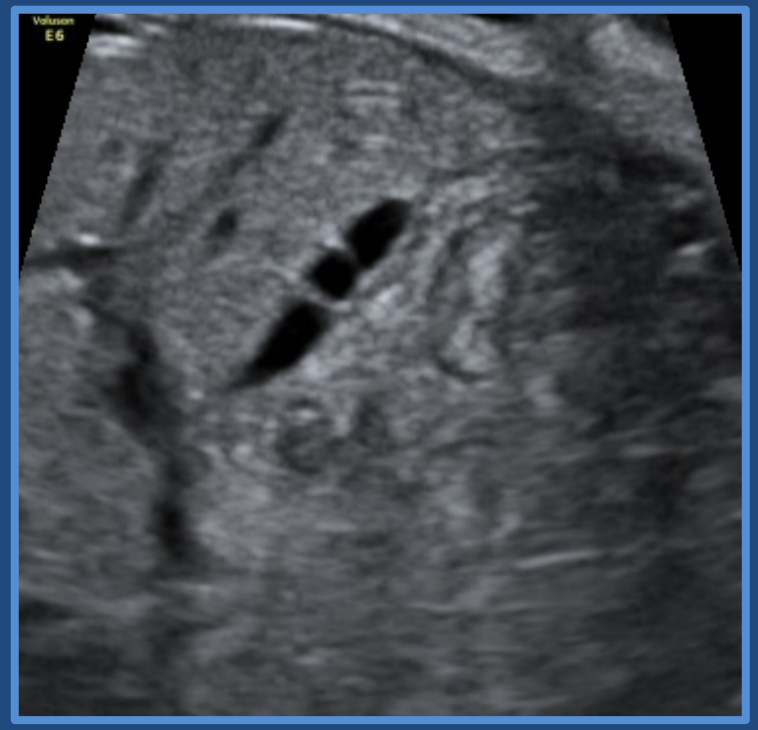


Septated fGB – 26WG

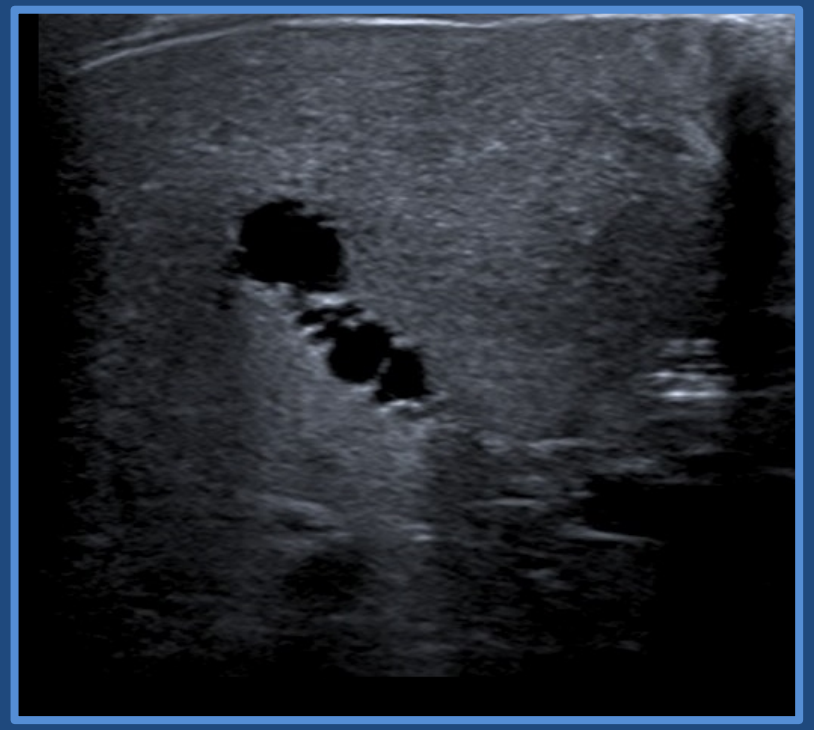


Convoluted GB pre-/postnatally

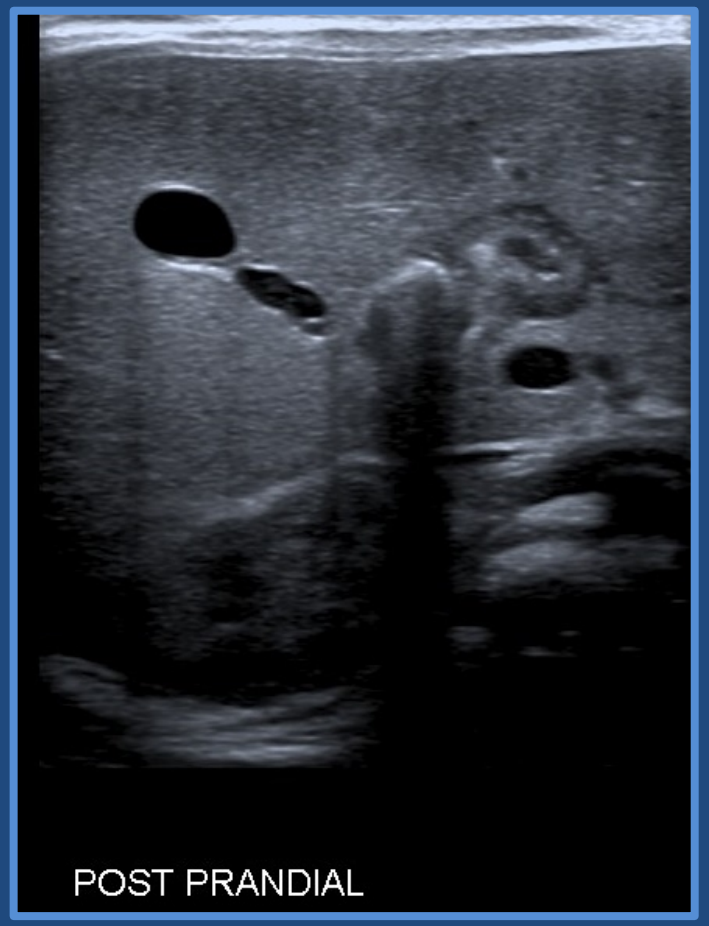
Septated GB



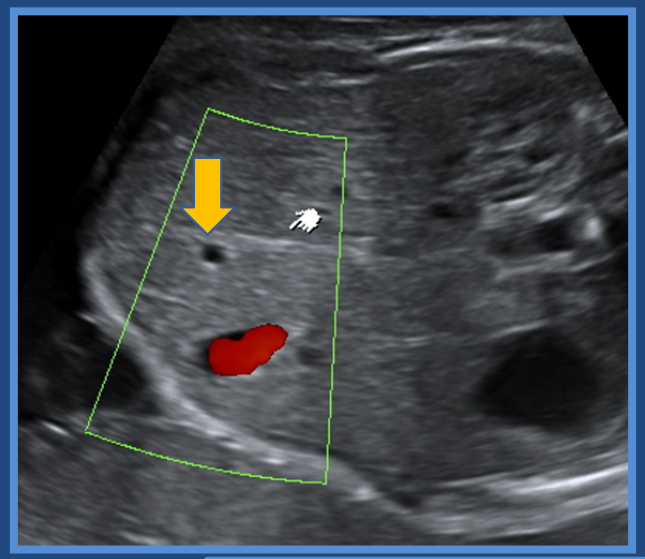
Fetal



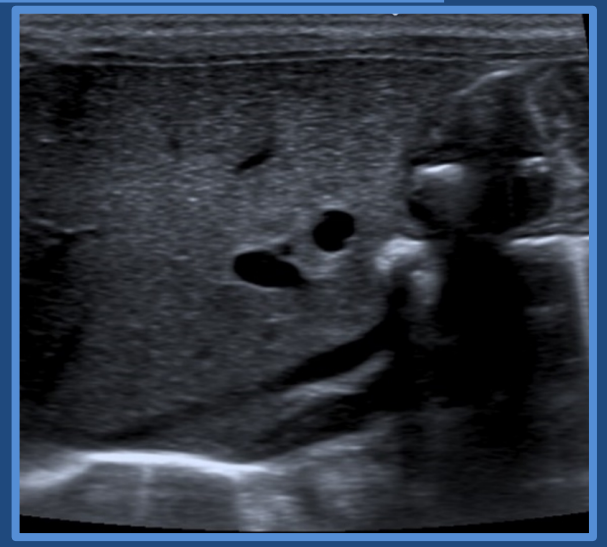
Day 1

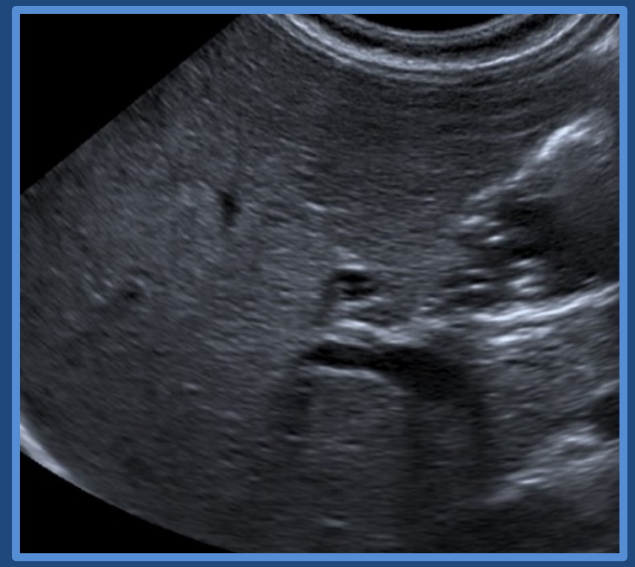


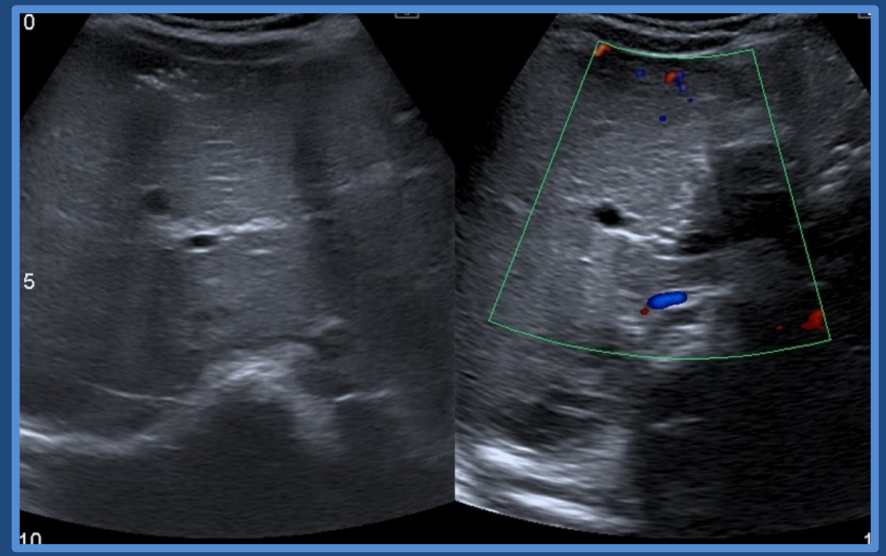
Day 1 after a meal



3rd trimester, unusual small round fGB (courtesy Le-Lez Soquet S)







At birth

3mo

10mo

no clinical or biological anomaly ➔ stop F-Up

fGB: Potential « anomalies » diagnosed by *obstetrical US*

- Agenesis of the GB
- Biliary atresia
- Non visualization of the fetal GB as a clue to polymalformative syndromes or to cystic fibrosis
- Biliary « sludge »
- GB duplication

Most diagnoses can be obtained by US - fetal MR imaging in few selected cases

J Clin Ultrasound 2019;1–6
J Gynecol Obstet Biol Reprod (Paris) 2014;43:581-6

Main challenge:
Non visualization of the fGB (during the 2d trimester)

1/875 pregnancies

1. *Technical and anatomical causes*
2. *« collapsed » fGB*
3. *Abnormal content shading the fGB*
4. *Congenital agenesis of the GB*
5. *Cystic fibrosis*
6. *Biliary atresia*

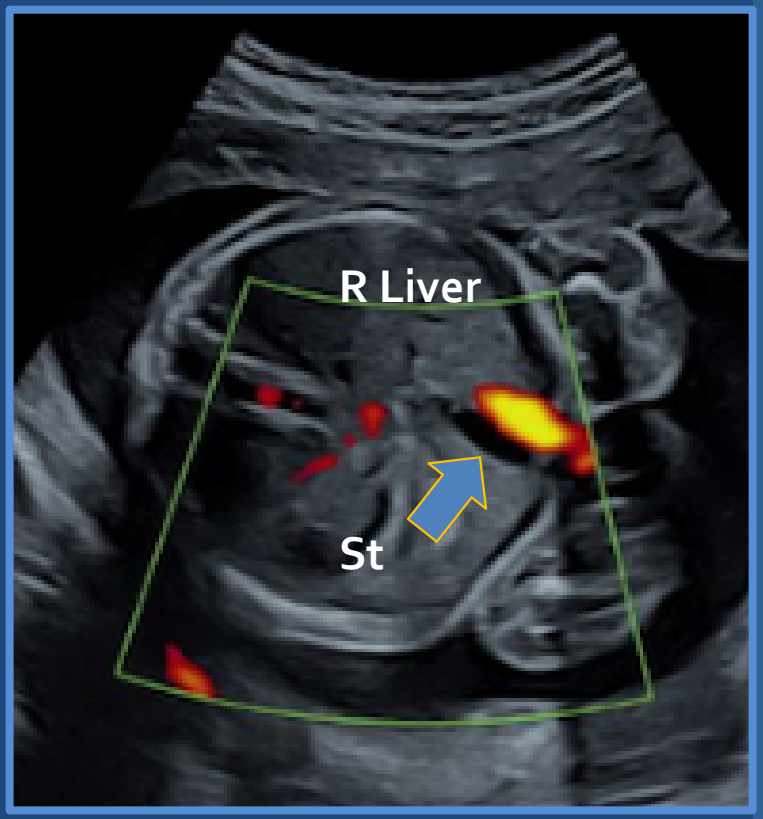
Isolated or part of polymalformative *syndrome*

J maternal fetal neonat med 2019; 32: 2643-2648
Ultrasound Obstet Gynecol. 2019;54:582-588.

Non - visualization of the fGB (during the 2d trimester)

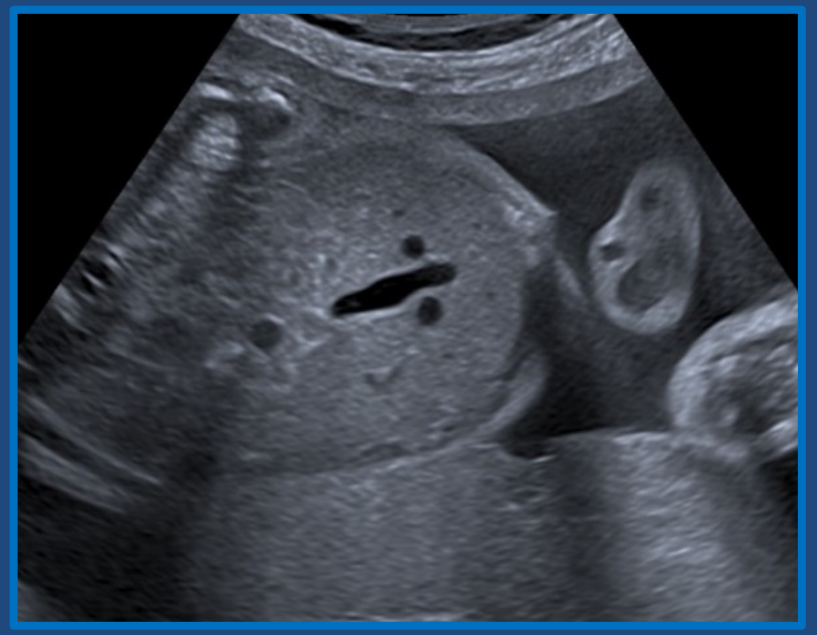
1) <u>Technical and anatomical causes</u>

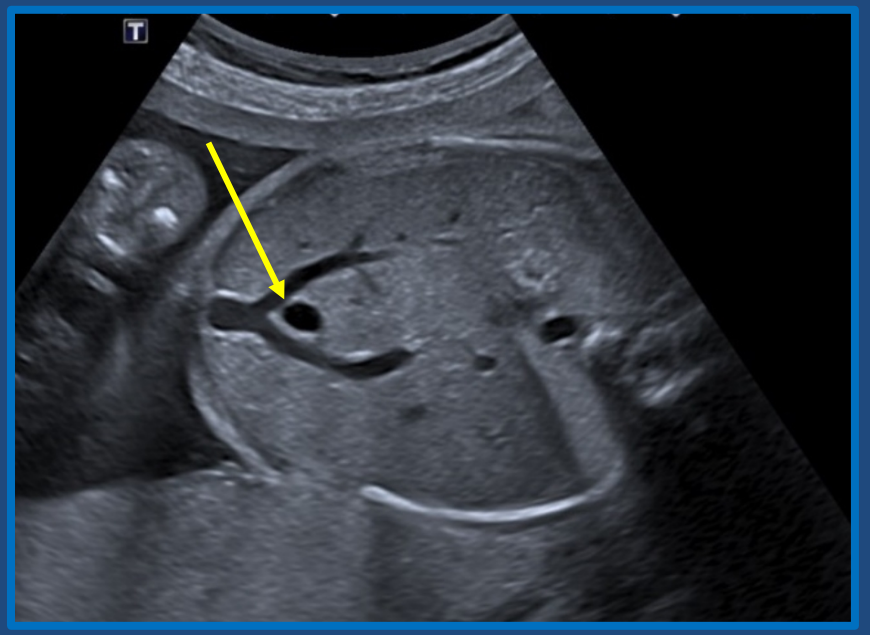
- *Mother's morphology*
- *Fetal lie*
- *« ectopic » fGB*
  - *Persisting R umbilical vein – usually isolated*
  - *Deep intra-hepatic fGB*



BMC Pregnancy and Childbirth (2020) 20:610

fGB - *unusual location*:



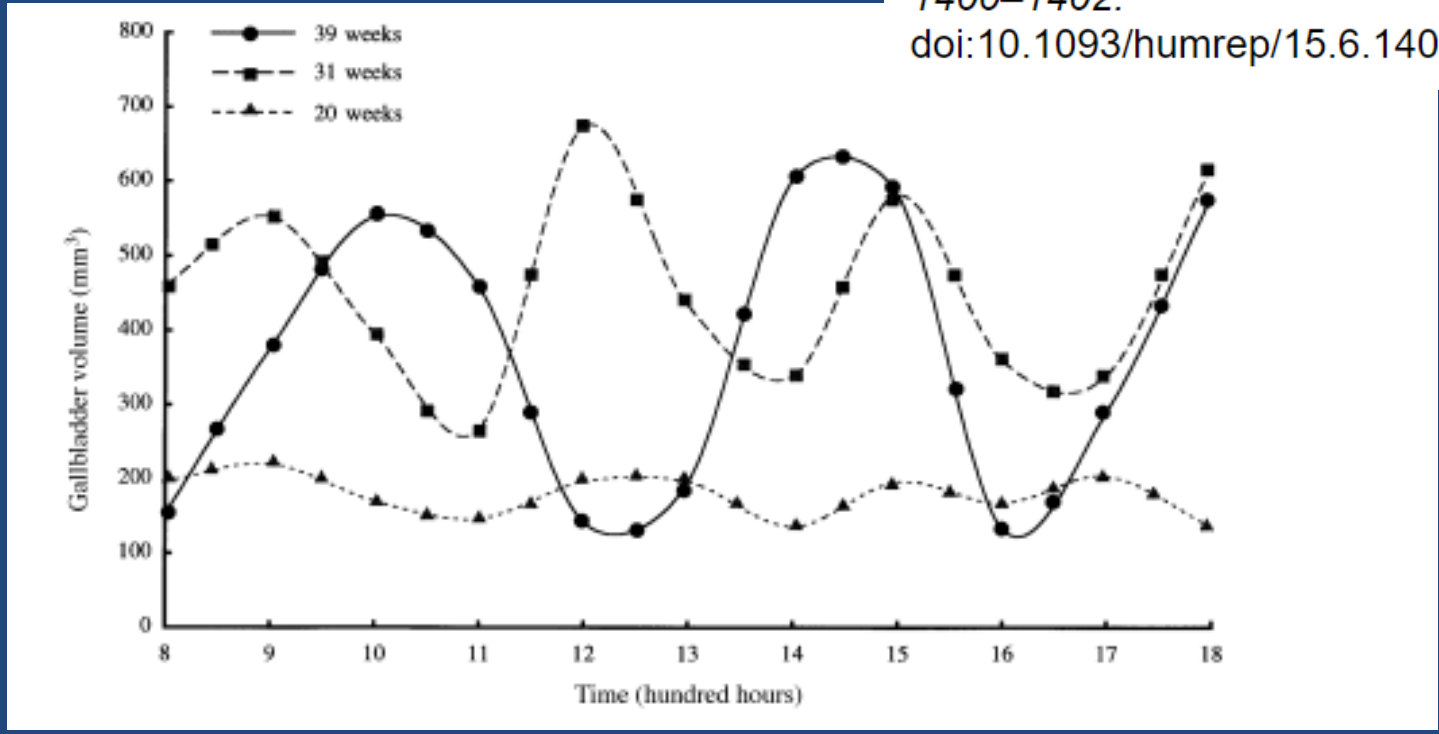


26 GW + 5 The fGB is located between an unusual proximal branching of the umbilical vein

Non-visualization of the fGB (during the 2d trimester)

2) « Collapsed » fGB: <Contractibility of the fGB during pregnancy ?

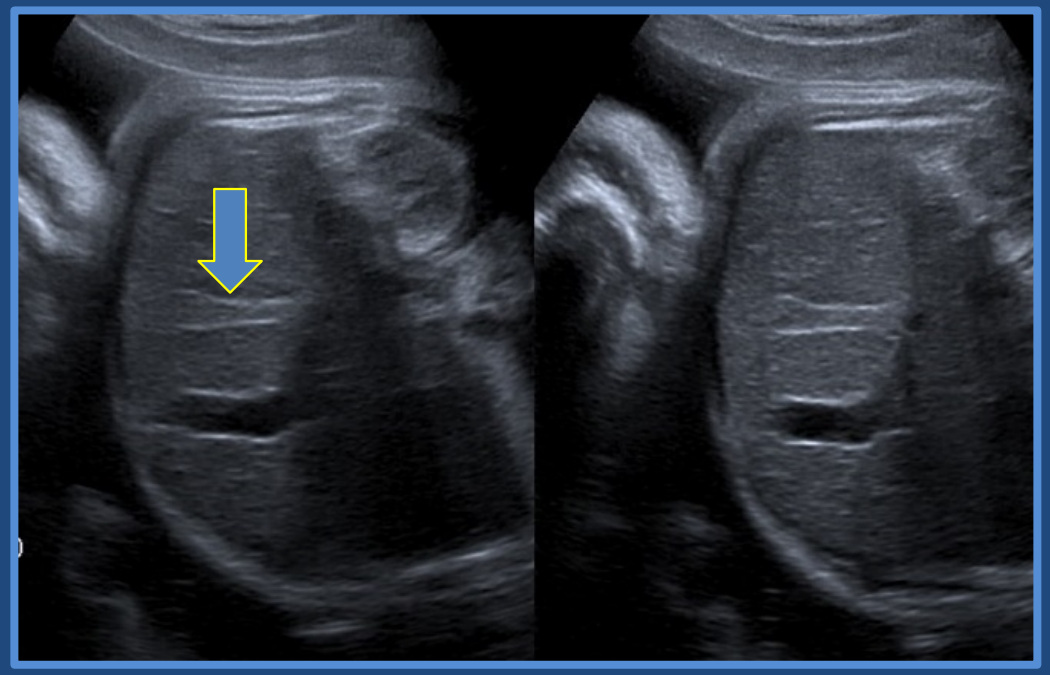
Tanaka, Y. (2000). *Is there a human fetal gallbladder contractility during pregnancy?. Human Reproduction, 15(6), 1400–1402.* doi:10.1093/humrep/15.6.1400



Non - visualization of the fGB (during the 2d trimester)

3) Shaded/ obscured fGB

- Abnormal content may prevent visualization



Non-visualization of the fGB (during the 2d trimester)

4) Congenital agenesis of the GB

- 1/ 6000 pregnancies
- Most cases diagnosed as isolated finding
- Besides expert US evaluation, no additional examination required
- Postnatal confirmation by US

! Important information to transmit to practionners (lifetime), to prevent wrong diagnosis of « cholecystitis »!

Oxf Med Case Reports. 2016 Aug; 2016(8): omw040.
Published online 2016 Aug 29. doi: 10.1093/omcr/omw040

49 year-old

Congenital agenesis of the gallbladder: a UK case report

Jenna L. Scobie* and Simon R. Bramhall

International Journal of Surgery Case Reports 53 (2018) 235–237

54 year-old

Contents lists available at ScienceDirect

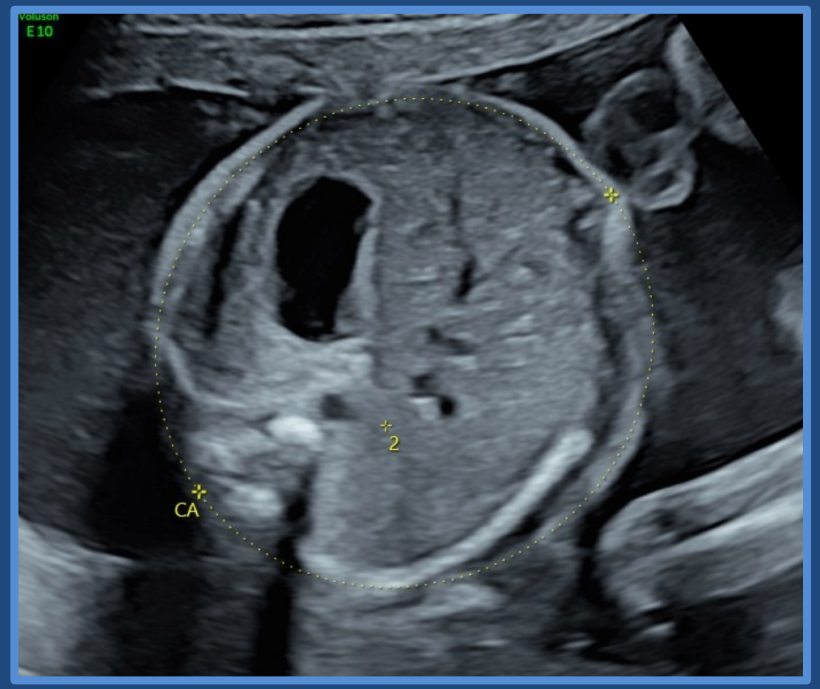
International Journal of Surgery Case Reports

journal homepage: www.casereports.com

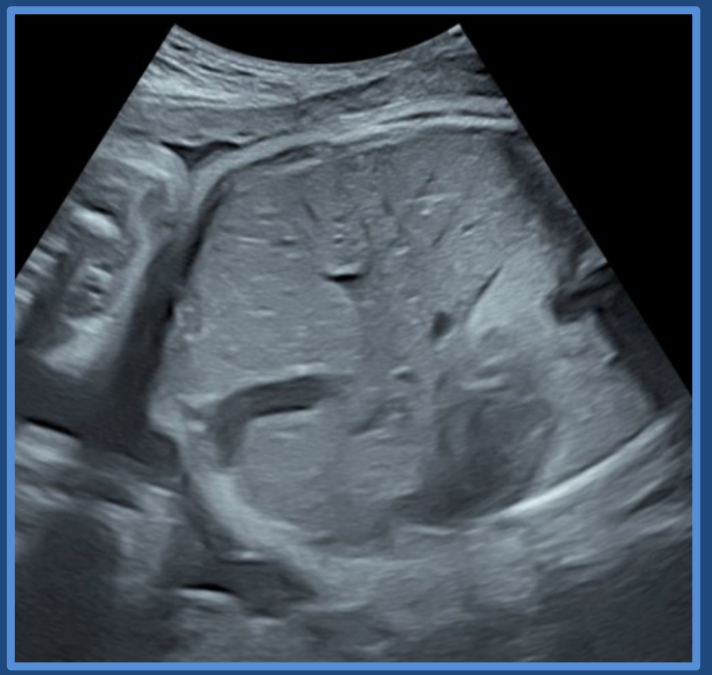
Gallbladder agenesis: A case report and review of the literature

Irakli Pipia[a,b], George Kenchadze[a,b], Zaza Demetrashvili[b,c,*], Grigol Nemsadze[d,e], Lika Jamburia[e], Tamari Zamtaradze[c], Ivane Abiatari[a]

Agenesis of the gallbladder: Antenatal US

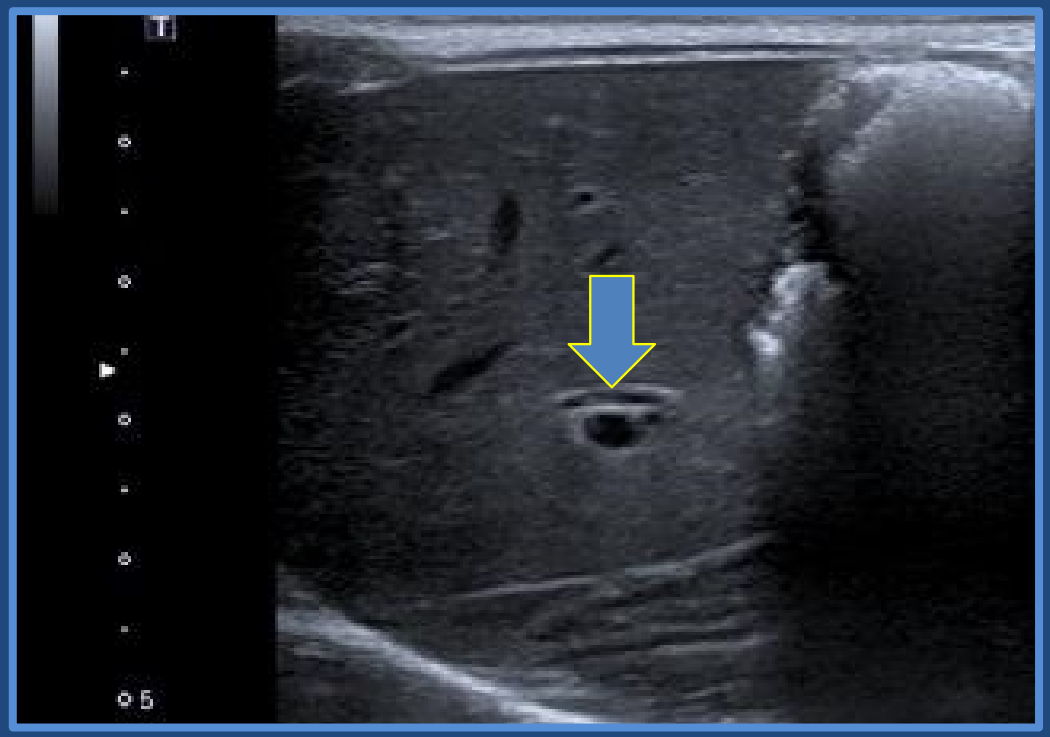


2nd trimester



3rd trimester

Agenesis of the GB: Postnatal US



Good visibility of the CBD, helps to exclude biliary atresia

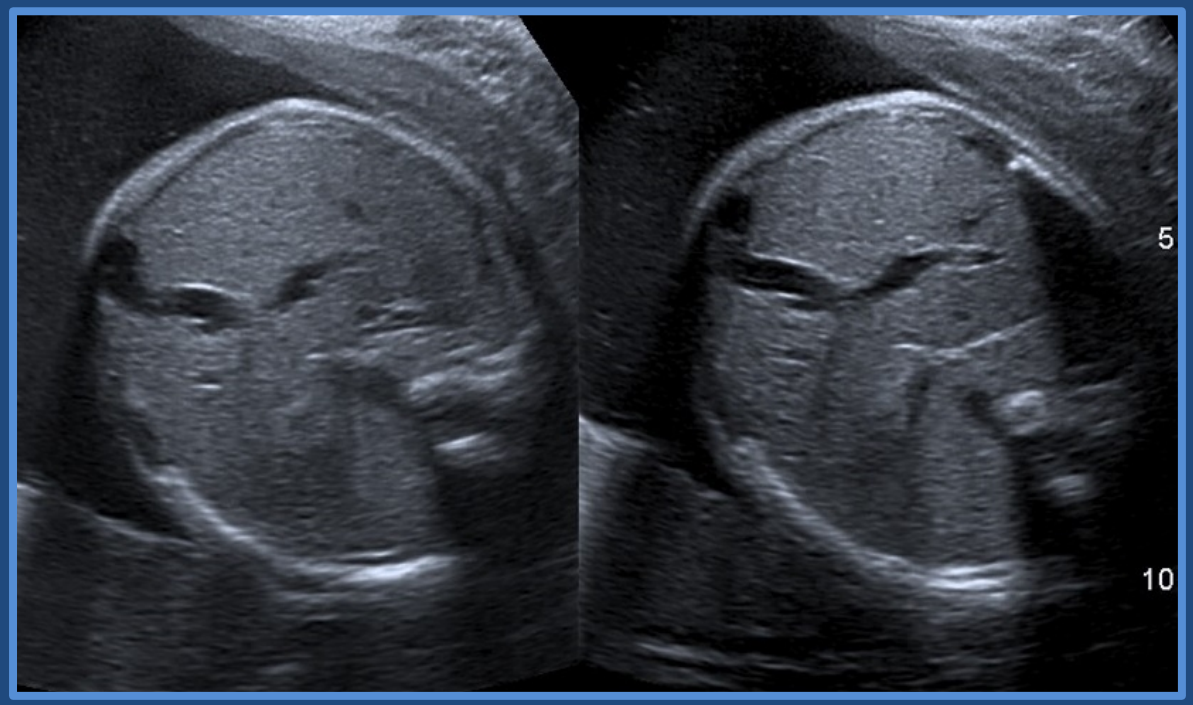
Non - visualization of the fGB (during the 2d trimester)

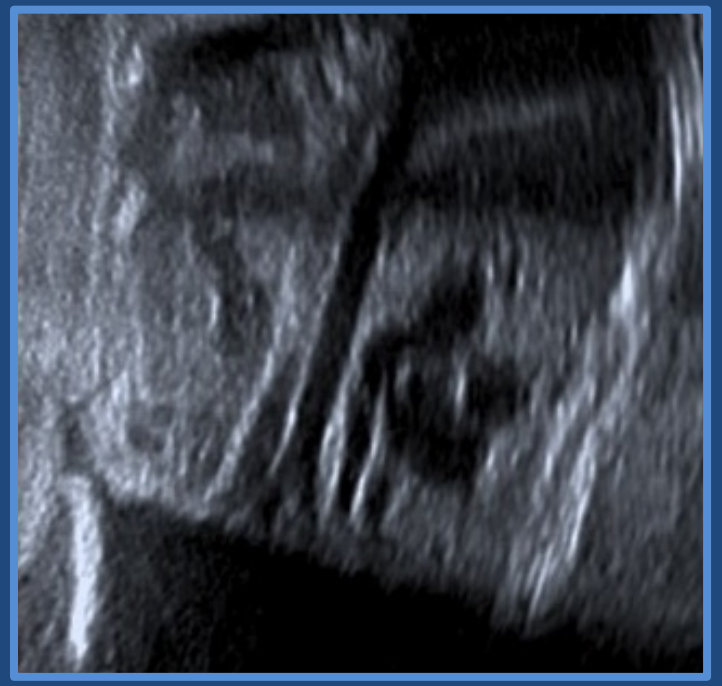
4bis) Congenital agenesis of the GB

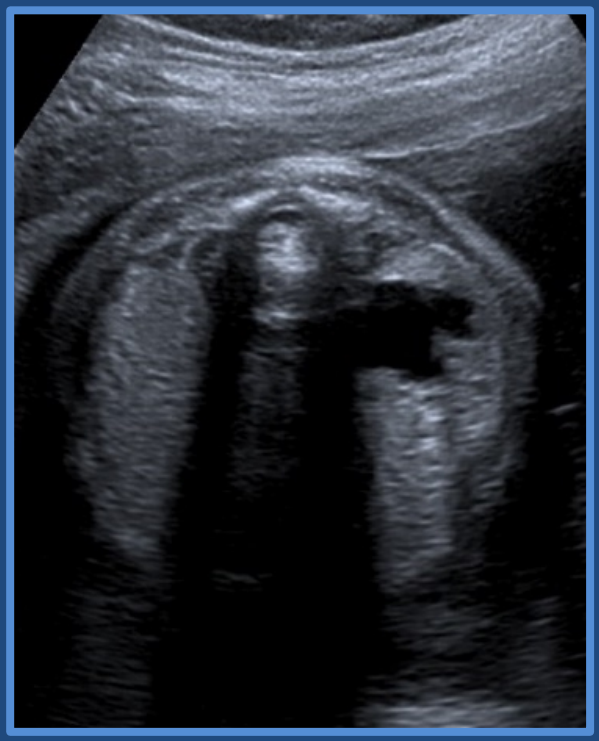
Can be part of polymalformative syndromes

- Steinfeld S., Alagille S., Vacterl S…
- Cardiovascular (58%) – GI (25%) - GU (25%) – CNS (6.5%) as associated malformations
- Chromosomal analysis warranted as well (Triploidy, XYY, T21 have been reported)

GB agenesis and polymalformative syndrome







28 GW – fGB never seen, polyhydramnios, left UT dilatation with obstructive dysplasia
+ *Esophageal atresia type IV (at histology)*

Non - visualization of the fGB (during the 2d trimester)

Preliminary comments:

- Common
- Mostly transient → *repeat obstetrical US*
- Mostly benign when isolated
- Detailed US to exclude associated anomalies
- If doubt persists → postnatal US

- Yet, …….

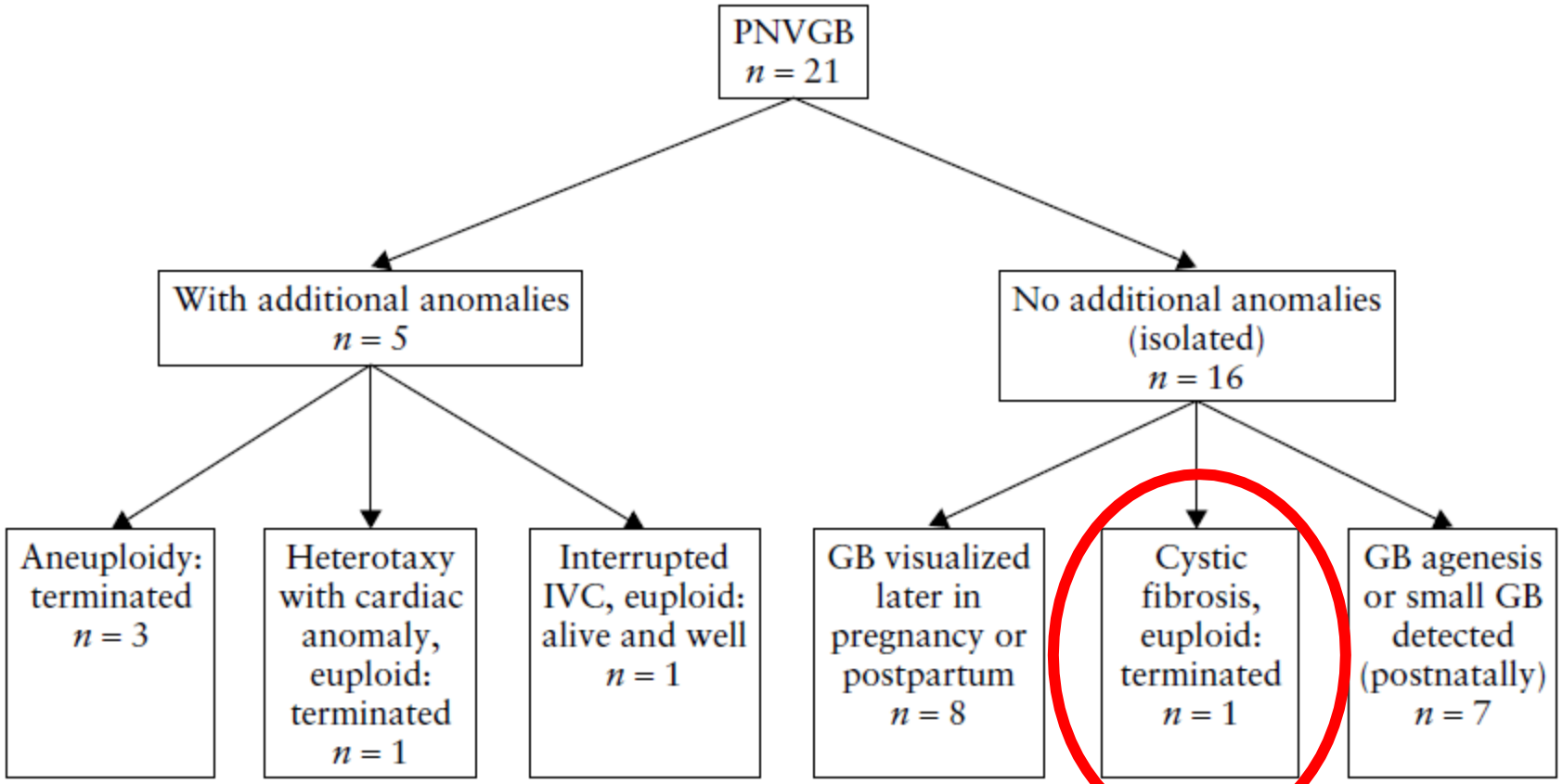


Figure 1 Summary of outcome of 21 cases of prenatal non-visualization of the fetal gall bladder (PNVGB). GB, gallbladder; IVC, inferior vena cava.

Ultrasound Obstet Gynecol 2011; 37: 673–677.

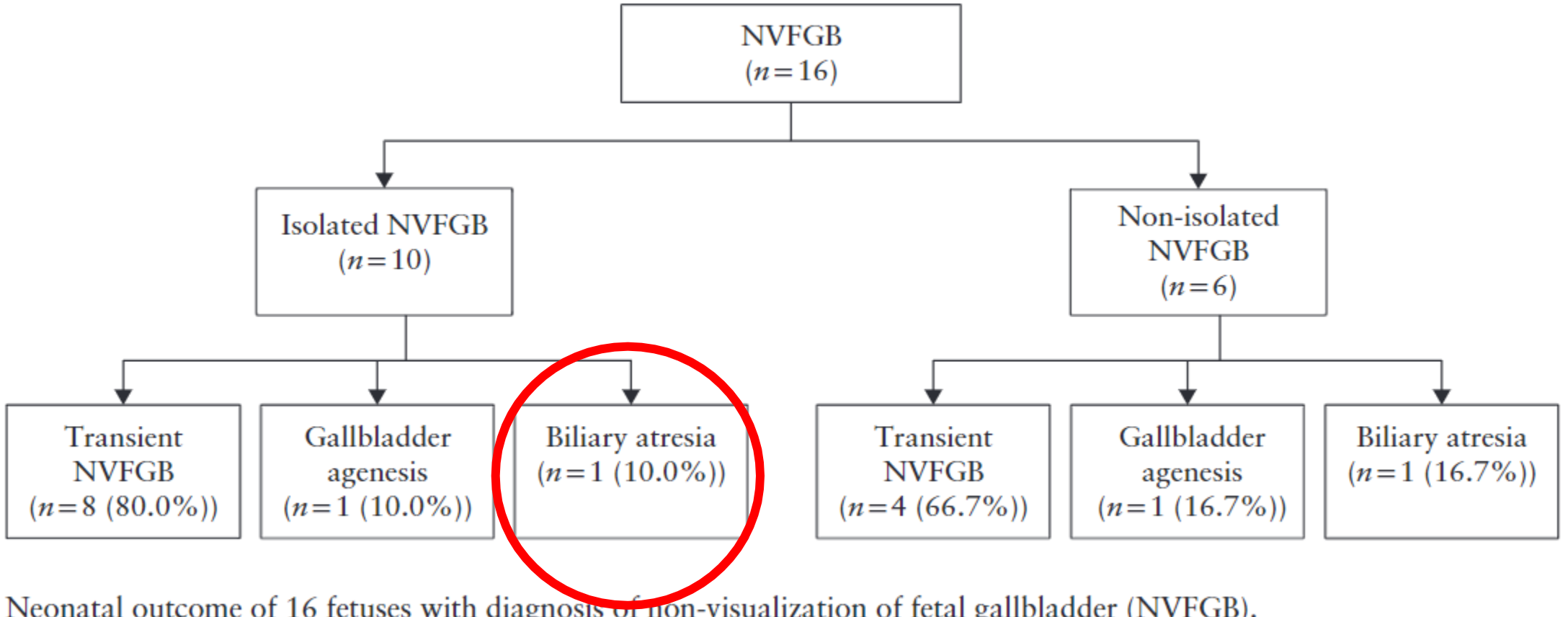


Figure 1 Neonatal outcome of 16 fetuses with diagnosis of non-visualization of fetal gallbladder (NVFGB).

Nonvisualization of fetal gallbladder in microarray era – a retrospective cohort study and review of the literature

Sagi-Dain Lena, Singer Amihood, Yarin Hadid, Sharony Reuven, Chana Vinkler, Bar-Shira Anat, Reeval Segel, Ben Shachar Shay & Maya Idit

To cite this article: Sagi-Dain Lena, Singer Amihood, Yarin Hadid, Sharony Reuven, Chana Vinkler, Bar-Shira Anat, Reeval Segel, Ben Shachar Shay & Maya Idit (2018): Nonvisualization of fetal gallbladder in microarray era – a retrospective cohort study and review of the literature, The Journal of Maternal-Fetal & Neonatal Medicine, DOI: 10.1080/14767058.2018.1443070

To link to this article: https://doi.org/10.1080/14767058.2018.1443070

45 own cases

Review of literature 173 cases

Prevalence :

- Cystic fibrosis: 7-9%
- Biliary atresia: 7%

Outcome of non-visualization of fetal gallbladder on second-trimester ultrasound: cohort study and systematic review of literature

E. DI PASQUO[1], M. KULEVA[2], A. ROUSSEAU[2], A. VITUCCI[2], P. SONIGO[3], C. CHARDOT[4], L. J. SALOMON[2,5] and Y. VILLE[2,5]

[1]*Obstetrics and Gynaecology Unit, University of Parma, Parma, Italy;* [2]*Maternité, Hôpital Necker–Enfants Malades, Assistance Publique, Hôpitaux de Paris, Université Paris Descartes, Paris, France;* [3]*Radiologie Pédiatrique, Hôpital Necker–Enfants Malades, Assistance Publique, Hôpitaux de Paris, Université Paris Descartes, Paris, France;* [4]*Chirurgie Pédiatrique, Hôpital Necker–Enfants Malades, Assistance Publique, Hôpitaux de Paris, Université Paris Descartes, Paris, France;* [5]*Société Française pour l'Amélioration des Pratiques Echographiques, Paris, France*

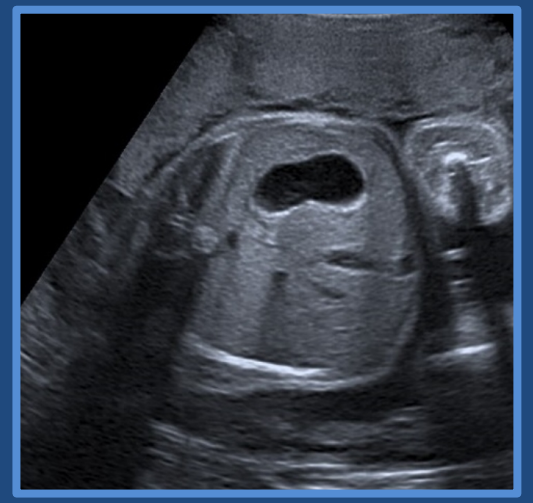
16 own cases

Review of the literature 280 cases

Prevalence :

- CF : 3.1%
- BA: 4.8%

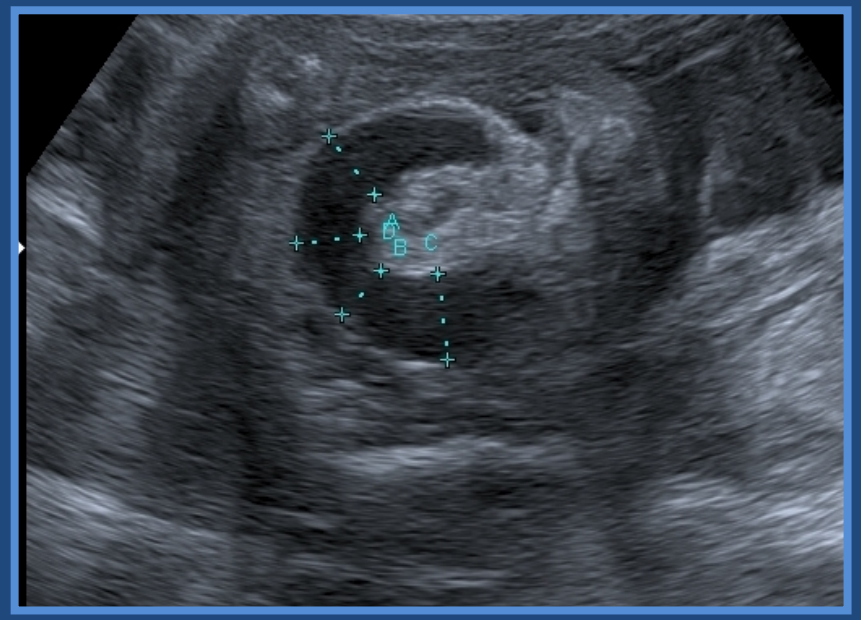
Non - visualization of the fGB (during the 2d trimester)

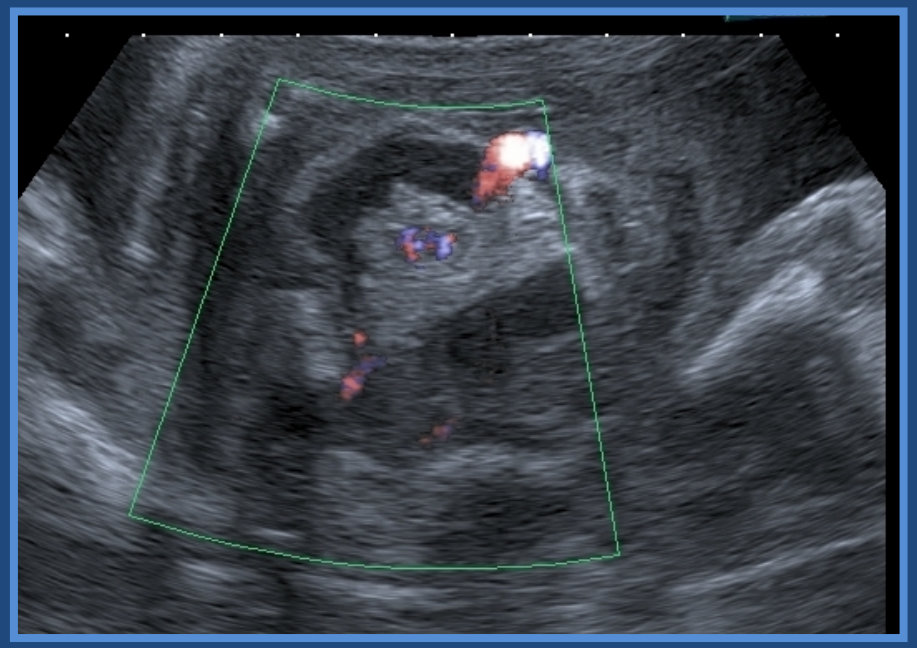


5) Cystic fibrosis

- *Could NVfGB be a clue to the diagnosis of CF?*
- High level of suspicion if associated with echogenic bowel loops and/or intestinal dilatation → genetic investigations of the parents and fetus
- If isolated, genetic evaluation controversial…..but understandable ? Of the parents only?

Fetal Diagn Ther 2019; 45: 312-316



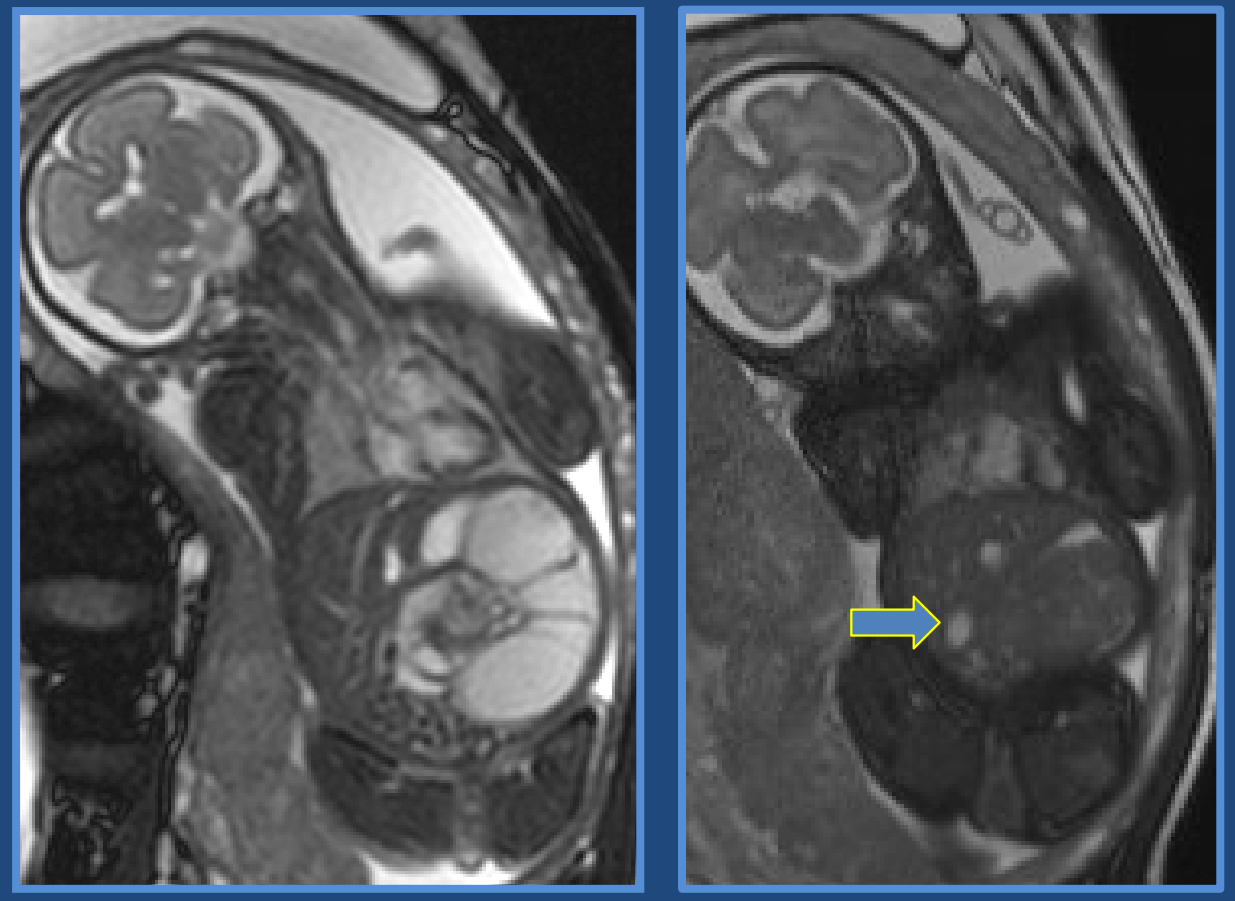


2d trimester
Dilatation of bowel loops ,
hyperechoic wall, fGB non visualized.

Suspicion of CF confirmed by genetic analysis of the parents and fetus :

*Maternal mutation p.Gln1411**
Paternal mutation DF 508

Courtesy of O Prodhomme MD, Montpellier



2d trimester
Bowel loops dilatation at 22 WG 4d (10-12 mm). Increasing dilatation at follow-up - fGB never visualized

fMR imaging at 26w : volvulus, fGB not seen

CF confirmed:
Maternal mutation Delta F 508 + paternal mutation 711+1GT

Courtesy of O Prodhomme MD, Montpellier

Non - visualization of the fGB (during the 2d trimester)

6) Biliary atresia:

Is this diagnosis achievable in utero???

Pediatr Radiol. 2021; 51:314-331
Ultraschall Med. 2022 Mar 8

Biliary atresia (BA)

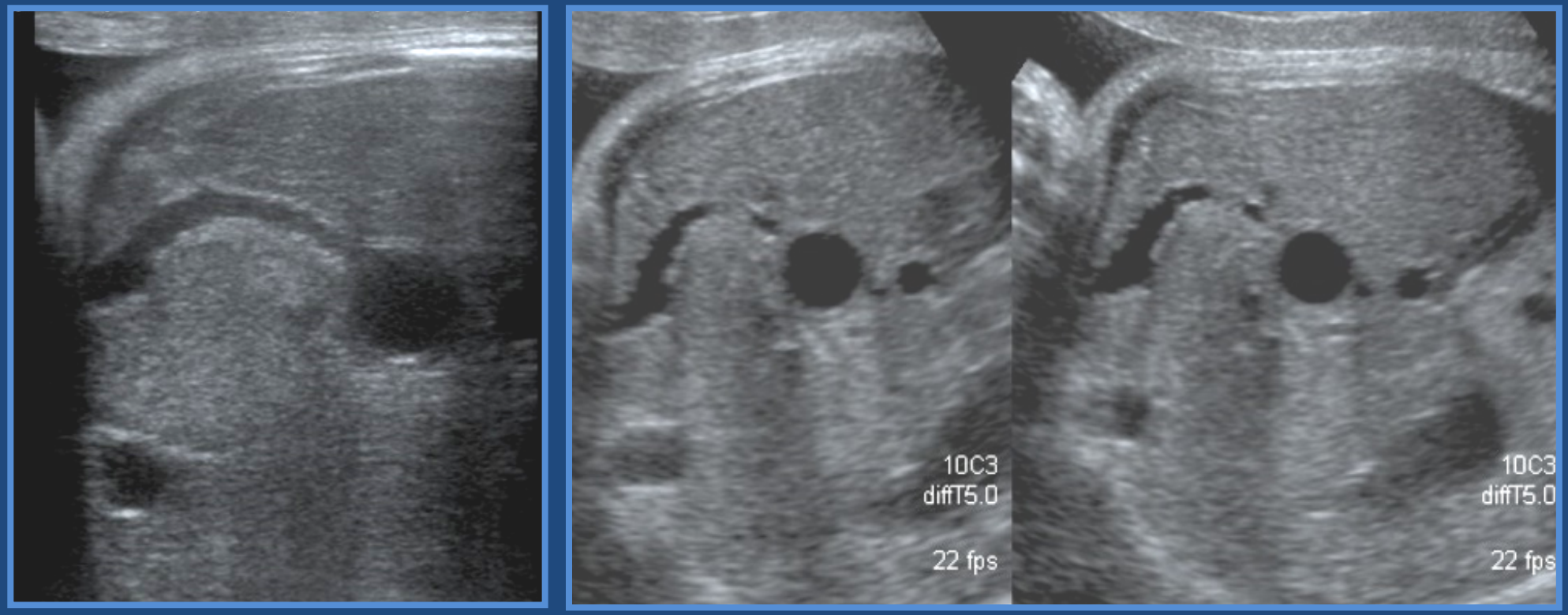
- Newborn (evolving) liver disease starting in utero
- Idiopathic progressive inflammatory and fibrosclerosing obliteration of large bile ducts
- Leading cause of liver-related death in children
- Incidence ranges from 1:5000 births in Taiwan to 1:20000 births in Europe
- Several clinical phenotypes
  - Isolated BA (90%) → *rarely diagnosed in utero*
  - Syndromic BA → *amenable to antenatal diagnosis*
  - « cystic -type BA » → *amenable to antenal diagnosis*
- Early diagnosis and early Kasai improve prognosis

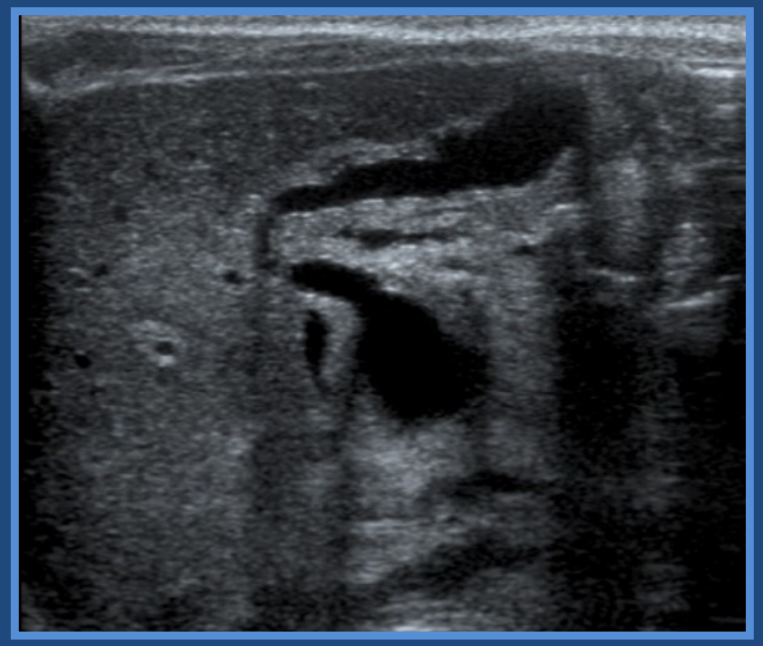
J. Clin. Med. 2022, 11, 999.

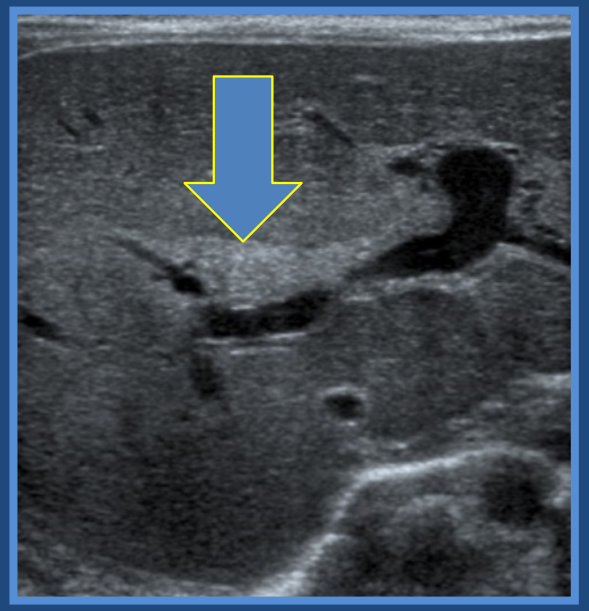
Biliary atresia: Prenatal US findings?

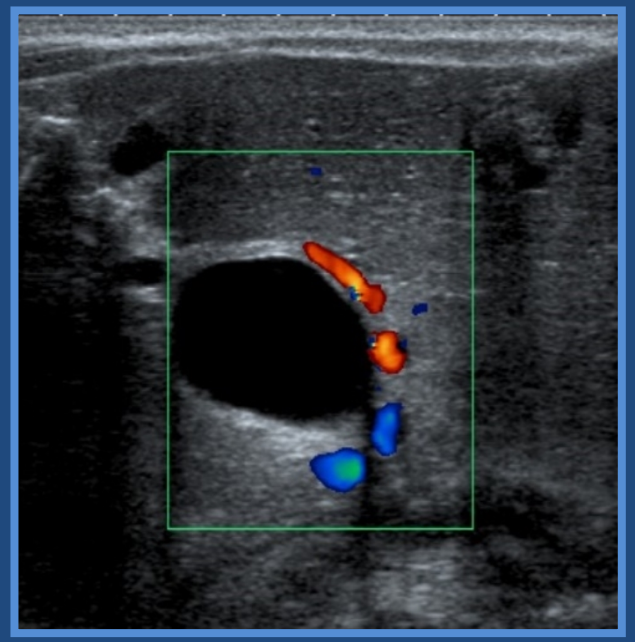
- Non visualization of the fGB – *weak sign*
- Small fGB – *weak sign*
- Large irregular fGB - *relatively good sign*
- Hilar micro- or macrocyst(s) – *good sign*
- Non visualization fGB + hilar cyst – *highly suspicious*
- Non visualization + hilar cyst + associated malformations (heterotaxy, polysplenia++) – *highly suspicious syndromic BA*

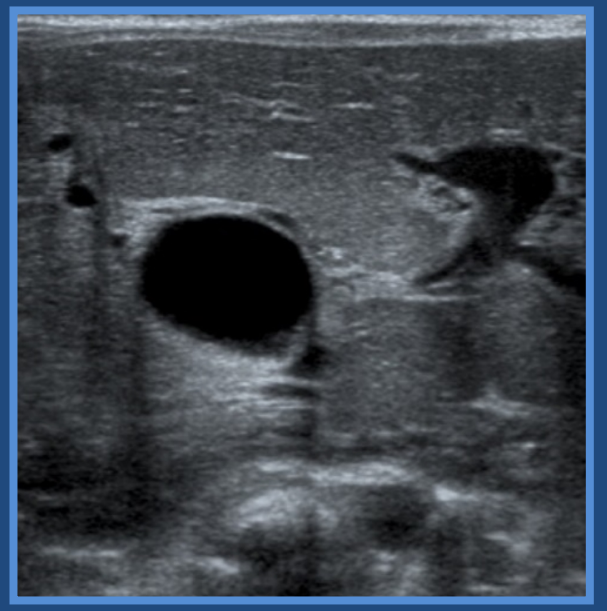
Prenatal US:
Hilar cyst + large irregular fGB











Postnatal US:
same findings +
Triangular cord sign
➔ Confirmation BA

Cases detectable in utero ?

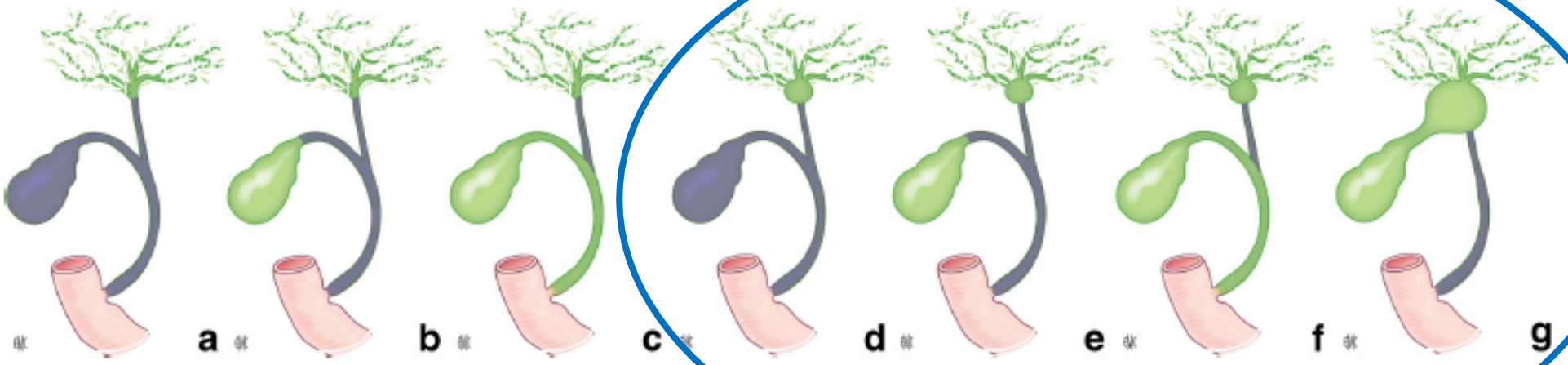
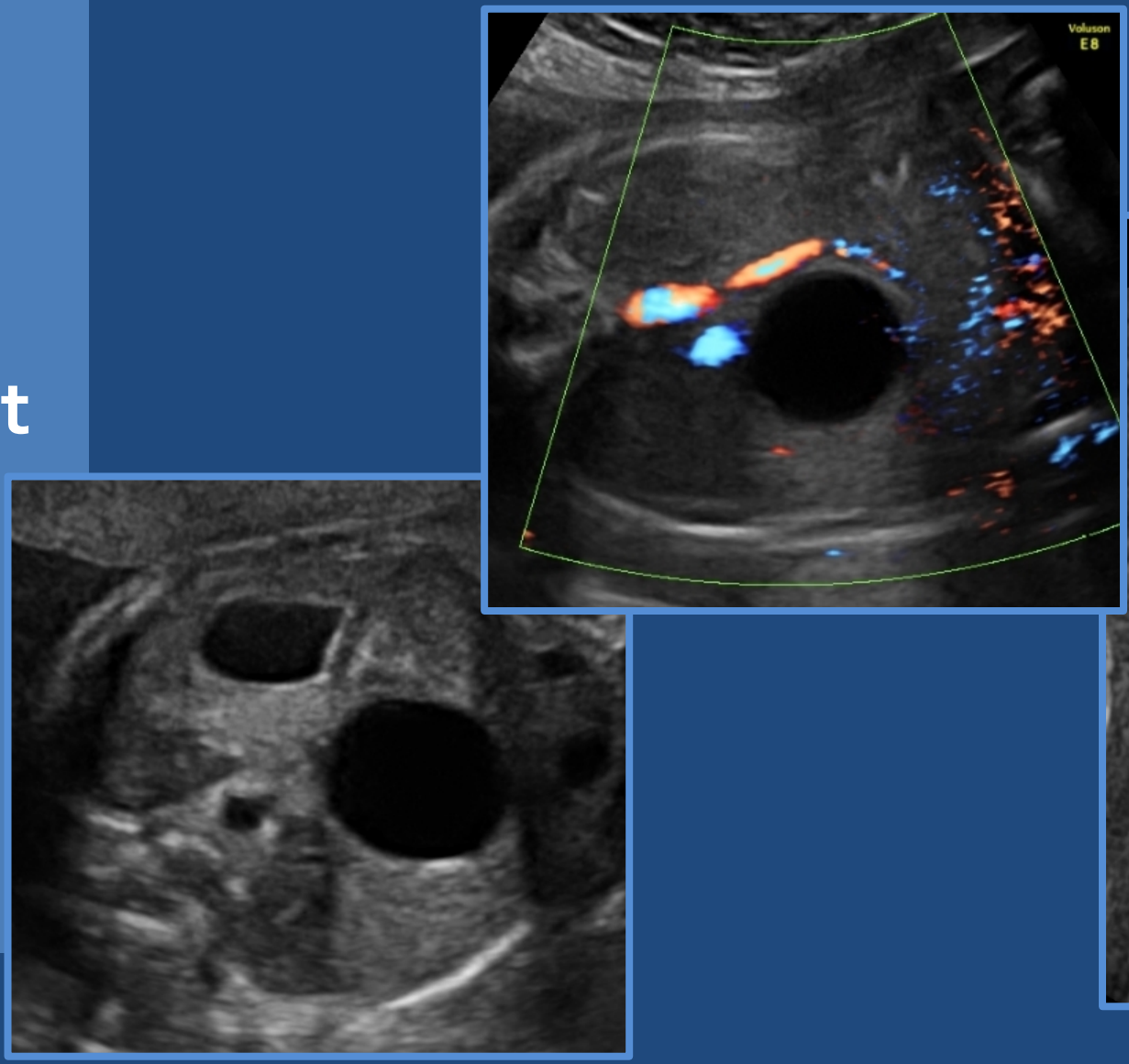
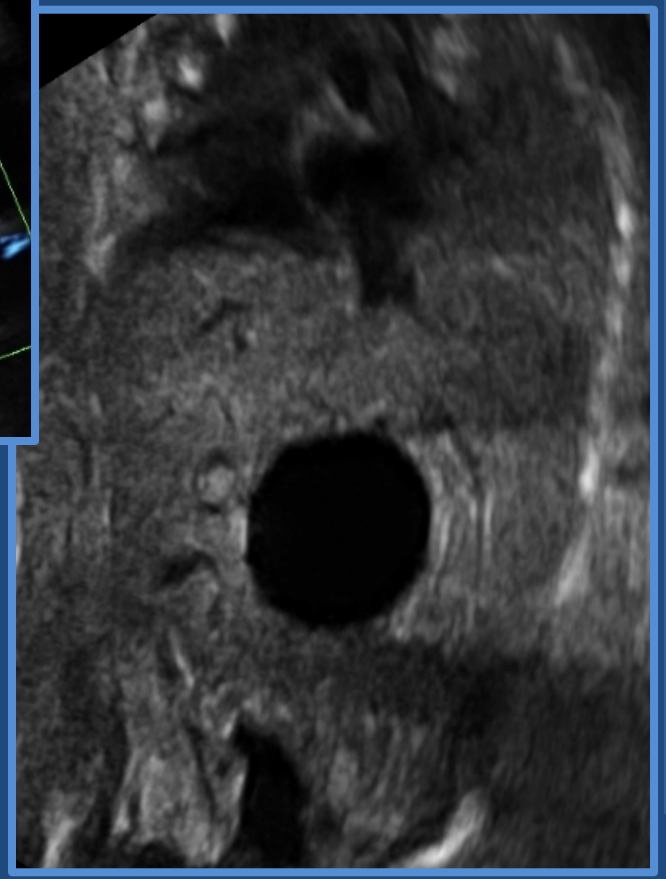


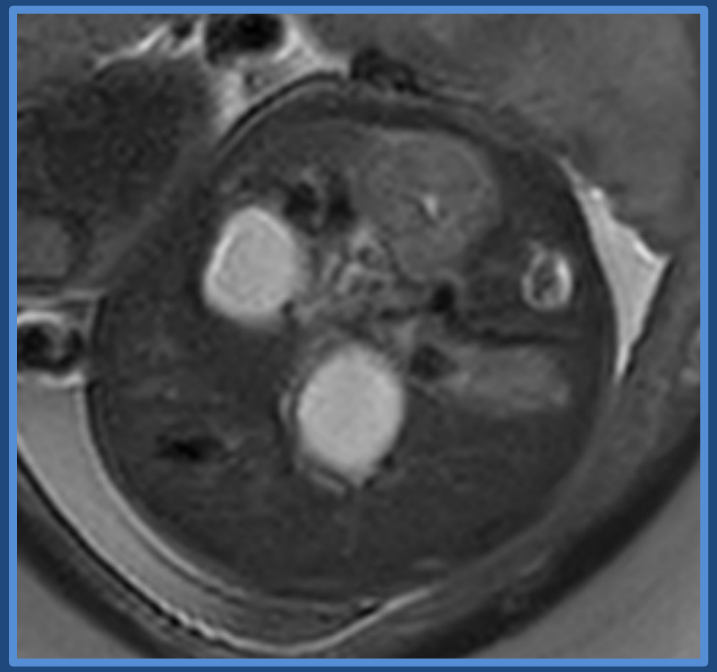
Fig. 1 Different types of biliary atresia — in grey the obstructed bile ducts or gallbladder, in green the patent parts. **a** Complete atresia of the extrahepatic bile duct and the gallbladder. This is the most frequent type, accounting for about 2/3 of patients. **b** Patent gallbladder with atretic cystic duct and extrahepatic bile duct. **c** Patent gallbladder, cystic duct and choledochus with atretic main common bile duct. **d**–**g** Cystic forms with macrocyst at the liver hilum and variable atresia of the gallbladder and the extrahepatic bile ducts. Note that intrahepatic bile ducts are always pathological; hence, they do not display dilation. With permission from Pariente et al. [6]

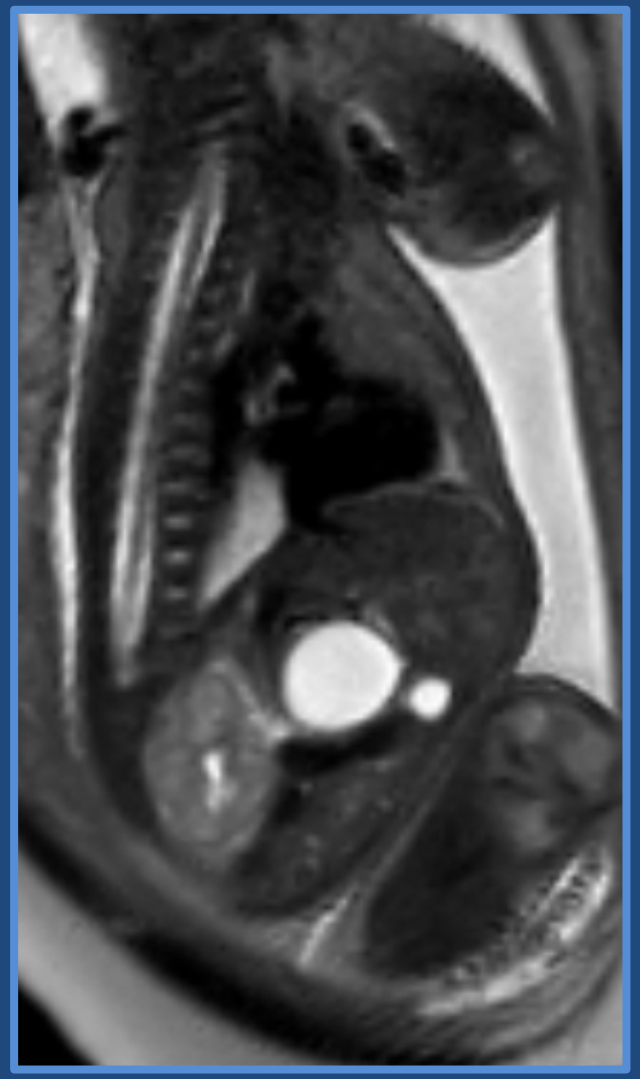
Hilar cyst « discovered » at 32 WG (Courtesy Marie Cassart (B))

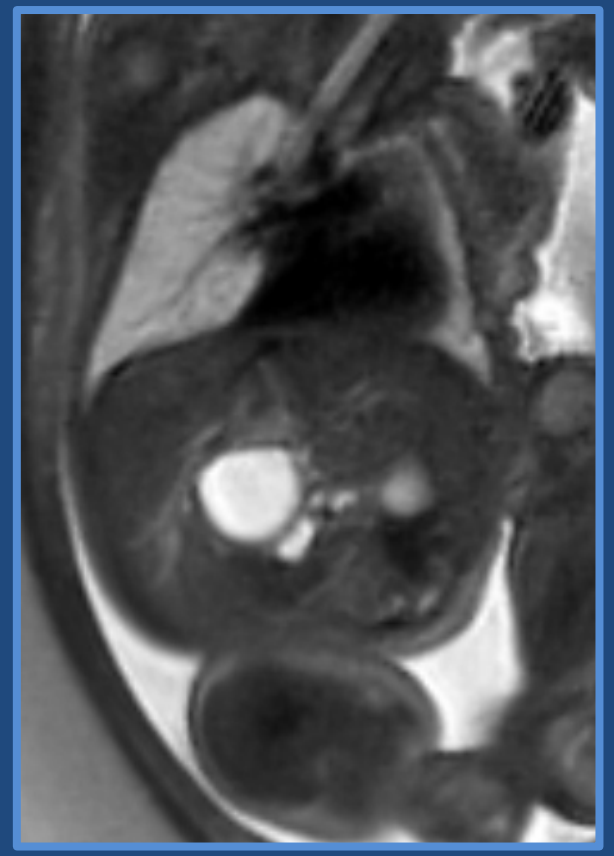




Fetal MR imaging

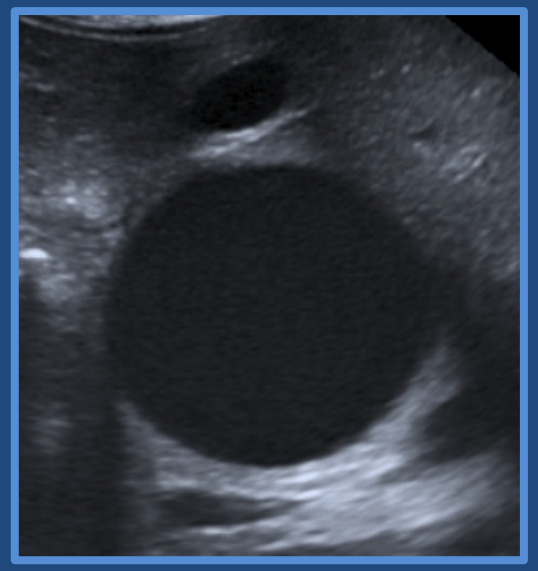


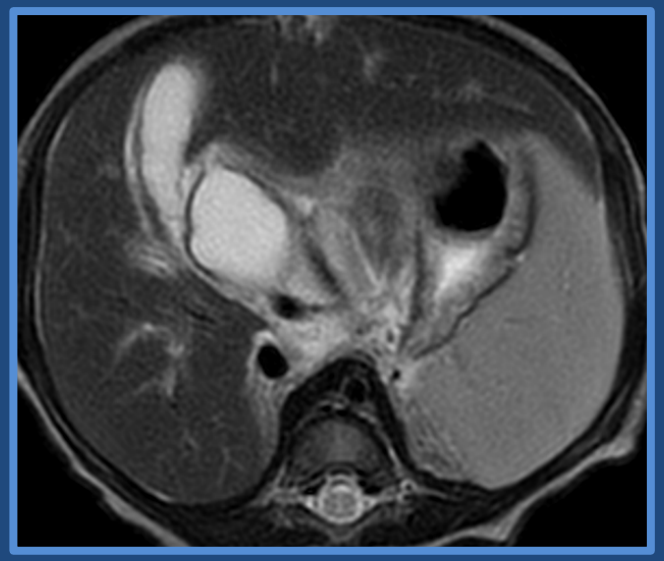




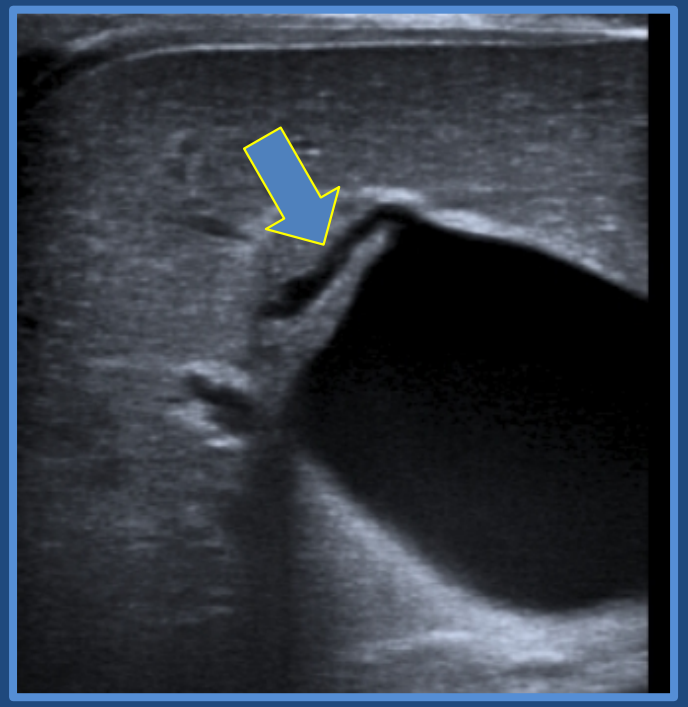
Hepatic hilar cyst: Differential diagnoses ?

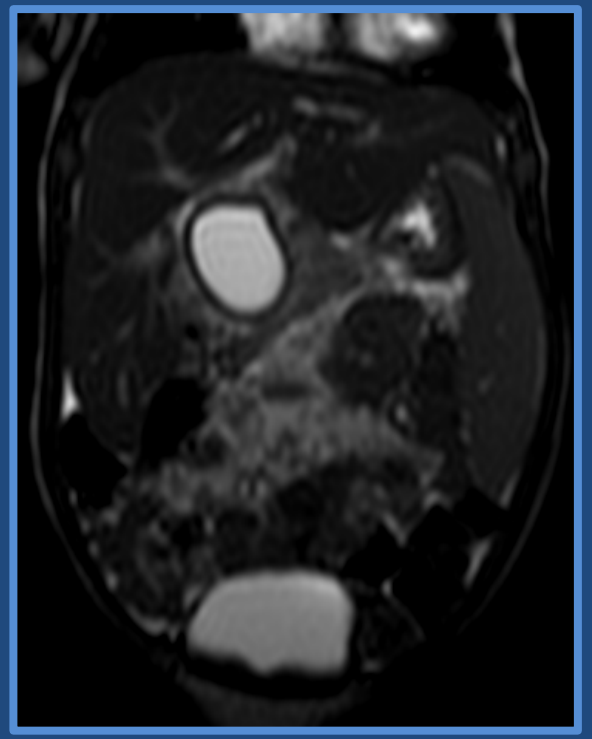
- Choledochal cyst
- Cystic biliary atresia
- Duodenal duplication
- Mesenteric cyst
- Liver (biliary cyst)
- Ovarian cyst
- .....

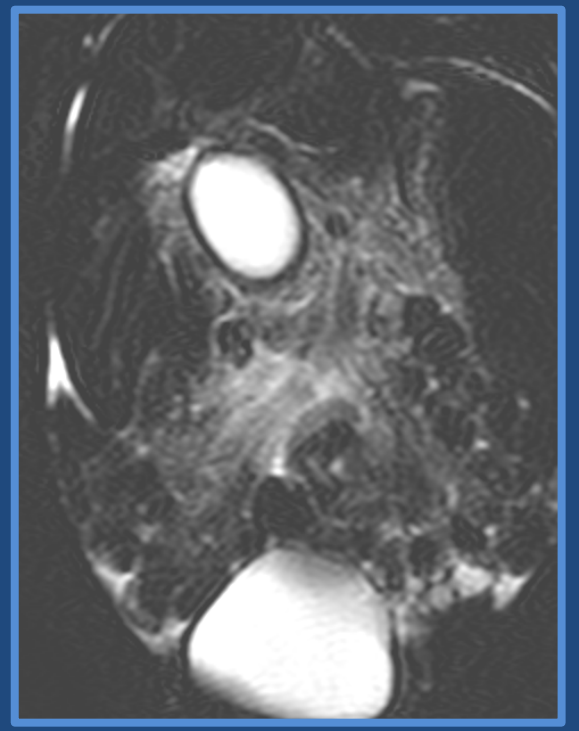


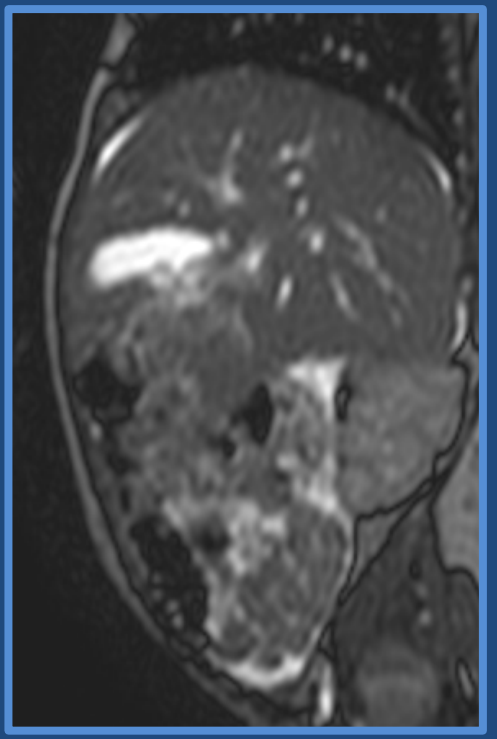


At birth…normal GB ➔ considered as CC,
Follow-up at 2 months:
poor clinic&l evolution ➔ final Diagnosis of *cystic type of BA*

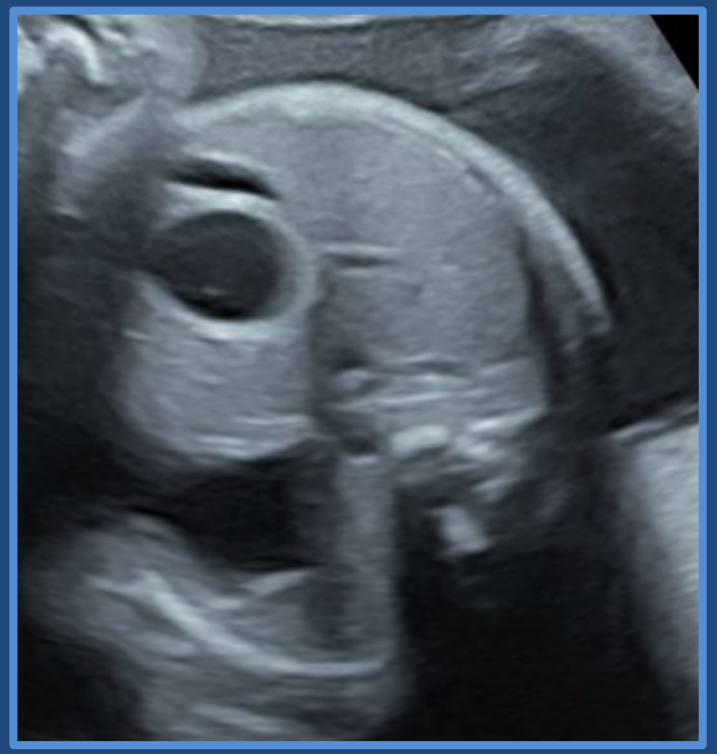


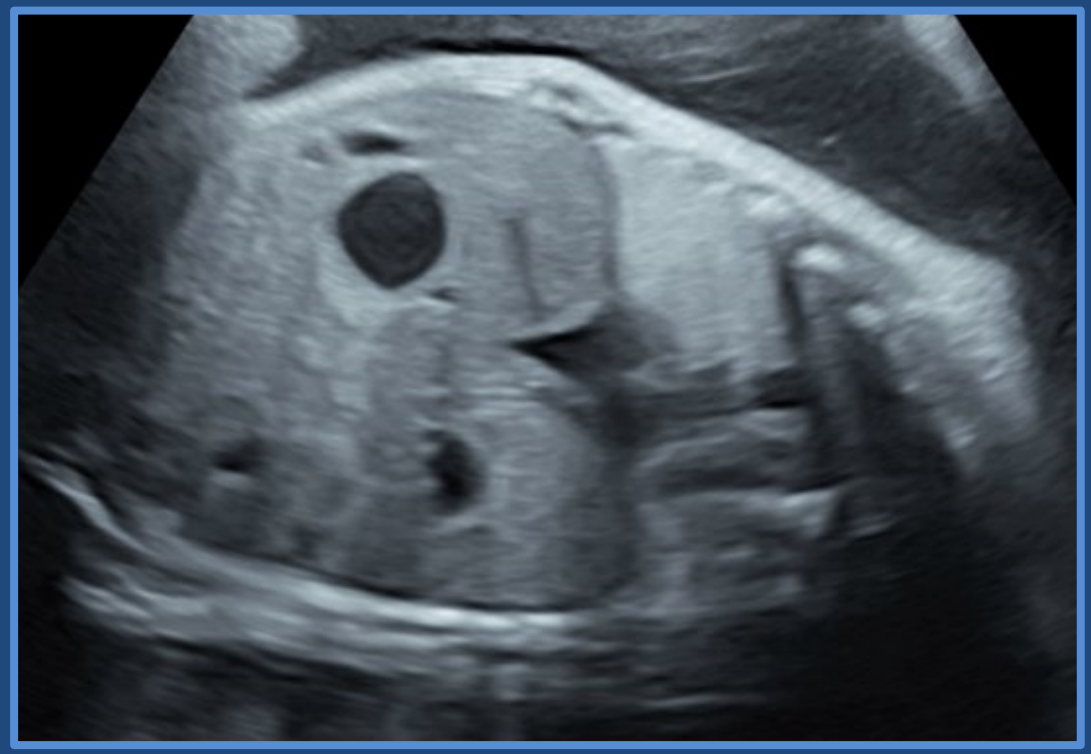




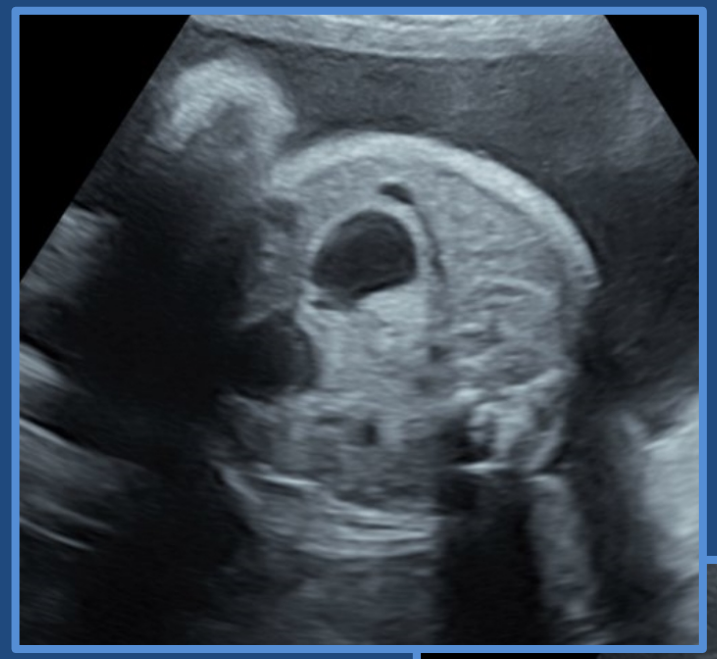


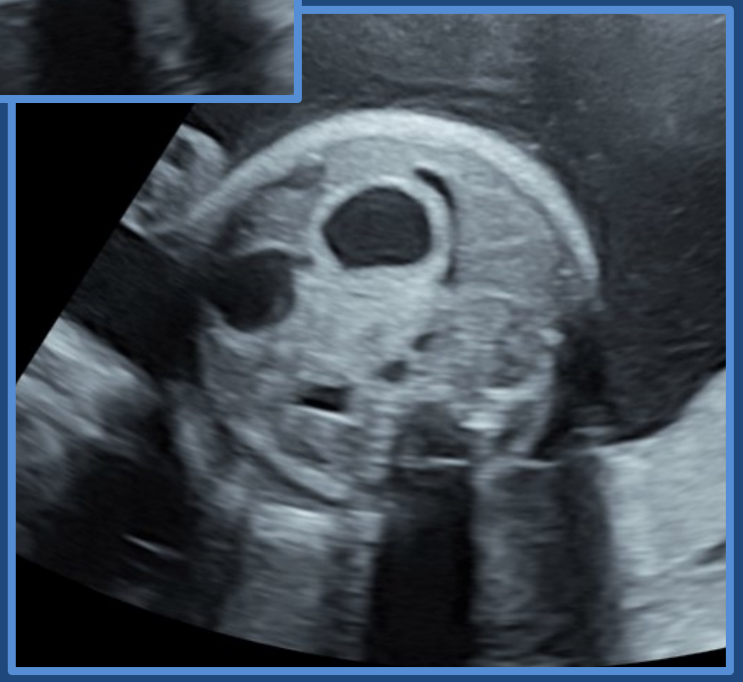
33 weeks gestation – Biliary tract anomaly?

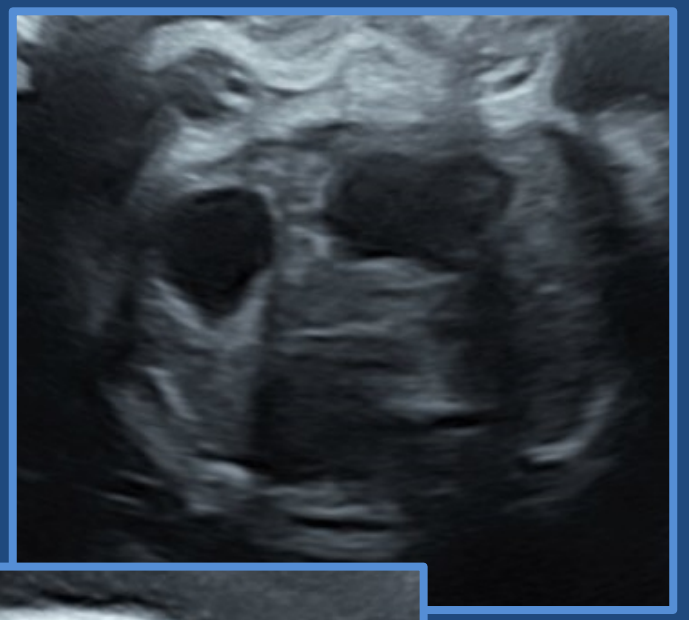


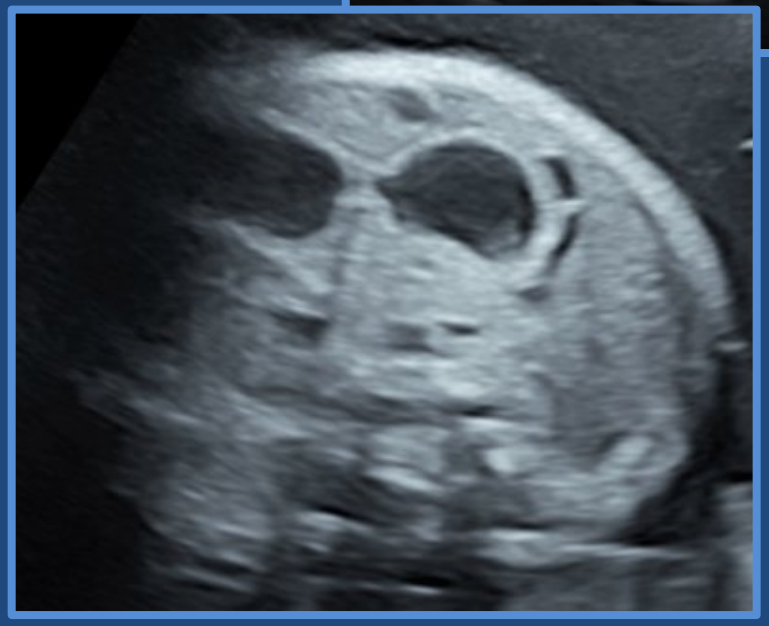


Double bubble sign ➔
Duodenal atresia!

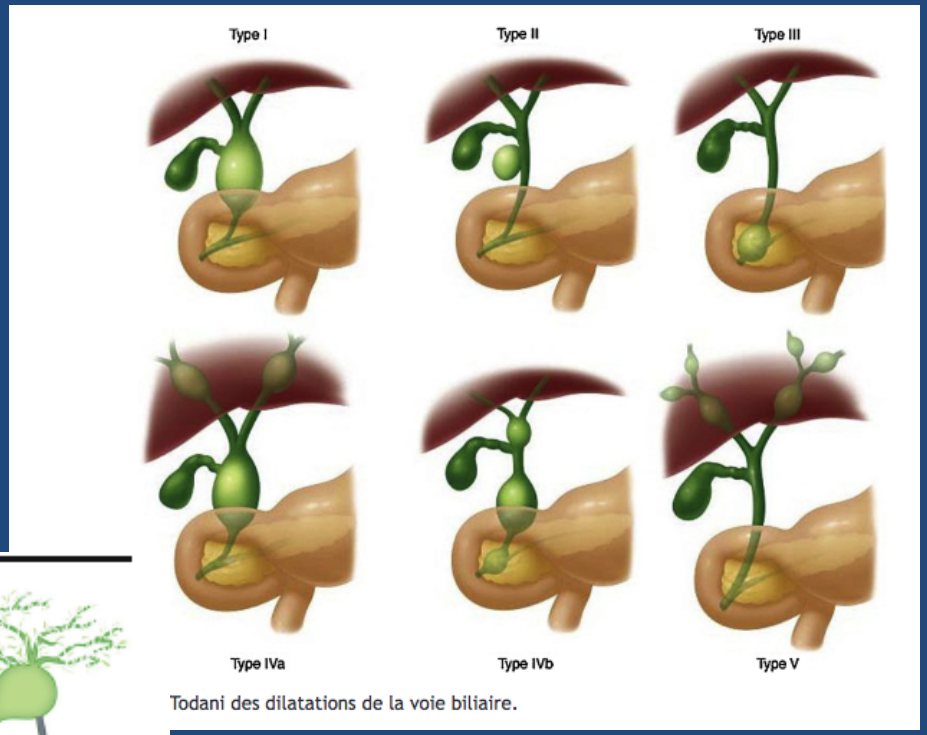




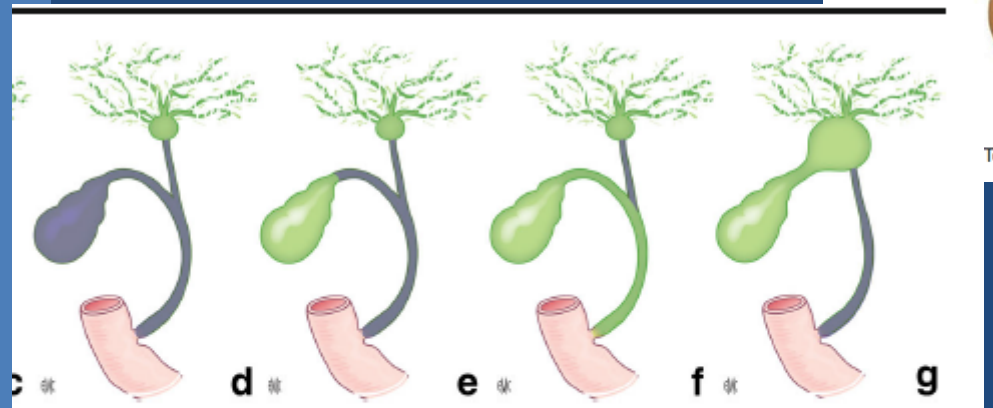




Main DDx: Biliary atresia (BA) vs Choledochal cyst (CC)



Todani des dilatations de la voie biliaire.

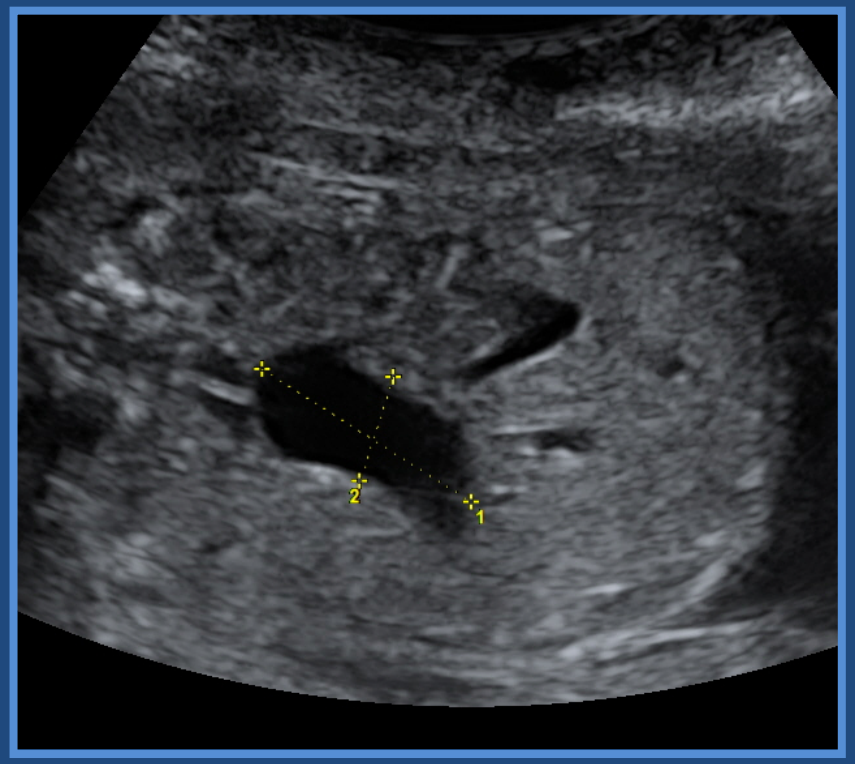


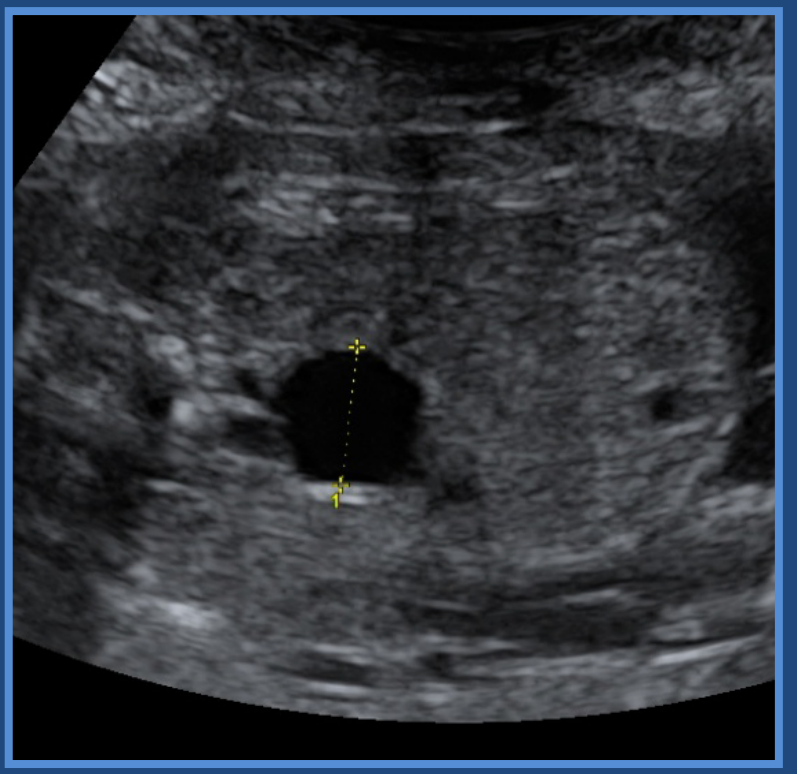
ucted bile
sia of the
uent type,
ith atretic
ystic duct

and choledochus with atretic main common bile duct. **d–g** Cystic forms with macrocyst at the liver hilum and variable atresia of the gallbladder and the extrahepatic bile ducts. Note that intrahepatic bile ducts are always pathological; hence, they do not display dilation. With permission from Pariente et al. [6]

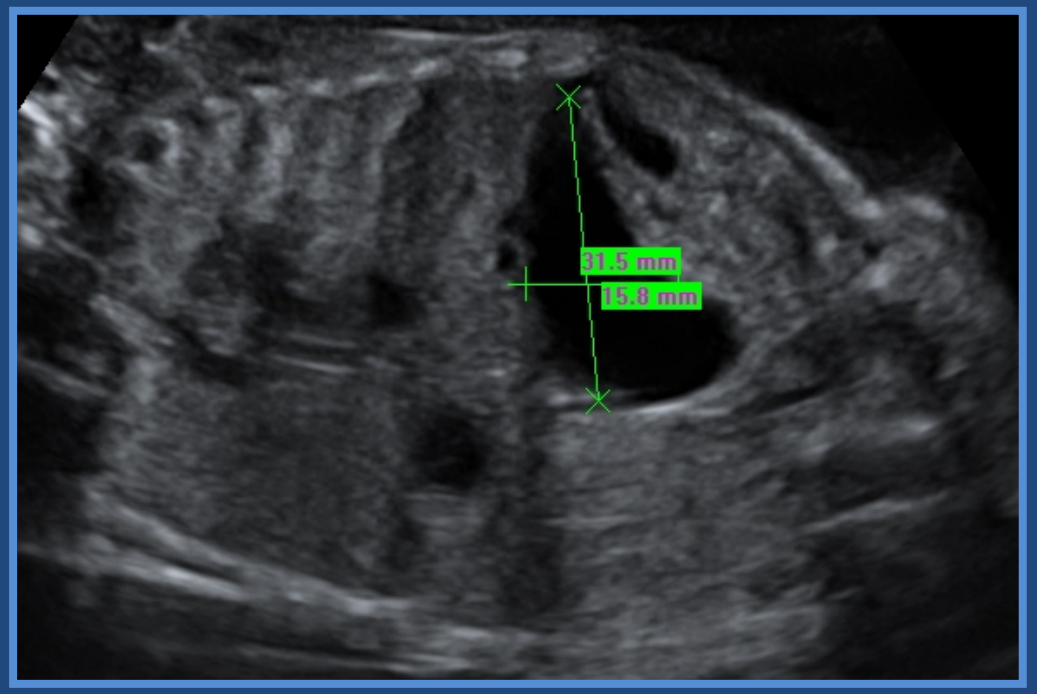
Ultrasonography 2022;41:140-149
Ultrasonography 2021;40:301-311

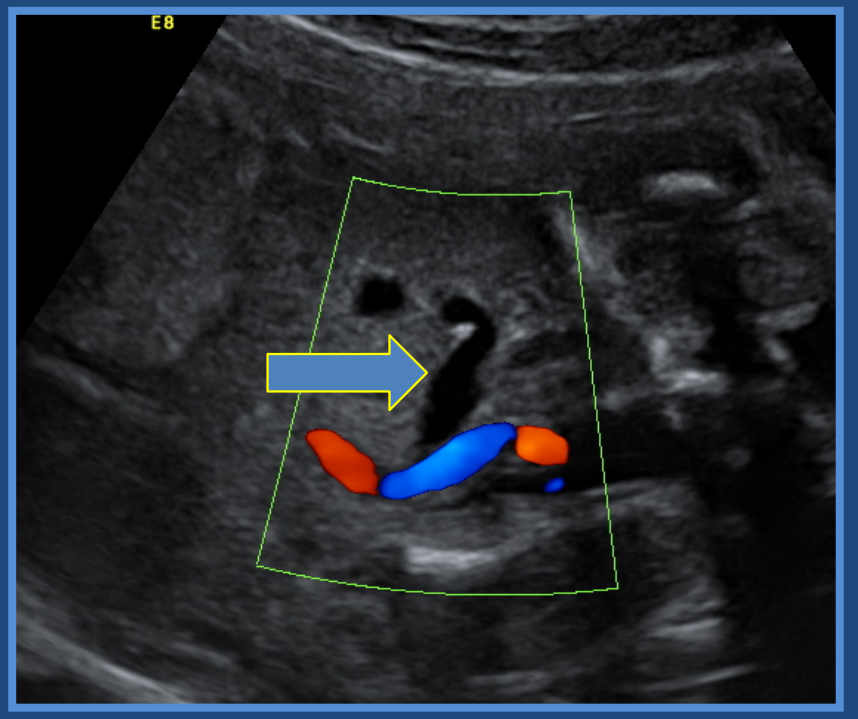
Hilar cyst « discovered » at 25 WG



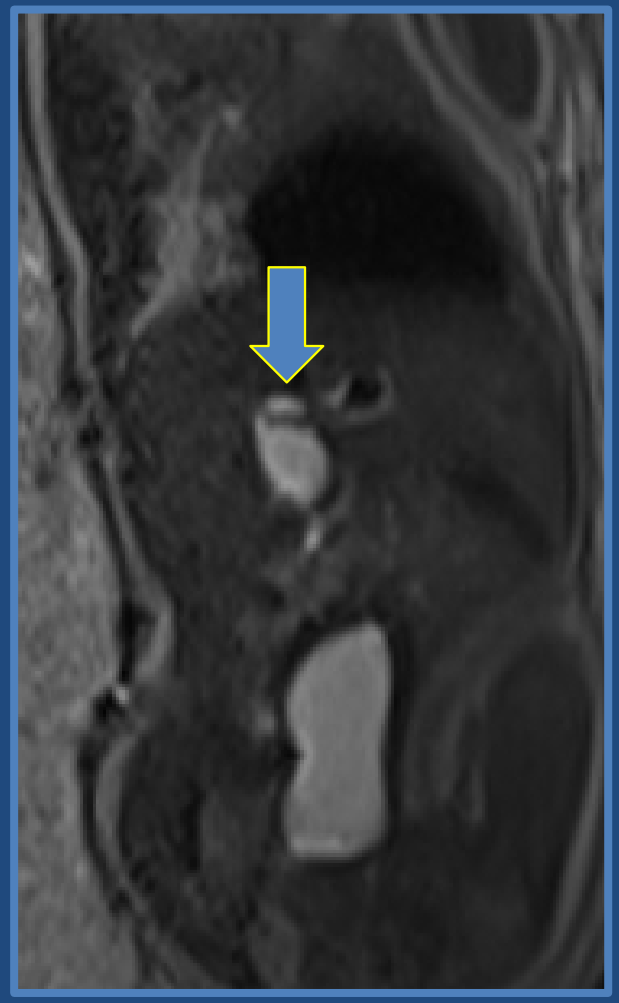


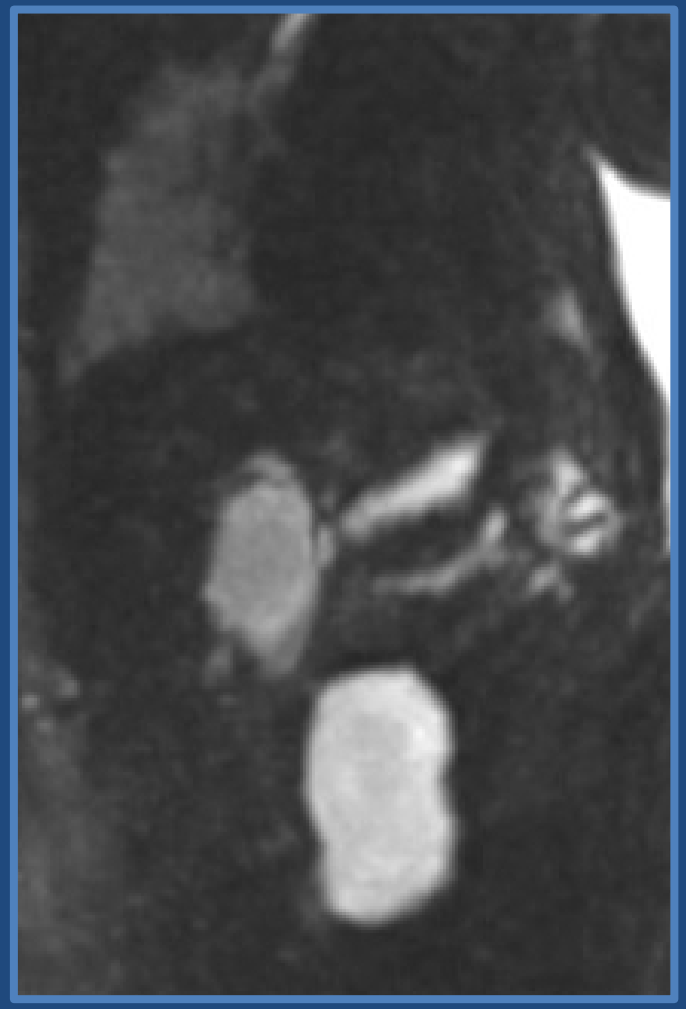
US GW 25+3
Increasing cyst + dilatation of left IH bilary ducts suggesting choledochal cyst



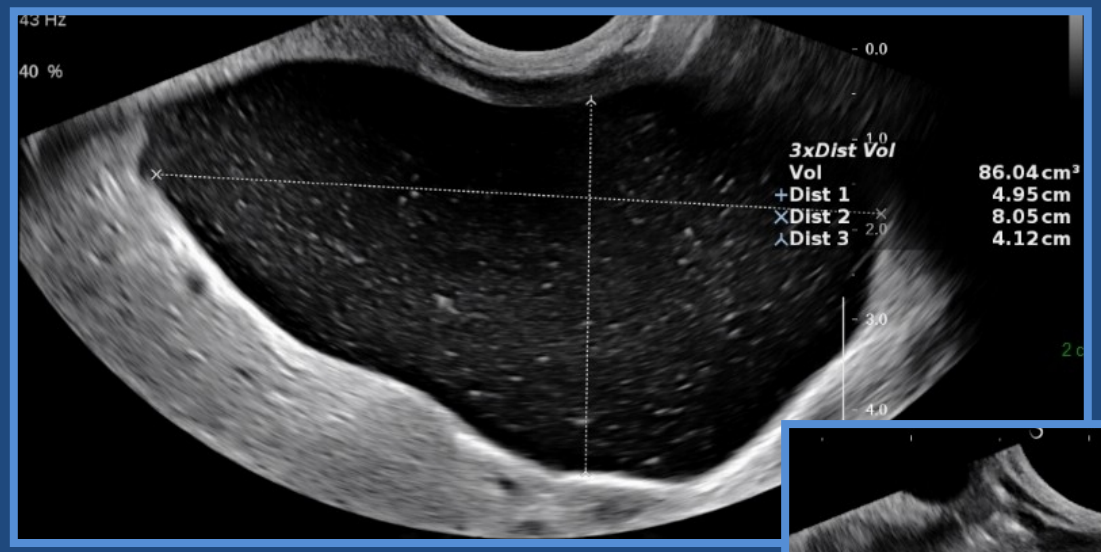


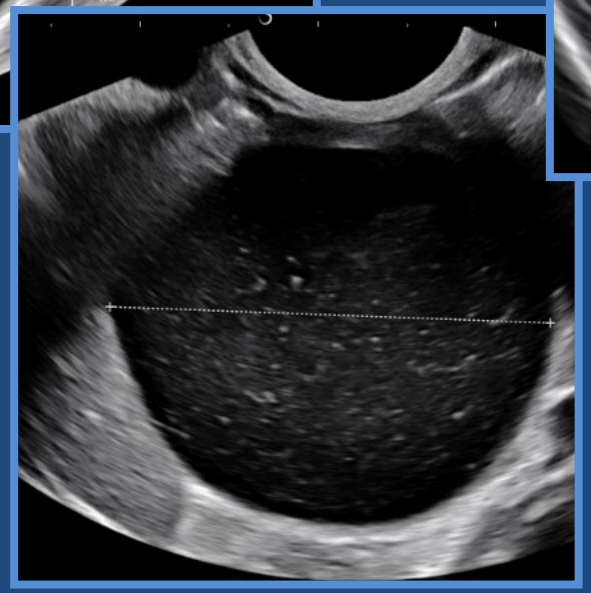
Fetal MR imaging in favour of CC

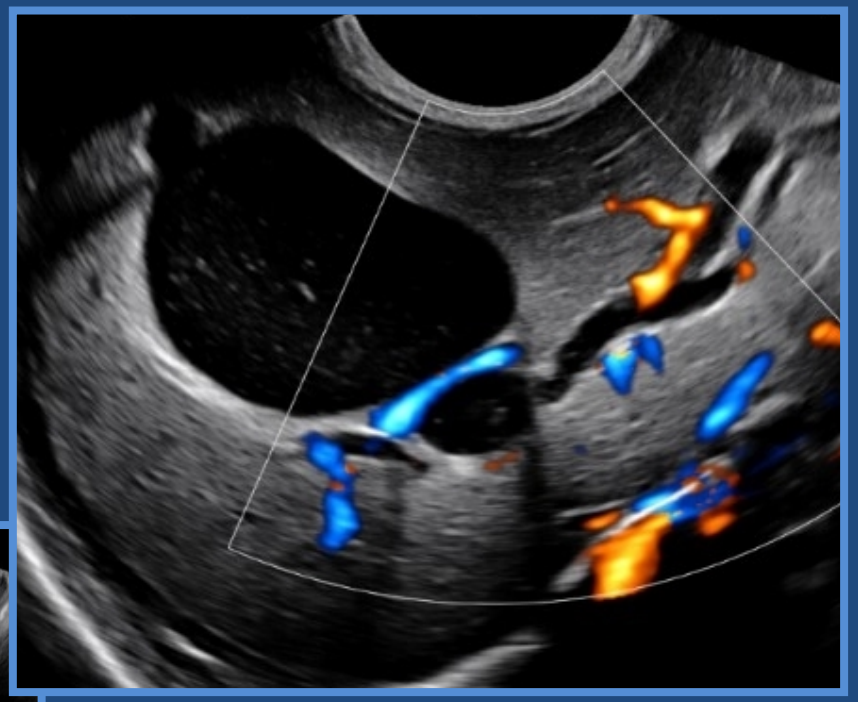




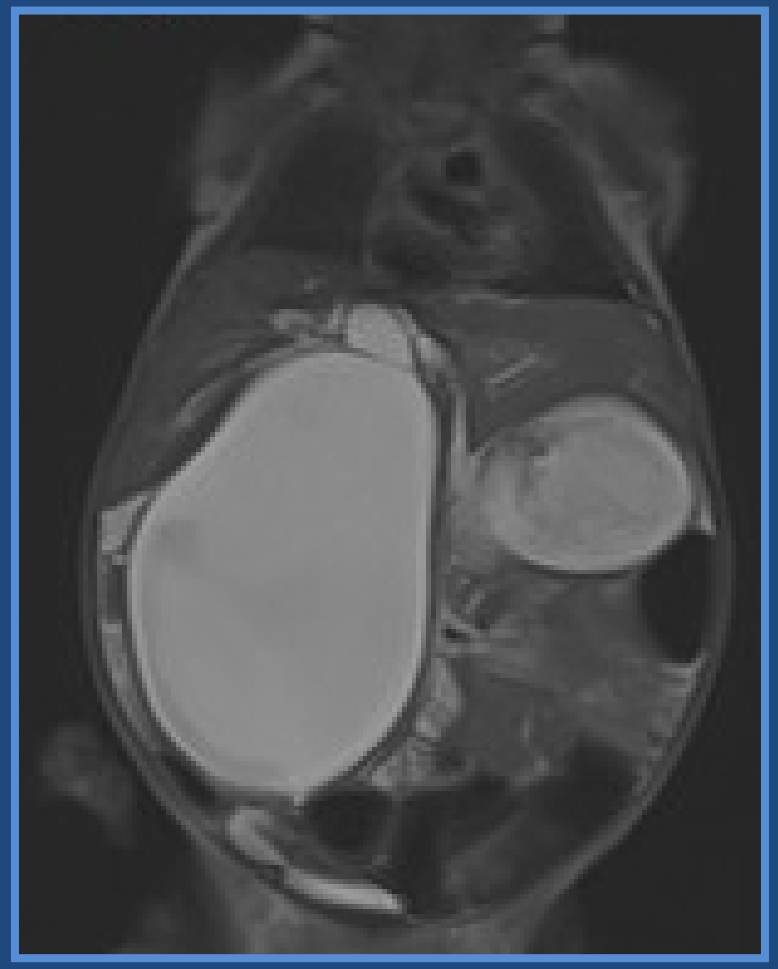
US at day 1: cystic dilatation of the common bile duct + left IHBD

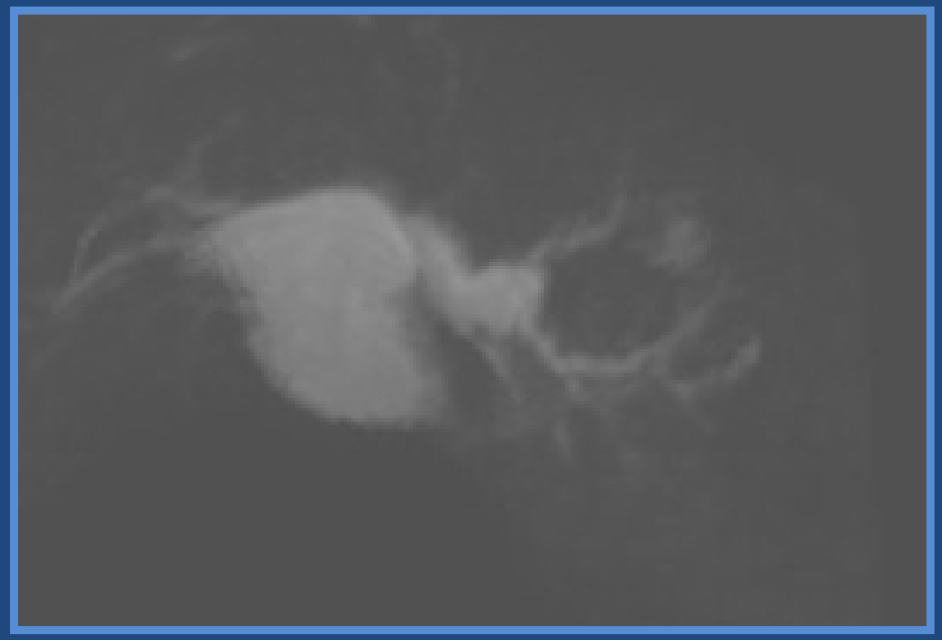






Neonatal MR cholangiography





Confirming the diagnosis of choledochal cyst ➔ surgery

DDx in utero: Biliary atresia (BA) vs Choledochal cyst

- The best differential feature would be the demonstration of intrahepatic bile ducts dilatation, connected with the hilar cyst favouring CC
- Large GB with irregular walls (with or without hilar cyst) would favour BA
- Polymalformative syndrome would favour BA

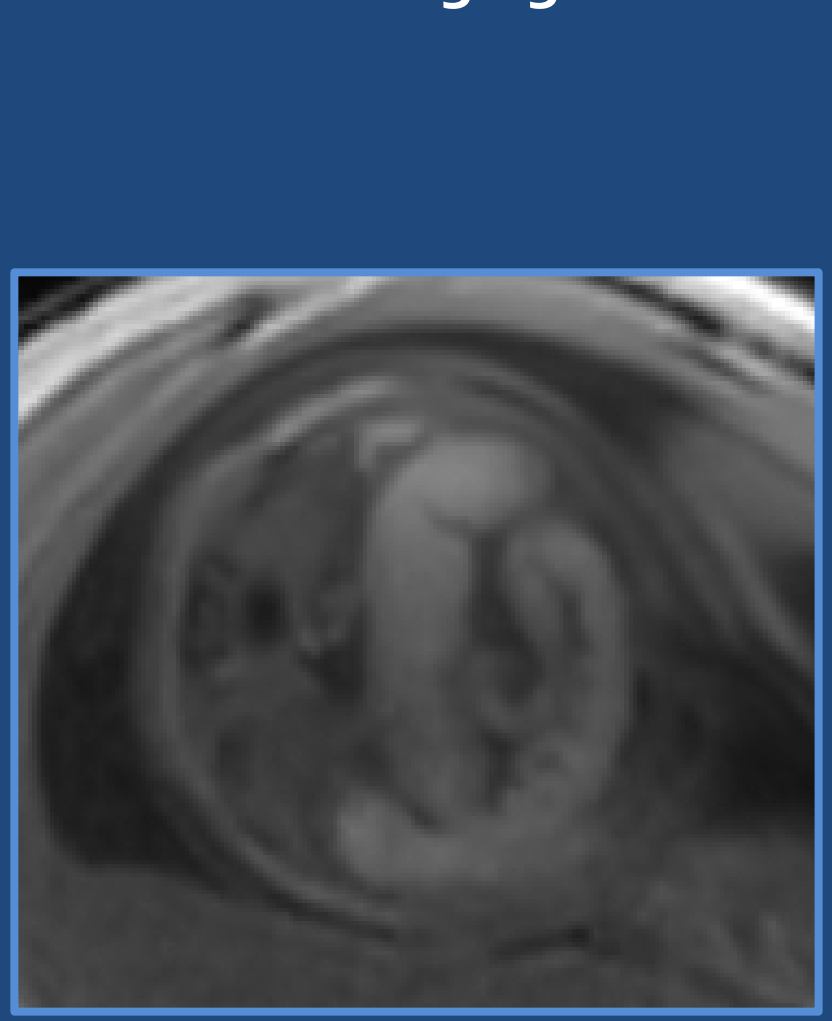
Ultrasonography 2022;41:140-149
Ultrasonography 2021;40:301-311

Syndromic biliary atresia

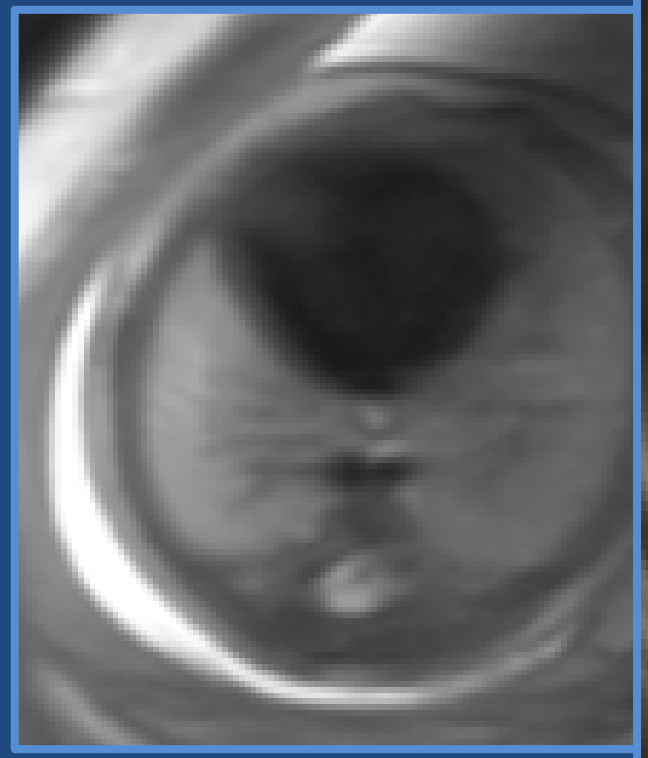
- **Syndromic (fetal or embryonic) form of BA includes various congenital anomalies:**
  - ***polysplenia, asplenia***, cardiac defects**, *situs inversus***, ***pre-duodenal portal vein***, absence of retro-hepatic inferior vena cava, ***intestinal malrotation***, annular pancreas, Kartagener's syndrome, duodenal atresia, esophageal atresia, polycystic kidney, cleft palate and jejunal atresia.
- **Represents 11 to 15% of cases of biliary atresia**

J Neonat surg 2014; 3(1): 9

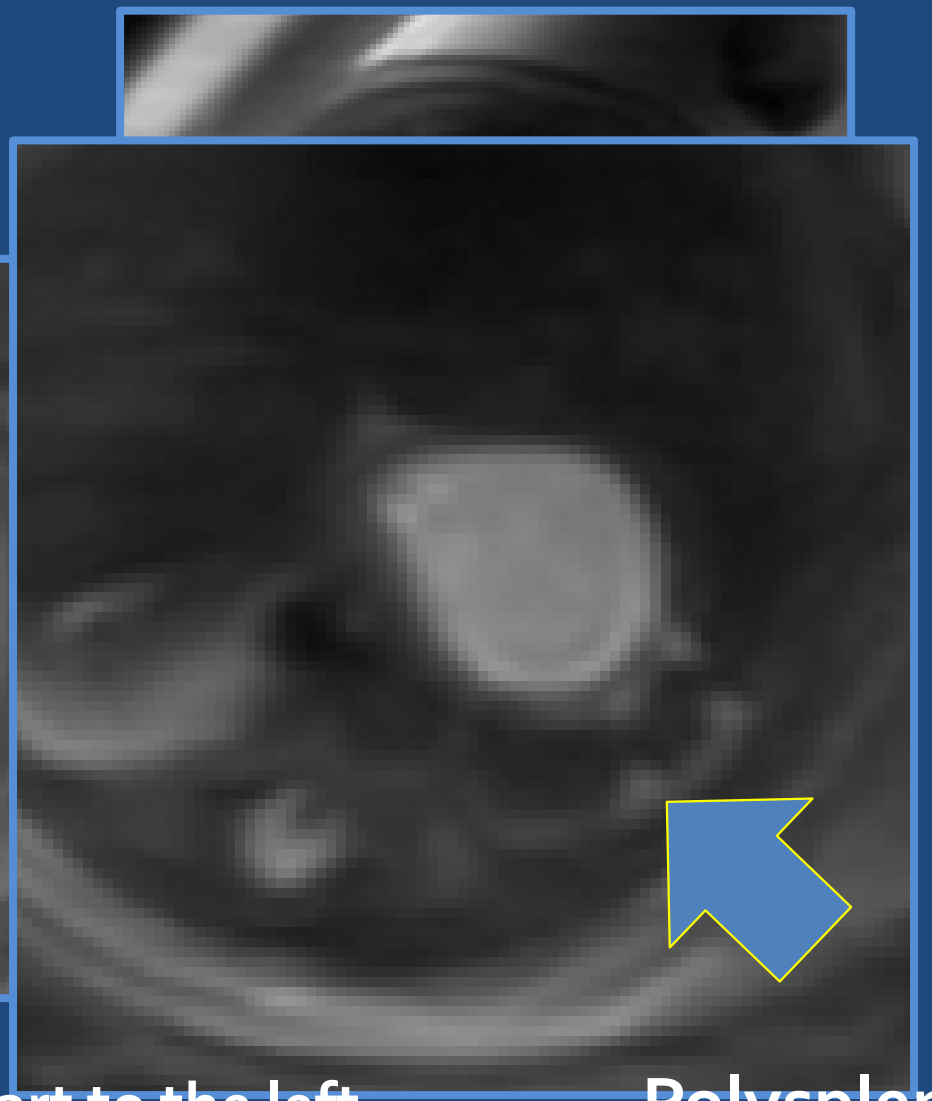
Fetal MR imaging at 26WG – US had shown intestinal obstruction



Volvulus

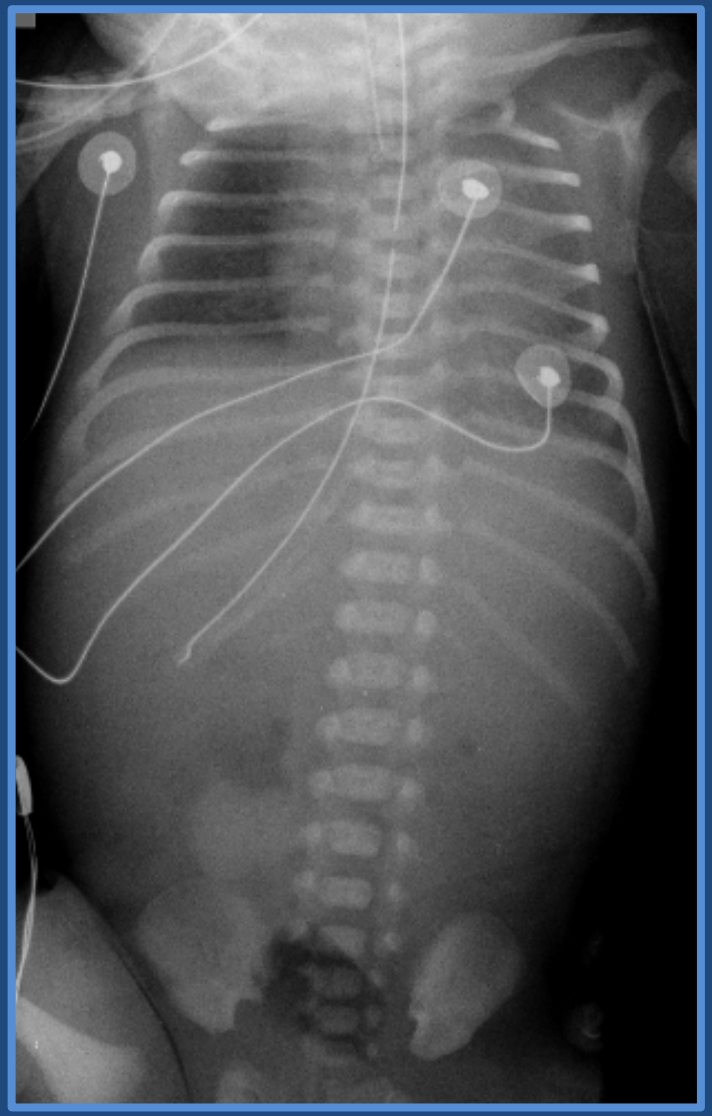


liver and heart to the left



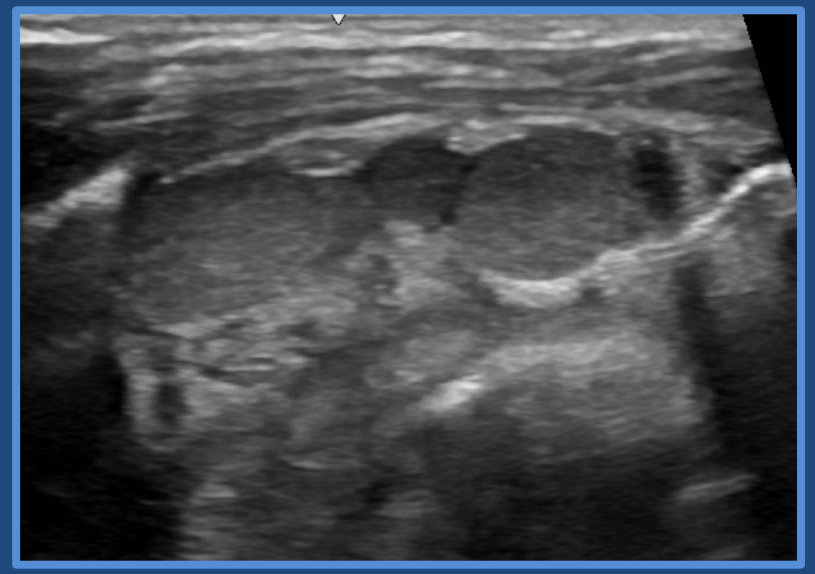
Polysplenia

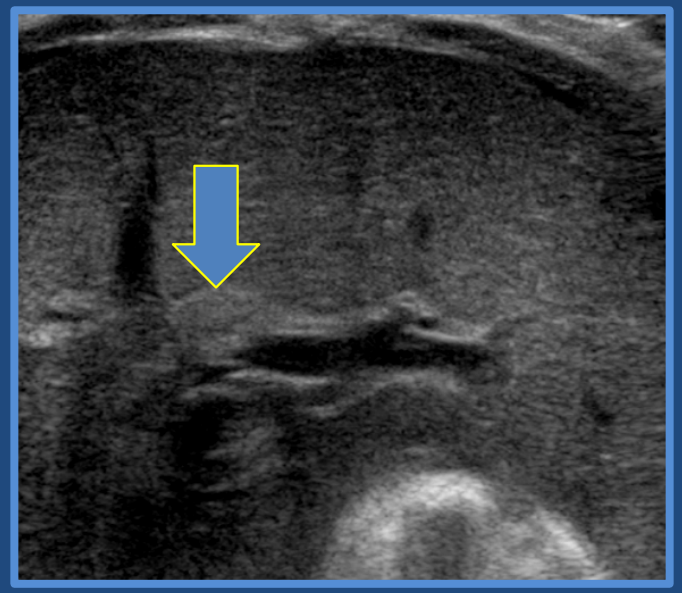
Birth at 26weeks 2days
Volvulus confirmed ➔ surgical cure

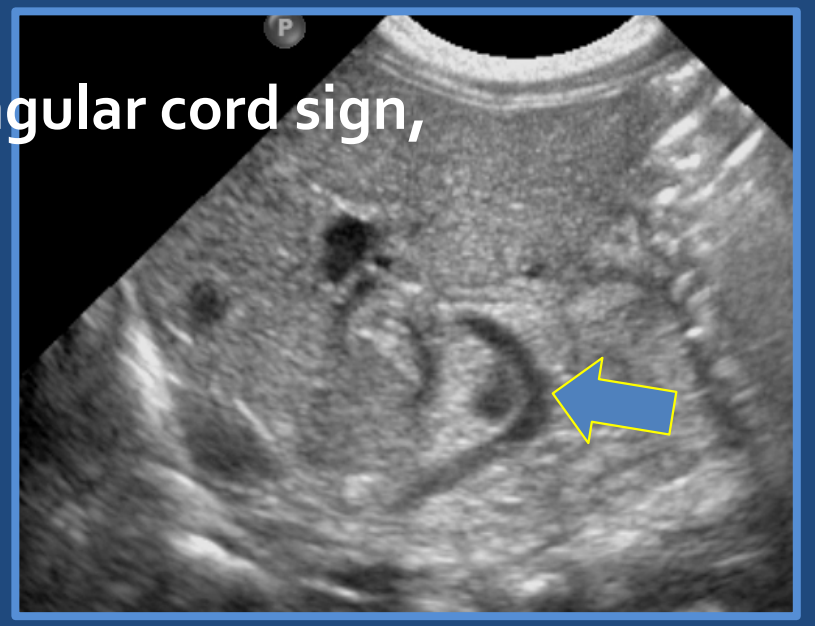


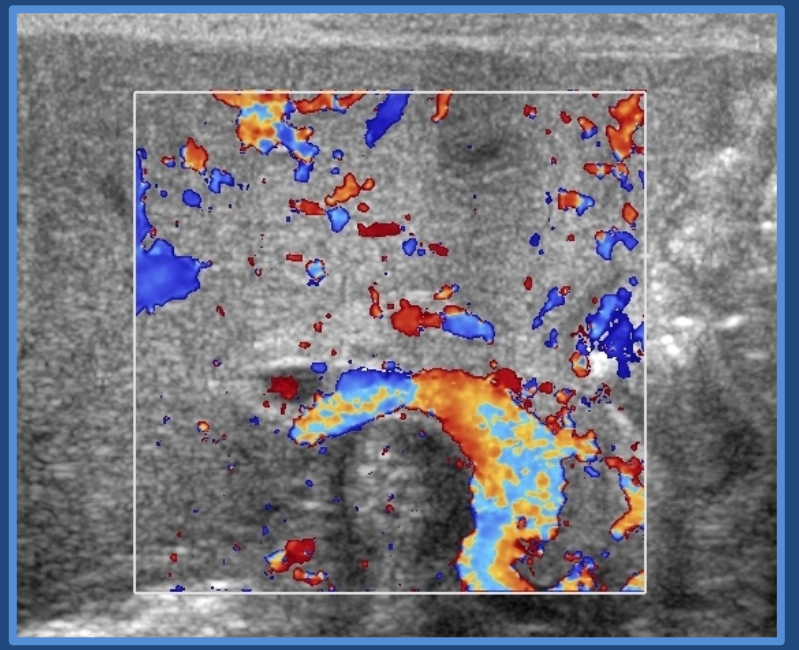
Post operative follow-up, first ok. Thereafter the patient developed progressive jaundice

Abdominal ultrasound at day 21: polysplenia, triangular cord sign, Pre-duodenal portal vein ➔ syndromic BA



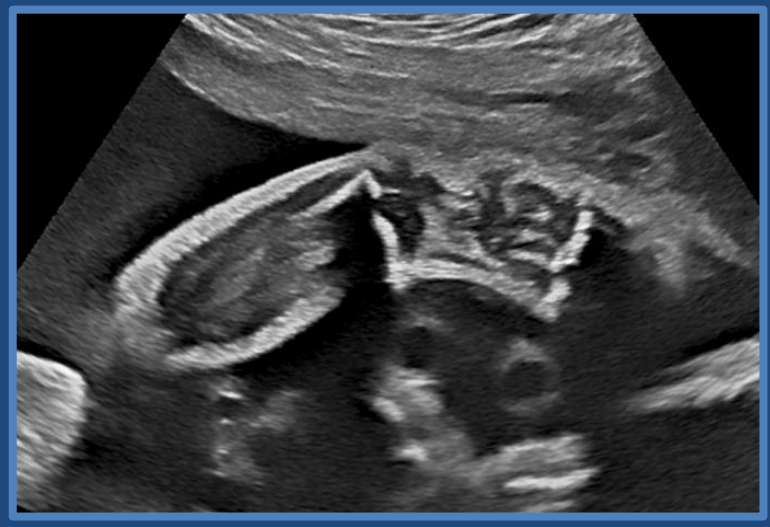


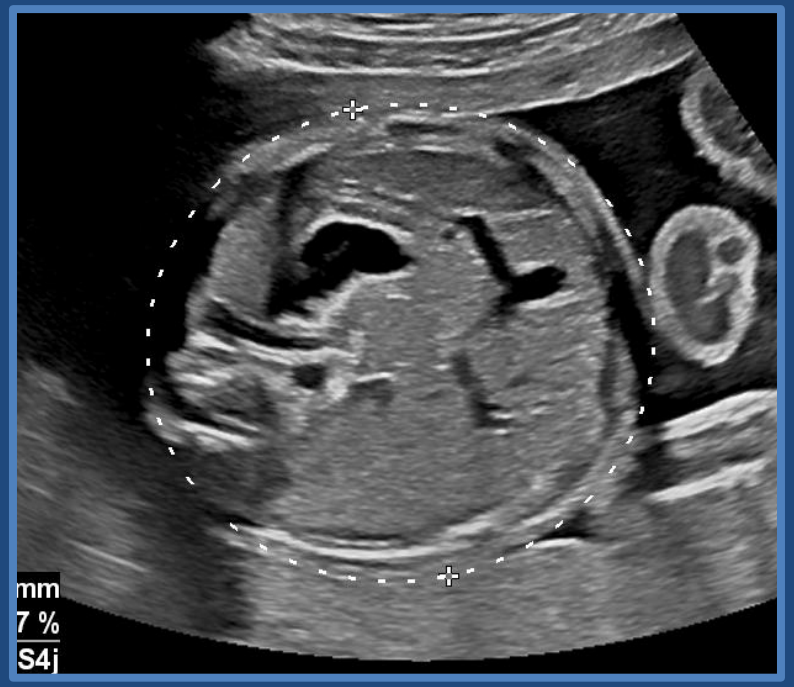




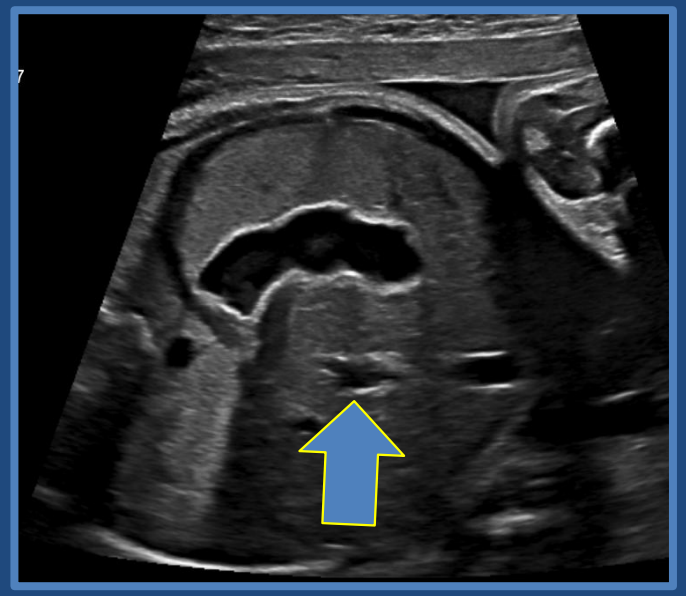
27 WG 4d
Refered after a diagnosis of Tetralogy of Fallot

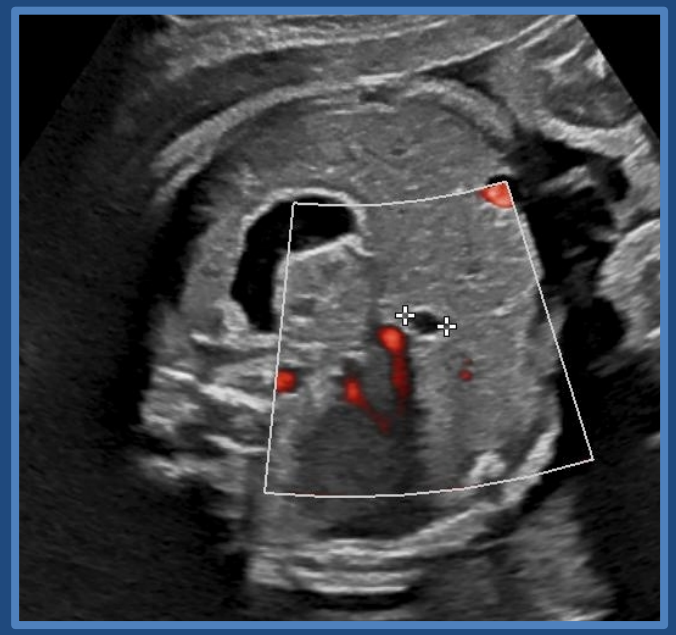
Confirmation of the cardiopathy
fGB not visualized
Club feet
(Courtesy of P Bach (F))

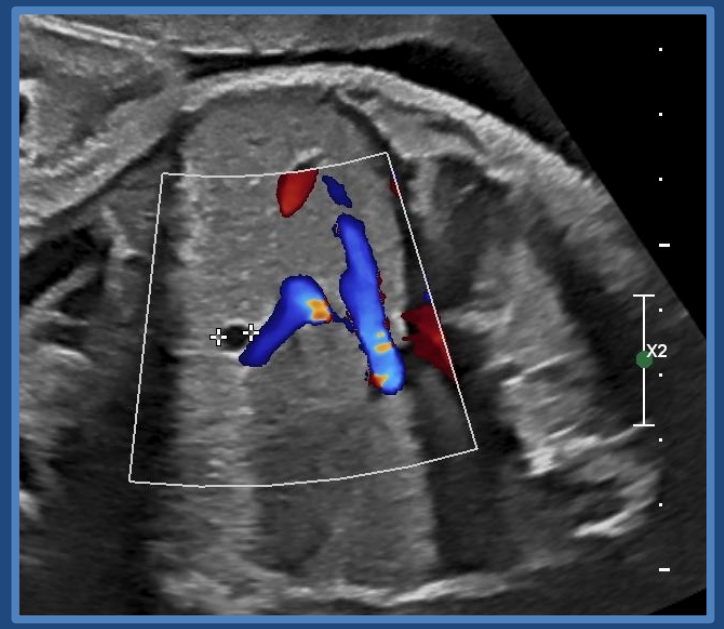




31 WG 4d
fGB not visualized
Hilar microcyst
Club feet
Growth 3^{d} percentile







Fallot and biliary atresia confirmed at histology

Biliary atresia (BA)

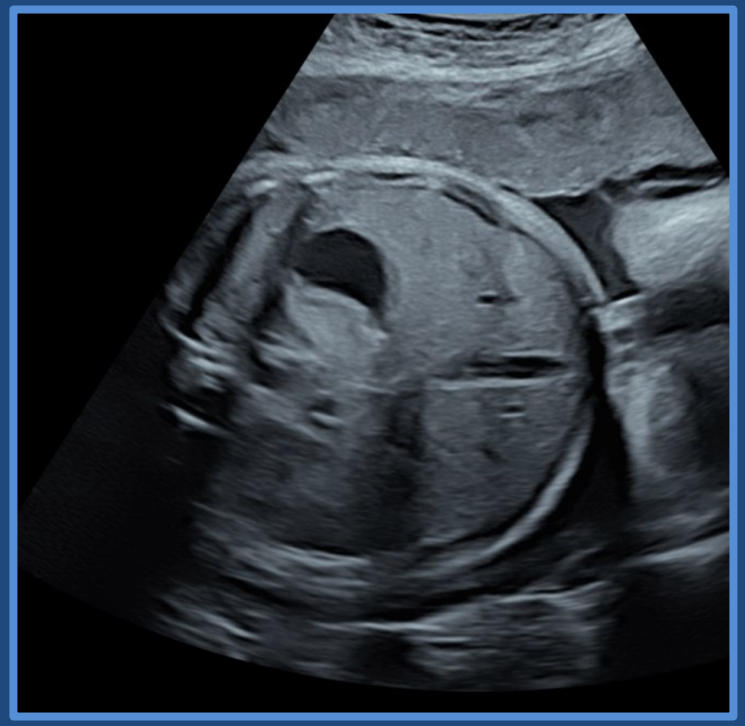
- Prenatal US may suspect BA
- Fetal MRI can provide additional information in case of US suspicion of biliary atresia (cystic type, syndromic type…, DDx)
- Any prenatal suspicion should lead to early postnatal biological, clinical and scintigraphic work up
- Early postnatal US ++, looking for:
  - GB anomalies
  - Hyperechoic cord sign
  - Hepatic artery
  - Associated malformations
- Dx → Earlier Kasai procedure, better prognosis

To summarize:
Non visualization of the fGB (during the 2nd trimester)

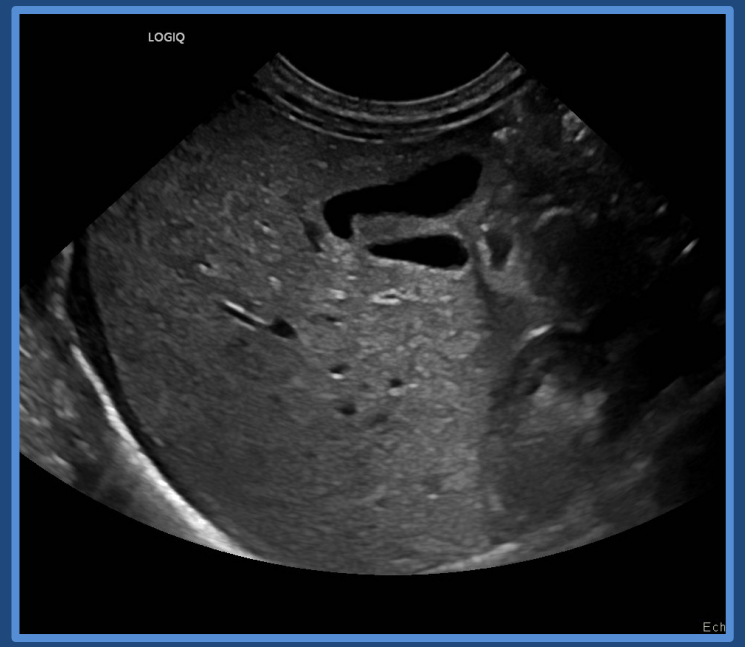
1. *Technical and anatomical causes*
2. *« Collapsed » fGB*
3. *Abnormal content shading the fGB*
4. *Congenital agenesis of the GB*
5. *Cystic fibrosis*
6. *Biliary atresia*

! In the majority of cases, transient finding, a fGB will be demonstrated subsequently in the majority of cases!

Non visualization of the fGB during the 2nd/3rd trimester ➔ postnatal US!



3rd trimester

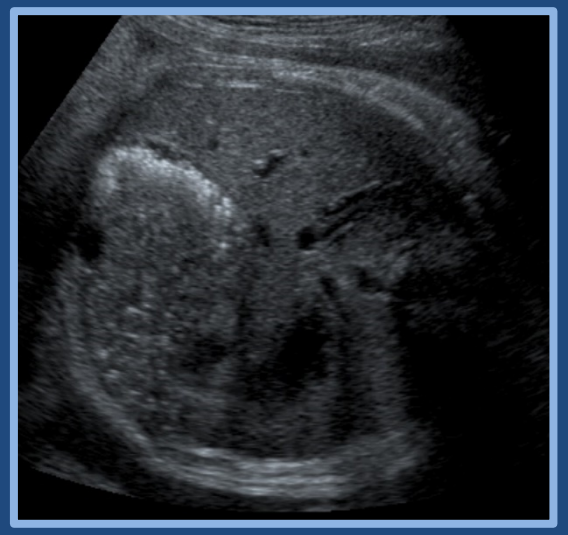


Day 1

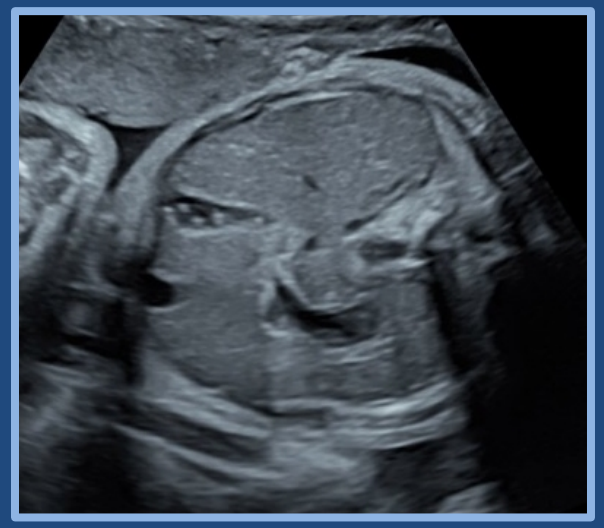
fGB
What else?
Abnormal GB content

- Echogenic material as diffuse homogeneous or inhomogeneous dense material in the fGB during the 3d trimester
- 0.5% pregnancies
- Origin? (maternal diabetes, twins, immaturity,…?)
- Spontaneous resolution in most cases
- Pre-lithiasis condition in some patients?
- Postnatal US to reassure

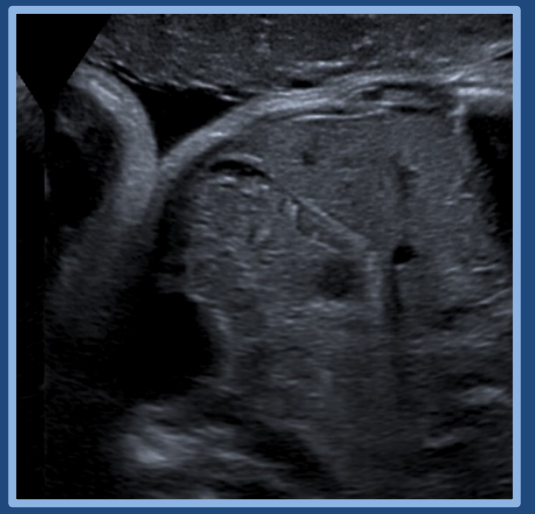
J Matern Fetal Neonatal Med. 2020; 33:1162-1170



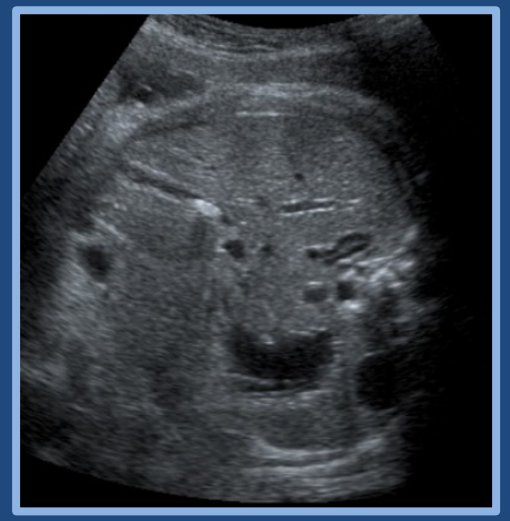
37 WG

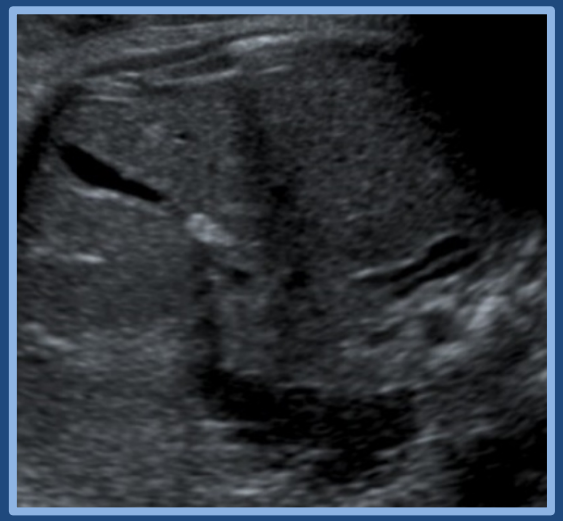


32 WG



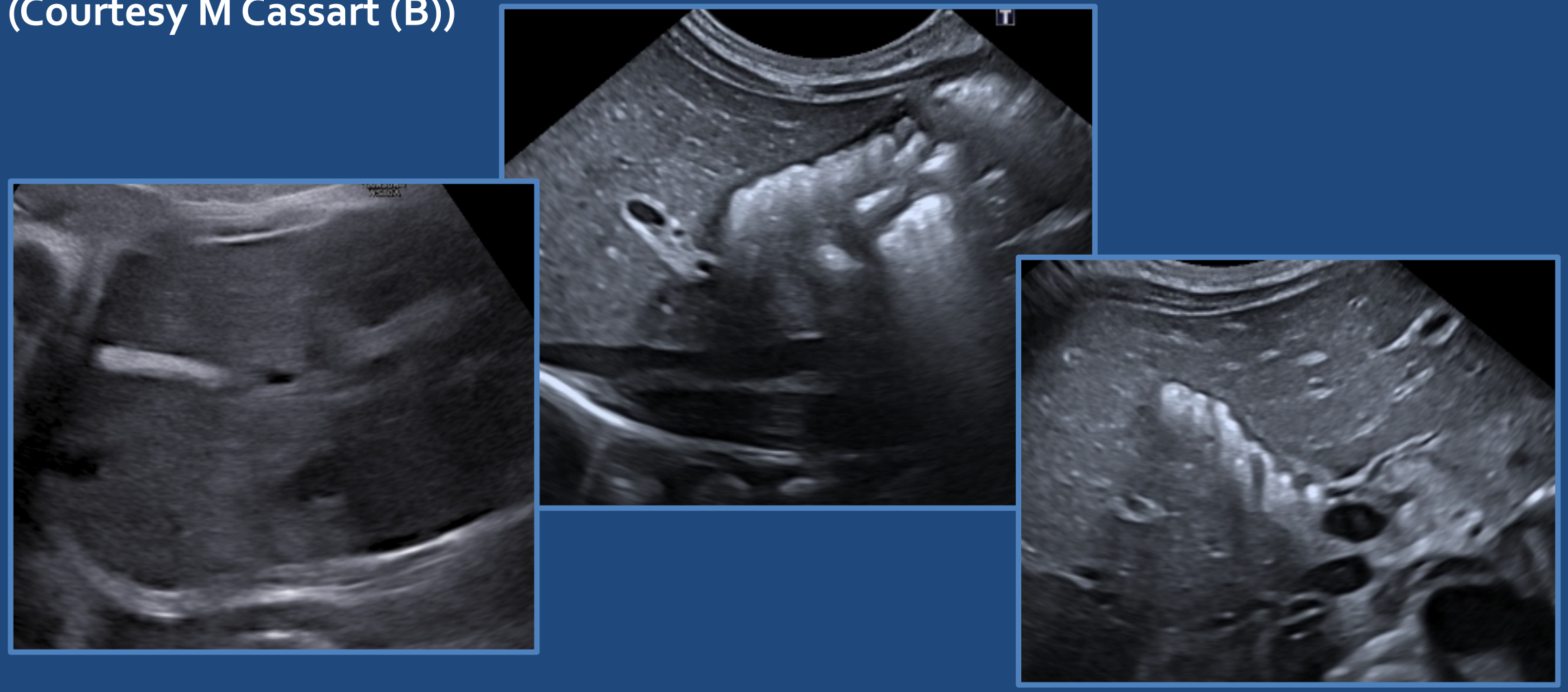
35 WG –
refered for non visualization of the fGB

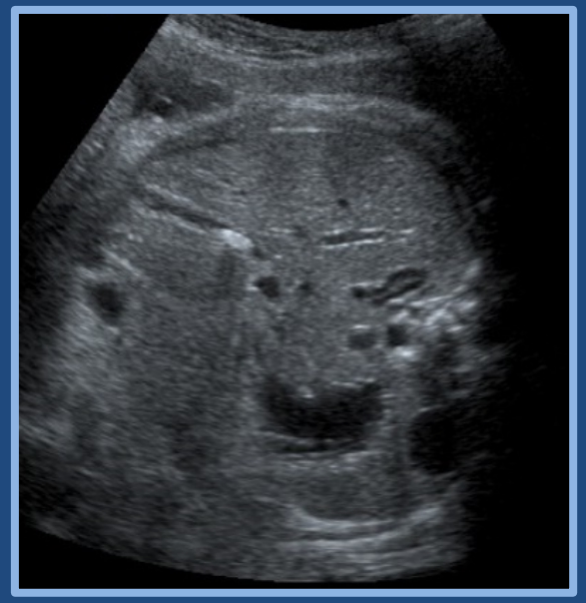


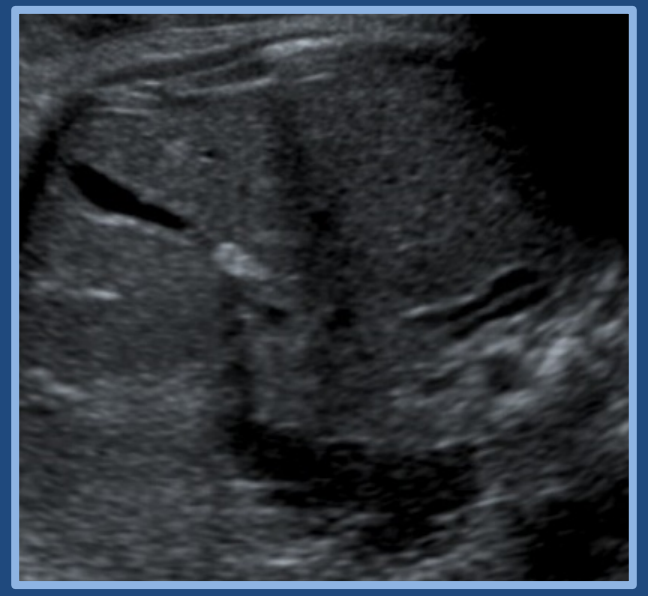


37 WG: fGB « lithiasis »?

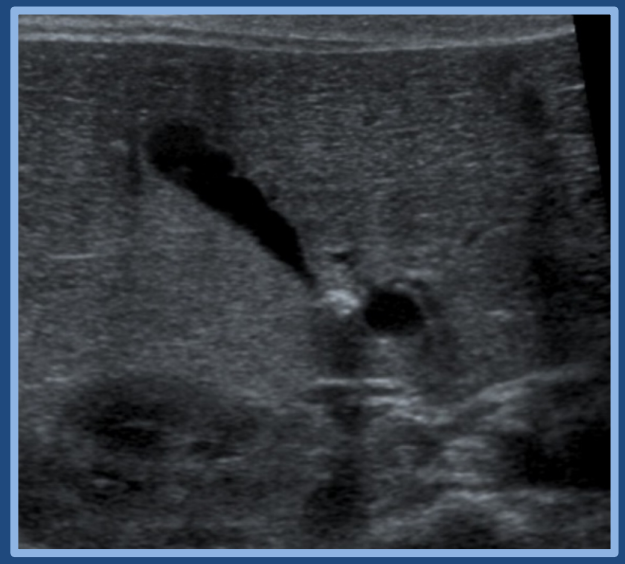
fGB sludge:
pre- and postnatal correlation
(Courtesy M Cassart (B))





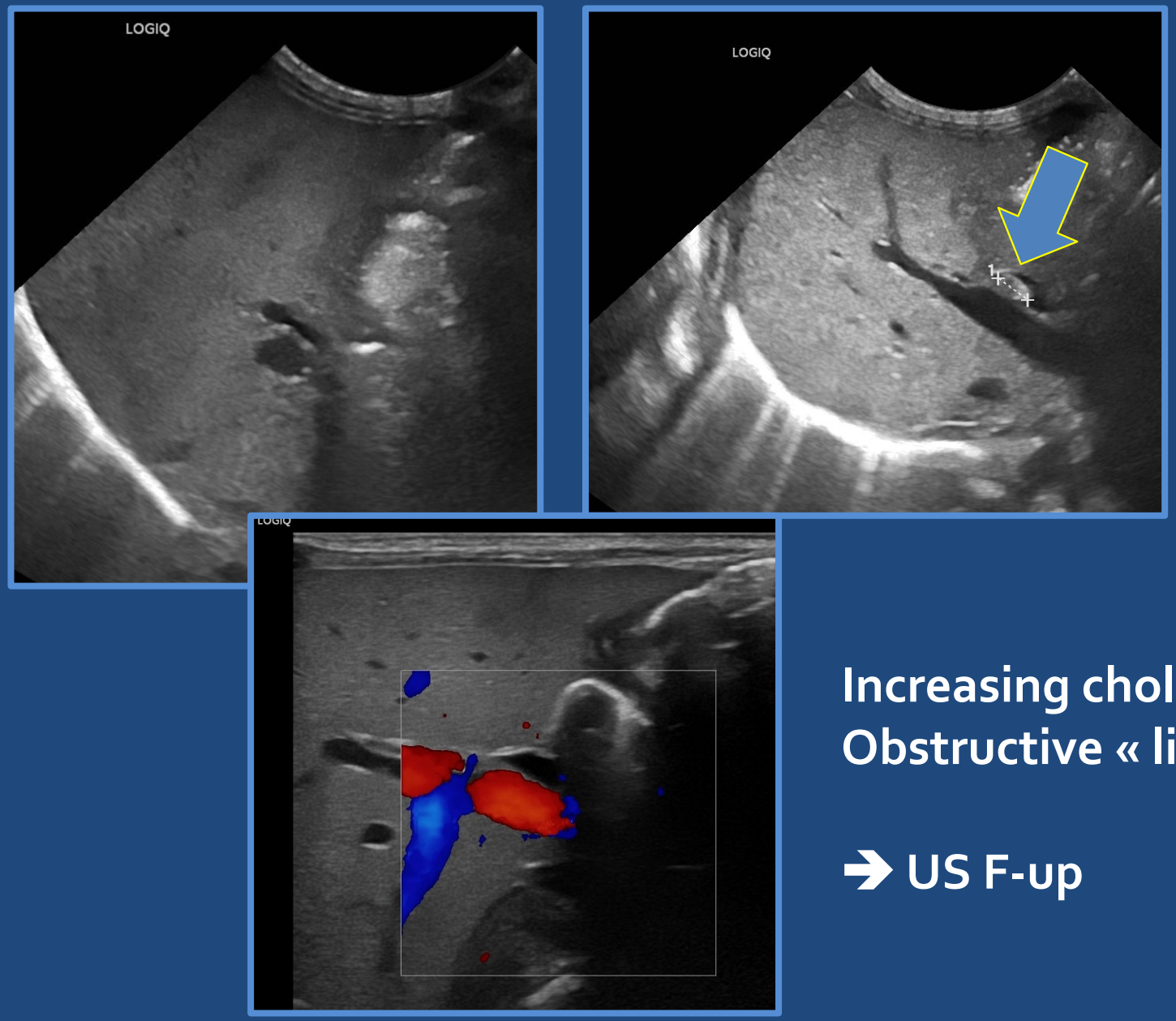


37 WG: fGB « lithiasis »



Persisting at day 30…, asymptomatic

Abnormal GB content :
Postnatal f-up?



Increasing cholestasis: Obstructive « lithiasis »

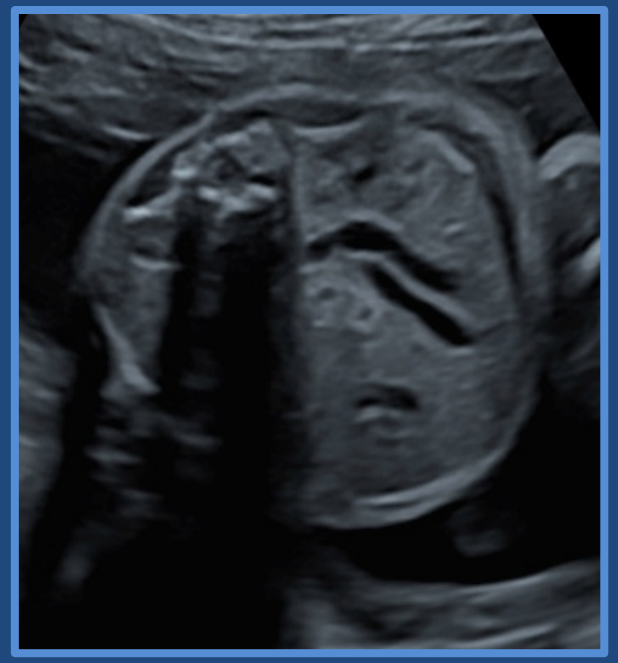
➔ **US F-up**

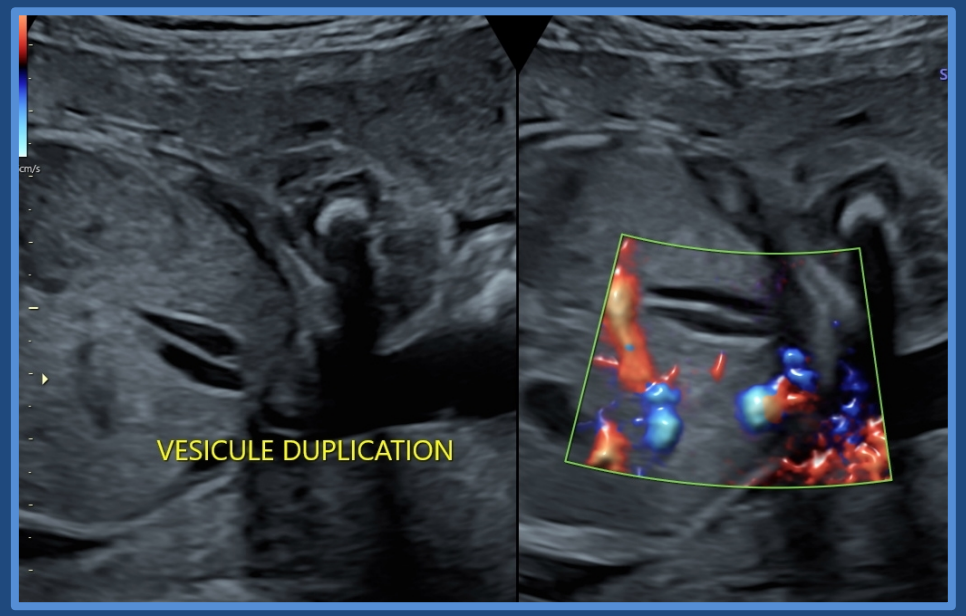
What else ?

GB DUPLICATION

- 1/4000 life births
- Two fGB parallel each to another
- Rare complications
- US follow-up

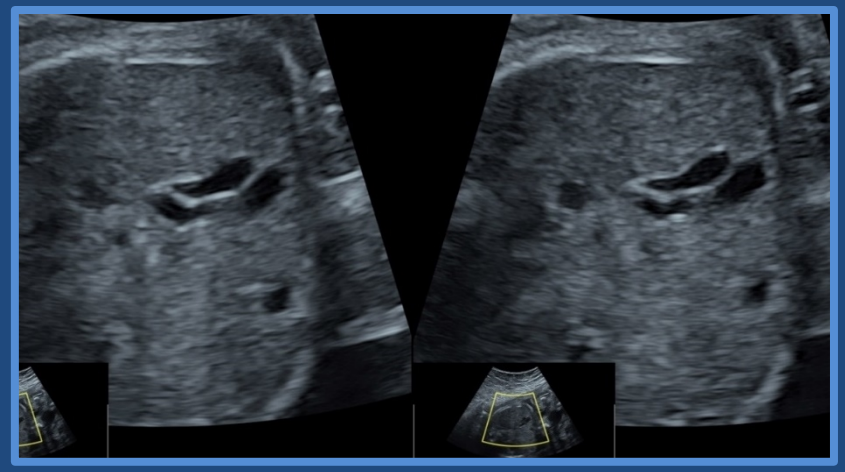
Arch Gynecol obstet 2020; 302; 377-382

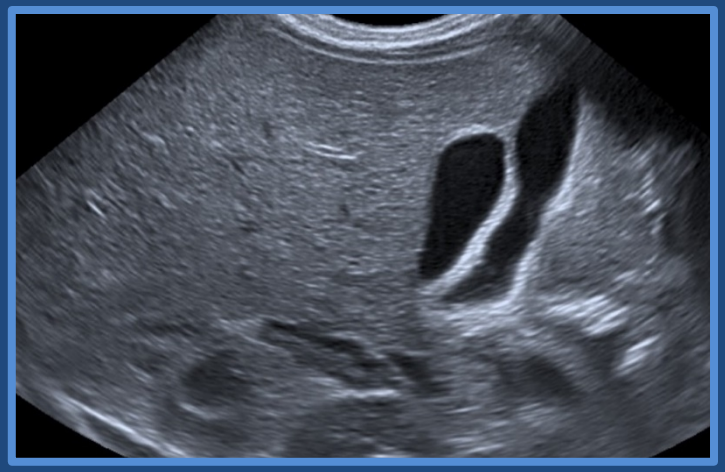




GB duplication

Courtesy G Levy (F)

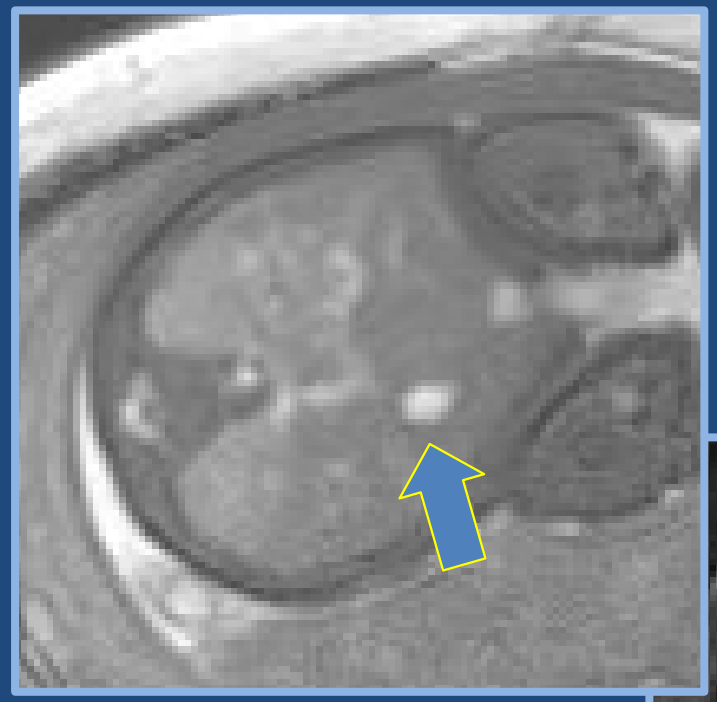


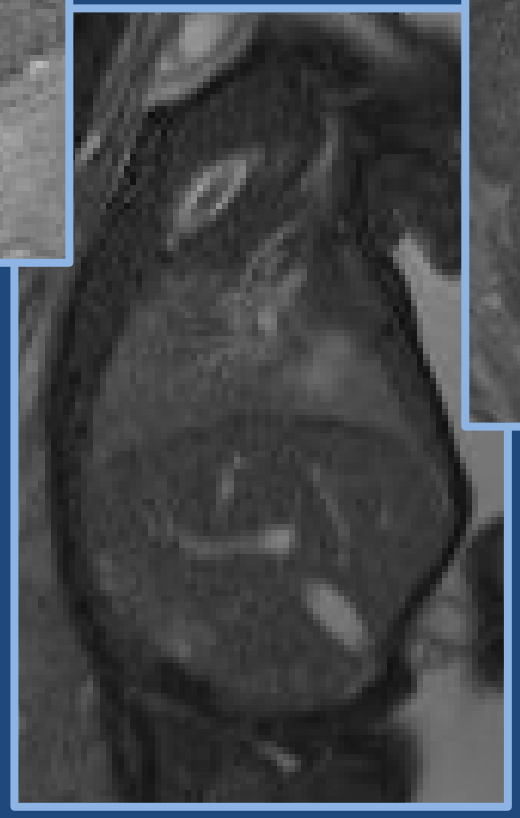


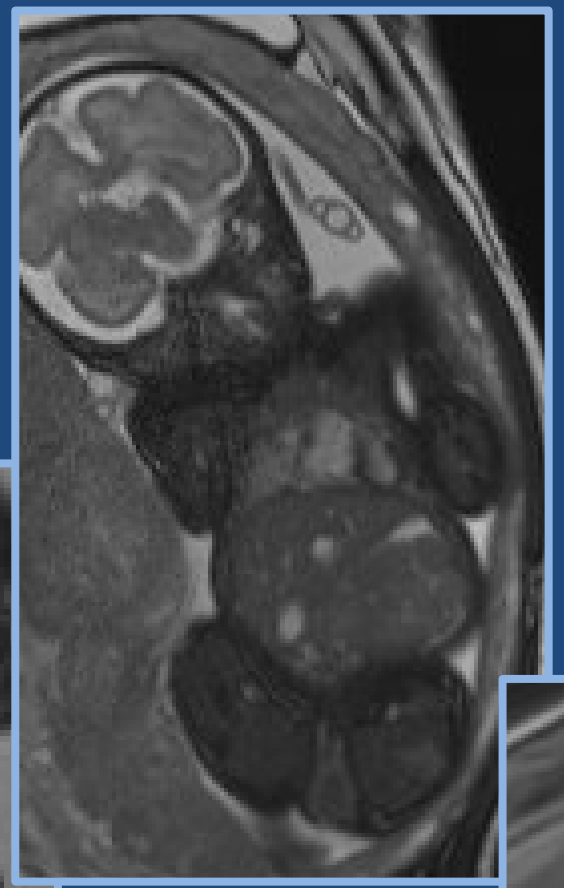
Pre- and postnatal F-up

fGB and MR imaging ?

- **Normal MR imaging findings**
  - The classical: GB content → hyperintense on T2 ws , hypointense on T1 ws

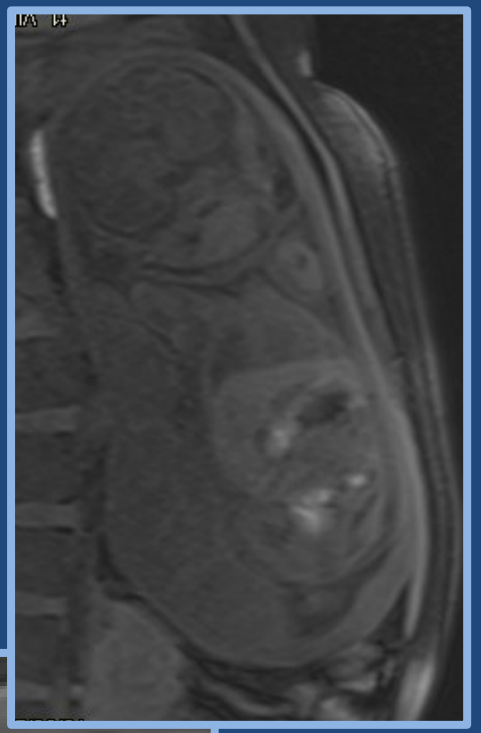


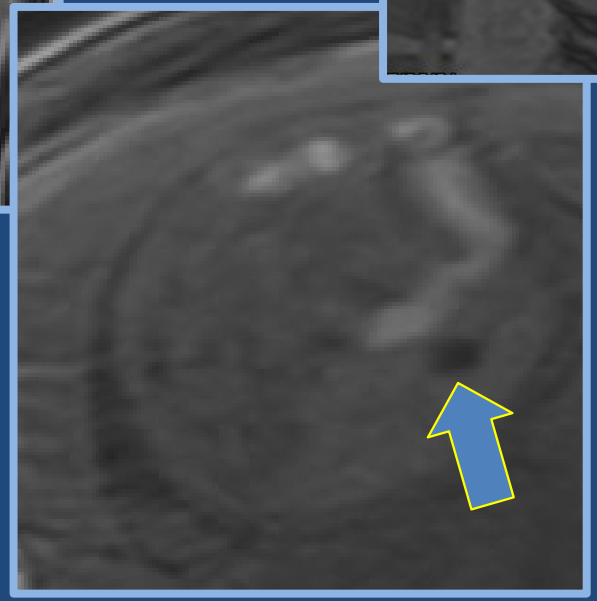




T2 WS

T1 WS

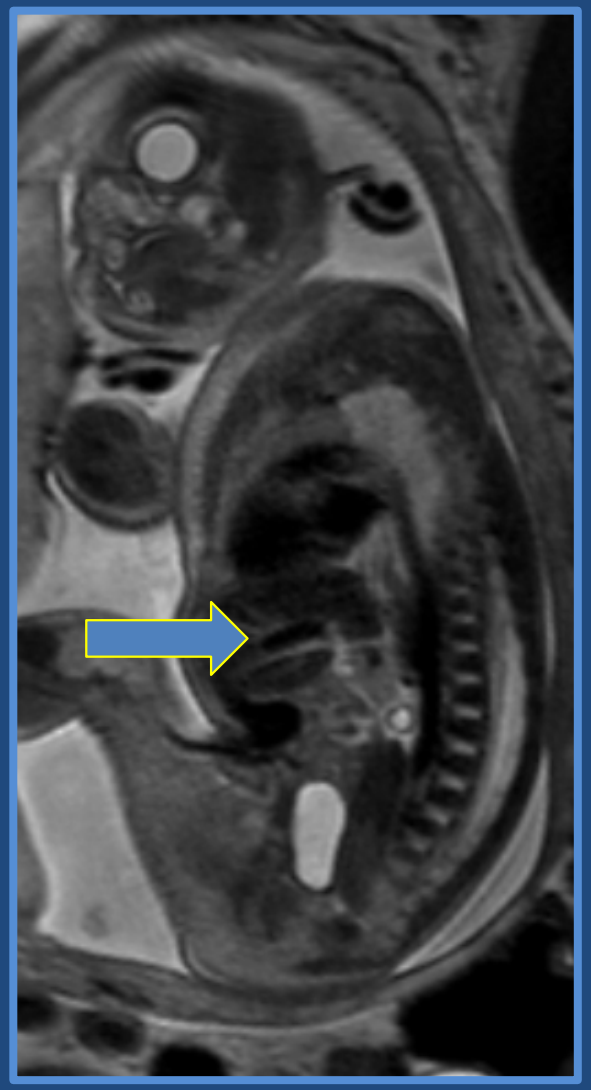


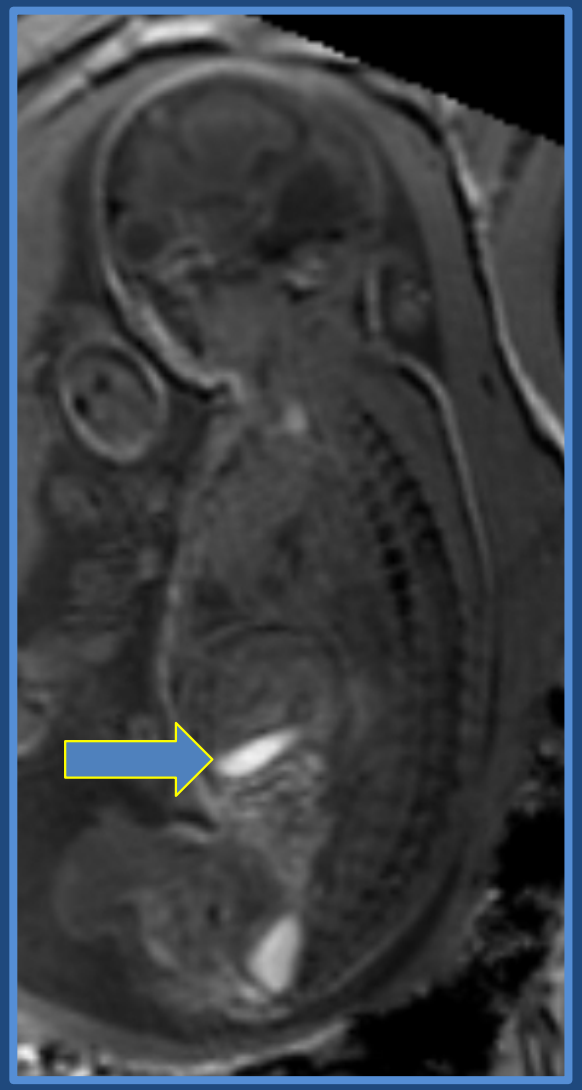


fGB and MR imaging

- **Normal MR imaging findings**
  - Can be hypersignal on T1 WS during the 3d trimester , origin unknown (< sludge?)

fGB not visualized on US (courtesy M Cassart (B))





<u>fGB anomalies</u>: What indications for fetal MR imaging?

- Non visualization of the fetal GB (?): *controversial*
- **DDx of hepatic hilar cystic masses ++**
- **Polymalformative syndromes ++**

fGB: Pre- and postnatal correlations

- A meticulous postnatal hepato-biliary US should always be performed after birth in any prenatal suspicion of GB (or biliary tract) anomaly (*US pre- and post meal if necessary*).
- Follow-up by US in unresolved case
- In few specific cases, postnatal MR imaging may provide additional information (i.e differentiating biliary atresia from a choledochal cyst)
- Findings to be correlated with clinical and biological data

Aknowledgment

This course has been made possible thanks to the helpful contributions of members of the GRRIF (Groupe **de** **R**echerche **en** **R**adiopédiatrie **et** **I**magerie **F**œtale**)**