Non-visualization of the fetal gallbladder – Can the level of amniotic fluid digestive enzymes predict fetal prognosis?
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Objective
The role of amniotic fluid digestive enzymes, specifically Gamma-Glutamyl Transpeptidase (GGT), as part of the workup, in cases of non-visualization of the fetal gallbladder is controversial. Thus, we aimed to determine whether amniotic fluid GGT can distinguish normal development or benign gallbladder agenesis from severe disease.

Methods
A retrospective cohort study between 2005 and 2012 in a single tertiary center was conducted. Pregnancies in which gallbladder was not visualized in the 2nd trimester anatomy scan were identified. Amniotic fluid GGT was analyzed prior to 22 weeks of gestation by amniocentesis. In all cases data regarding other fetal malformations, fetal karyotype and screening result for CFTR gene mutations were collected. Severe neonatal disease included mainly biliary duct atresia (BA) cystic fibrosis (CF) whereas healthy newborn considered as either normal gallbladder subsequently detected or isolated gallbladder agenesis.

Results
Overall, 31 cases of non-visualization of the fetal gallbladder were detected, 27 of which with normal values of GGT in amniotic fluid and four (13%) had low levels of GGT. In 30/31 patients both karyotype and CFTR gene screening were found normal, in 3 out of the four cases with low levels of GGT had additional findings subsequently terminating pregnancy (two with BA, one with severe gastrointestinal anomaly). The 4th case was later diagnosed with gallbladder agenesis. Among the entire cohort of 31 cases, in 22 (71%) gallbladder was subsequently detected.

Conclusion
Our data shows that non-visualization of the fetal gallbladder concomitant with abnormally low levels of GGT in amniotic fluid might be an ominous sign for severe disease while isolated NVFGB with normal levels of GGT carries good prognosis.