SRYAHWA PUBLICATIONS

Archives of Gastroenterology and Hepatology
ISSN: 2639-1813 | Volume 7, Issue 1, 2025
https://doi.org/10.22259/2639-1813.0701003

CASE REPORT

Two Case Reports of an Abnormally High Alkaline Phosphatase in Pregnancy

Mohammed Ali Hasabalrasoul[1], Rita Awal[2], Cliffort Kiat[3]

[1,3]Department of gastrornterology and hepatology-Cork University Hospital –Ireland.
[2]Matenity Hospital-Cork-Ireland.

Received: 02 June 2025 Accepted: 18 June 2025 Published: 01 July 2025

Corresponding Author: Mohammed Ali Hasabalrasoul, Department of gastrornterology and hepatology-Cork University Hospital–Ireland.

Abstract

Alkaline phosphatases are enzymes that can be released by liver, bile ducts, intestine, bone, kidney, placenta, and leukocytes .The normal range in adults is between 85 and 110 IU/L .During pregnancy and due to placental contribution and fetal growth the ALP can increase by 2 folds. Here we describe two case reports of very high ALP during pregnancy where the level jumped upto 20 folds .In both situations the level fell to normal post delivery . The first lady was a 33 year old Her routine blood by her doctor at 34 weeks of gestation showed an ALP of 1336 which continued to rise to 2224 U/L at 37 ..The second lady was 34 year old who was admitted due to the fact that her routine GP blood showed ALP of 1884 which jumped to 2512 during her admission .Both patients were asymptomatic and were initially sent to hospital for further workup and,observation.The scans showed no hepatic or biliary tree abnormalities and all the non invasive liver screening was normal. Serial fetal growth scan for the first lady demonstrated fall of fetal growth and AFI at 3 6 weeks .yet she was delivered expectantly by caeserian section at 37 weeks and the product was a baby with good APGAR score.. Serial growth scan for the second lady showed a macrosomic baby and reduced AFI at 34 weeks of gestation .Patient attended the emergency department with reduced fetal movement at 34 weeks of gestation and was delivered by emmergency caeserian section. The outcome was a male baby with good APGAR score (9/10).In both situations the ALP isoenzymes pattern showed placenatal and bone isonenzyme only... Our cases demonstrate an extremely high level of ALP in the setting of normal pregnancy but reduced AFI and some placental abnormalities in histopathology.

Keywords: Alkaline Phosphatse (ALP), High Alkaline Phosphatse in Pregnancy, Placental ALP, Cholestatsis in Pregnancy, Case Report, Expectant Management, Pregnancy.

1. Introduction(Background)

Serum alkaline phosphatase mainly reflects the hepatic and bone isoforms; the intestinal form may account for 20 to 60% of the total after a fatty meal

Elevations in the serum alkaline phosphatase activity can be seen in cholestatic hepatobiliary disease, bone disorders like Paget disease, osteomalacia and bone metastases ALP can also be high during rapid bone growth in children, in the later stages of pregnancy, with chronic renal failure and, occasionally, in the presence of malignancy not involving bones or liver. The source of high ALP is usually clear but when it is not, fractionation techniques can distinguish hepatobiliary alkaline phosphatase from other forms(1).

Serum ALP levels higher than the reference range are normal in children and in pregnancy There is a substantial placental contribution to the alkaline phosphatase level late in pregnancy; the Regan isozyme, a variant that appears identical to the placental

Citation: Mohammed Ali Hasabalrasoul, Rita Awal, Cliffort Kiat. Two Case Reports of an Abnormally High Alkaline Phosphatase in Pregnancy. Archives of Gastroenterology and Hepatology. 2025;7(1): 13-16.

form, is associated with hepatocellular cancer , lung cancer , and other neoplasms.{1} placental ALP isozymes can be detected in the maternal serum by 15 to 26 weeks of pregnancy{2}.These isozymes are likely produced by syncytiotrophoblasts in the placenta and are theorized to play a role in transport across cell membranes and metabolism [2, 3].

An extremely elevated levels of ALP have not been reported much in the literature .Higher levels of ALP have been linked to low birth weight [4,5], intrauterine growth restriction [6], preterm delivery [7, 8], and hypertensive disorders of pregnancy [9]. It has been thought that ALP may be a marker of uteroplacental vascular disease [10}

We describe 2 case reports of extremely high ALP during pregnancy that proved to be placental and bony in origin .The pregnancy was complicated by reduced AFI and histological changes in placeta in both situations.

2. Case Presentation

Case 1 : A 33 years old , gravida 6 para 5 ,Body mass index (BMI) 35 kg /M2, was attending a low risk antenatal clinic for her routine prenatal care. She has no specific symptoms

She has no background history of note and significant family history.Her past pregnancies were unremarkable, with four vaginal deliveries and one lower segment caesarean section (LSCS) for breech presentation..She has o history of alcohol consumption, recent antibiotics,paracetamol ingestion,nonsteroidal anti-inflammatory drugs,intravenous drugs or herbal supplements . Clinical exam showed no peripheral stigmata of liver disease

Her routine booking blood test was unremarkable with normal oral glucose tolerance test (OGTT) at 28 weeks of gestation. Anatomy scan at 21 weeks of gestation was normal .

Her blood work up at 34 weeks of gestation showed elevated ALP of 1381 U/L. So her ALP was serially monitored ,which was gradually rising and reached a peak of 2224 U/L at 37 weeks of gestation.

Full blood count, kindnty function test, bilirubin, GGT,ALT were all normal.Her basic liver screening including hepatitis serology ,CMV,EBV were negative.The immunoglobulins , liver autoantibodies, iron studies were normal as well as Alpha 1 antritrypsin and caeruloplasmin. Her routine Covid swab test came back as positive for SARS Cov-2 RNA and ANA was also weak positive nucleolar pattern. The bile salt was normal at 2.6.

The ultrasound liver showed normal liver and hepatobilary system and the fetal scan showed single pregnancy with no fetal or placental abnormalities apart from some calcification

Serial fetal growth scan demonstrated fall of fetal growth from 34 % centile to 26.9 % centile at 36 weeks of gestation .The AFI was also low, 9 cm though the patient declined any history of leaking of amniotic fluid and per speculum examination was normal.

Mother was happy with fetal movement and umbilical artery doppler was normal.

She was managed expectantly and delivered by elective LSCS at 37/40 .

Placenta was sent for histopathology, showed mild to moderate distal villous immaturity and small intervillous thrombus.

Neonatal outcome : A male baby of 3.08 Kg was born with APGAR score of 9/10 but subsequently was diagnosed with pulmonary hypertension with moderate VSD and mild ASD . The ALP isoenzymes pattern showed 90% placenatal isonenzyme and 10% bone isonenzyme.Postpartum follow up : ALP returned to the level of 56 U/L at 8 weeks postpartum.

Case 2: A 34 years old , gravida 3 para 2 , BMI 34. 65 kg /M2 was attending a low risk antenatal clinic for her antenatal care. Her past obstetric history was uneventful with two vaginal deliveries.She did not give any significant family history.She did not have any medical condition and no history of alcohol consumption or substance misuse.

Her routine booking blood test was normal but subsequently diagnosed with gestational diabetes at 28 weeks of gestation. Anatomy scan at 21 weeks of gestation was normal. She had good glycemic control with dietary modification.

Her blood work up at 33 weeks of gestation showed raised ALP of 1068 U/L and reached to a level of 1336 U/L in a week time with normal bilirubin and other liver enzymes. He kidney function and FBC were normal. and the work up for a cause revealed normal immunoglobulins , viral markers, iron studies and liver autoantibodies l. Her liver US showed no hepatic or biliary abnormalities.

Serial growth scan showed a macrosomic baby, estimated fetal weight more than 99 % and reduced AFI from 16.97 cm to 10. 67 cm at 34 weeks of gestation.

Patient attended the emergency department with reduced fetal movement at 34 weeks of gestation and was delivered by Emergency LSCS (Category 1) for antenatal non reassuring CTG at 34 +4 weeks of gestation .

The histopathology of the placenta revealed placentomegaly with mild to moderate delayed villous maturation/distal villous immaturity with acute chorioamnionitis.It also showed. avascular ectasia of chrionuic plate and chronic plasma cell basal deciduitis.

Neonatal outcome : A male baby was born with a birth weight of 2.8 kg . APGAR score was 9/10 .

He has been admitted to SCBU for prematurity but had good neonatal recovery .

ALP electrophoresis revealed PALP 83 % and bone ALP 17 %.

Her ALP came down to 740 U/L immediately and returned to normal in 4 weeks.

3. Discussion

ALP is an endogenously produced enzyme that may be raised due to a number of pathologies namely HELLP syndrome , intrahepatic cholestasis , liver malignancy or bone disease[4]. As such, it is imperative that in cases with raised ALP, these aforementioned causes are firstly ruled out.

ALP can be classified into different isoenzymes according to the sites where they are produced. PALP is produced by syncytiotrophoblast and is heat stable[11].

Literature review and case control studies in regards to raised ALP during pregnancy were looked at to draw correlation between high serum levels and complications during pregnancy. Our literature review found several cases of raised ALP during pregnancy, few of them complicated by hypertension and preeclampsia [11].

Of the 8 cases of raised serum ALP reviewed, 4 cases showed normal pregnancy outcomes with no fetal or maternal complications.[12] Of the remaining 4 with recorded complications, the cases to note were one with pre eclamptic toxaemia and preterm labour and another one with IUGR which developed at 33 weeks of gestation with high resistance index of umbilical artery doppler (UAD) with intermittent absent end diastolic volume[13].

Furthermore, a case control control study was conducted by Rajagambeeram to investigate the correlation of pre-existing chronic hypertension and raised ALP during pregnancy in 60 pregnant patients. The results showed significantly raised ALP and PALP values in the hypertensive group (p value < 0.5)[14].

As outlined in the Case presentations above, Case 1 showed fall off fetal growth with reduced AFI but with normal umbilical artery doppler whereas with Case 2, the fetus was observed to be macrosomic but low AFI noted in the third trimester. In order to understand and correlate the deviations from normal fetal growth and development it is important to take into consideration the role of the placenta during pregnancy. The placenta plays an essential role in modulating foetal growth and placental dysfunction and pathology may cause IUGR, low AFI and abnormal UAD.

Given the findings above, the challenge is that we cannot categorically conclude whether the complications namely low AFI and IUGR can be singularly attributed to raised ALP or if this precipitates as a result of other factors and therefore need to be explored further.

4. Conclusion

The literature proposes that elevation of the placental isotype of ALP could be a marker for placental insufficiency, preterm delivery, or infants born large for gestational age. We report a case with delivery of a normal infant and no placental pathology at term.

While the select cases discussed above showed maternal and foetal complications in a small sample size, we cannot conclusively state correlation of a causative nature nor can we suggest that raised ALP be used as a biomarker for placental pathology. This will require a larger scale study of such cases to arrive at a definitive conclusion. From my experience however, I would suggest that in pregnant patients with raised ALP or a history of raised ALP, the fetus should be closely monitored by serial growth scan to avoid adverse outcomes.

5. Refrences

1. Lee Goldman MD, in Goldman-Cecil Medicine, 2020
2. A. Boronkai, N. G. Than, R. Magenheim et al., “Extremely high maternal alkaline phosphatase serum concentration with syncytiotrophoblastic origin,” Journal of Clinical Pathology, vol. 58, no. 1, pp. 72–76, 2005.4 View at: Publisher Site | Google Scholar
3. B. Ferro, I. Marques, J. Paixão, and M. D. C. Almeida, “Incidental finding of extreme elevation of serum

alkaline phosphatase in pregnancy," Cureus, vol. 13, no. 8, article e17211, 2021.View at: Publisher Site | Google Scholar

4. R. G. Best, R. E. Meyer, and C. F. Shipley, "Maternal serum placental alkaline phosphatase as a marker for low birth weight: results of a pilot study," Southern Medical Journal, vol. 84, no. 6, pp. 740–742, 1991. View at: Publisher Site | Google Scholar

5. D. J. Brock and L. Barron, "Measurement of placental alkaline phosphatase in maternal plasma as an indicator of subsequent low birthweight outcome," British Journal of Obstetrics and Gynaecology, vol. 95, no. 1, pp. 79–83, 1988. View at: Publisher Site | Google Scholar

6. S. McErlean and C. King, "Does an abnormally elevated maternal alkaline phosphatase pose problems for the fetus," BMJ Case Reports, vol. 12, no. 4, p. e229109, 2019. View at: Publisher Site | Google Scholar

7. R. E. Meyer, S. J. Thompson, C. L. Addy, C. Z. Garrison, and R. G. Best, "Maternal serum placental alkaline phosphatase level and risk for preterm delivery," American Journal of Obstetrics and Gynecology, vol. 173, no. 1, pp. 181–186, 1995. View at: Publisher Site | Google Scholar

8. A. H. Moawad, R. L. Goldenberg, B. Mercer et al., "The preterm prediction study: the value of serum alkaline phosphatase, alpha-fetoprotein, plasma corticotropin-releasing hormone, and other serum markers for the prediction of spontaneous preterm birth," American Journal of Obstetrics and Gynecology, vol. 186, no. 5, pp. 990–996, 2002 View at: Publisher Site | Google Scholar

9. R. Rajagambeeram, S. Abu Raghavan, S. Ghosh, S. Basu, R. Ramasamy, and S. B. Murugaiyan, "Diagnostic utility of heat stable alkaline phosphatase in hypertensive disorders of pregnancy," Journal of Clinical and Diagnostic Research, vol. 8, no. 11, pp. Cc10–CC13, 2014. View at: Publisher Site | Google Scholar

10. McErlean S, King C, "Does an Abnormally Elevated Maternal Alkaline Phosphatase Pose Problems for the Fetus?" BMJ Case Reports CP 2019;12:e229109.

11. Courtney T. Connolly, Olivia Grubman, Zainab Al-Ibraheemi, and Tatyana Kushner " A Case of Markedly Elevated Isolated Alkaline Phosphatase in the Third Trimester of Pregnancy" Case Reports in Obstetrics and Gynecology Volume 2022, Article ID 1611304,

12. Yulia A, Wijesiriwardana A "Extremely high isolated maternal alkaline phosphatase serum concentration – 2 case reports and literature review" Archives of Disease in Childhood - Fetal and Neonatal Edition 2012;97:A65-A66.http://dx.doi.org/10.1136/fetalneonatal-2012-301809.212

13. McErlean S, King C, "Does an Abnormally Elevated Maternal Alkaline Phosphatase Pose Problems for the Fetus?" BMJ Case Reports CP 2019;12:e229109.

14. Rajagambeeram R, Abu Raghavan S, Ghosh S, Basu S, Ramasamy R, Murugaiyan SB. "Diagnostic Utility of Heat Stable Alkaline Phosphatase in Hypertensive Disorders of Pregnancy. J Clin Diagn Res. 2014 Nov;8(11):CC10-3.doi: 10.7860/JCDR/2014/10895.5084. Epub 2014 Nov 20.https://pubmed.ncbi.nlm.nih.gov/25584211/