CASE REPORT

Case Report: Hyperemesis gravidarum, high transaminases level and prolonged prothrombin time: is it an acute liver injury? [version 1; peer review: awaiting peer review]

Rym Ennaifer, Yosr El Mouldi, Bochra Bouchabou, Abdelwahab Nakhli, Nesrine Hemdani, Amel Triki

Department of Gastroenterology, Mongi Slim La Marsa Hospital, Tunis, 2046, Tunisia

Abstract

Background: Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting in the first trimester of pregnancy. It is considered a benign condition, but severe complications, fortunately rare, have been reported. Frequently, this condition is associated with a perturbed liver function tests, which remains without severe consequences. The clinical presentation may be suggestive of an acute liver injury (ALI), especially as the end of the first trimester approaches, pregnancy specific and non-specific liver diseases should be considered.

Case: A 28-year-old primigravida, 14-week pregnant woman affected by hyperemesis gravidarum, developed high transaminases level and spontaneously low prothrombin time (PT) ratio. An ALI was suspected as transaminases were very high and our patient was at the end of the first trimester. An exhaustive etiological work-up was negative. In the second line, the factor V assay was conducted, which showed a normal activity, and the vitamin K level was low. We therefore concluded that it was hyperemesis gravidarum complicated by fluid and electrolyte disorders and vitamin K deficiency. She had parenteral rehydration and a proton pump inhibitor. She received intravenous vitamin K 10 mg daily for three days. The outcome was excellent without any maternal or fetal impact.

Conclusion: Hyperemesis gravidarum is a common condition in the first trimester of pregnancy that usually has a favourable outcome. However, it is important to be attentive to possible complications, including vitamin K deficiency with its maternal and fetal consequences. On the other hand, in case of major disturbance of the liver function tests, we should not overlook acute liver injury and should not hesitate to initiate an adequate etiological investigation.

Keywords

Hyperemesis, Acute liver injury, prothrombin time, vitamin K
Corresponding author: Yosr El Mouldi (yosrelmouldi@gmail.com)

Author roles: Ennaifer R: Supervision, Validation, Writing – Review & Editing; El Mouldi Y: Writing – Original Draft Preparation, Writing – Review & Editing; Bouchabou B: Supervision, Validation, Writing – Review & Editing; Nakhli A: Supervision, Validation, Writing – Review & Editing; Hemdani N: Supervision, Validation, Writing – Review & Editing; Triki A: Resources, Supervision, Validation

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2022 Ennaifer R et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.


First published: 09 Jun 2022, 11:634 https://doi.org/10.12688/f1000research.111040.1
Introduction
Nausea and vomiting are common in the first trimester of pregnancy and usually have an excellent outcome: most cases recover around week 20. However, some patients present a more severe form: hyperemesis gravidarum (HG). It is defined by incoercible vomiting leading to a weight loss of more than 5%, hydro-electrolytic disorders and ketosis. Frequently, this condition is associated with a perturbed liver function tests, mainly a mild elevation of transaminases and more rarely jaundice, which remains without severe consequences, particularly without hepatocellular failure.

Case report
A 24 year-old primigravida patient, with no familial or personal medical history, was admitted at week 14 of pregnancy for severe vomiting refractory to the usual symptomatic treatment since one month with asthenia and recent bodyweight loss.

On admission, she presented an altered general condition, signs of extracellular dehydration, and epigastric sensitivity in abdominal examination. Her axillary temperature was normal, the skin and mucous membranes were normal, the haemodynamic status was stable and there was no palpable goiter. The patient has no active bleeding and no abnormalities on neurological examination. Obstetrical examination was also normal. The urine test showed ketonuria without proteinuria.

Abdominopelvic ultrasound ruled out anomalies of the biliary tract, hepatic veins thrombosis and obstetric emergencies.

Laboratory analysis showed hypokalaemia at 2.4 mmol/l without other electrolyte disorder, elevated transaminases: serum aspartate aminotransferase (ASAT) 201 IU/l and serum alanine aminotransferase (ALAT) 648 IU/l (normal value < 40) without cholestasis, total bilirubin 32 umol/l, spontaneously low prothrombin time (PT) ratio 40%, haemoglobin 10 g/dl. Thyroid function tests were normal. Bacterial urine sampling was negative in culture. Serum markers for viral hepatitis (A, B, C, E, EBV, CMV and HSV) were not detectable. Autoimmune antibodies were absent.

Drug-induced hepatotoxicity was also ruled out, as the patient did not ingest any recent medicine or pharmacological therapy.

Acute liver injury (ALI) was suspected. However, Factor V assay showed a normal activity, with low vitamin K levels. The diagnosis of HG complicated by fluid and electrolyte disorders and vitamin K deficiency was retained.

As her PT continued to decrease, she received intravenous vitamin K 10 mg daily for 3 days. She had parenteral rehydration with correction of hypokalaemia. For vomiting, a proton pump inhibitor was prescribed.

The outcome was excellent, with regression of vomiting, correction of water-electrolyte balance and a normal PT of 85%. On the other hand, liver function tests normalization was slower.

Discussion
HG is the most severe form of nausea and vomiting in the first trimester of pregnancy. Its prevalence is 0.3 to 1% of pregnancies. Its pathophysiology remains unclear, but it is certainly multifactorial. This condition is considered a first trimester pregnancy-related liver disease as it is associated with liver function abnormalities in half of the cases. The transaminase elevation is usually moderate but can reach 1000 IU/L in rare cases. It predominates over ALAT. Alkaline phosphatase may double, and bilirubin increases up to 4 mg/dl. However, synthetic liver function remains intact, with normal coagulation profile and serum albumin levels, except in case of severe malnutrition. Usually, these disorders disappear after the vomiting has stopped and the fluid and electrolyte disorders have been resolved.

The aetiology of liver damage during HG is not well known, but several factors may be involved: dehydration, malnutrition, human chorionic gonadotropin (HCG) and placental-derived cytokines such as tumor necrosis factor-alpha.

Normal pregnancy has no effect on ASAT and ALAT. Therefore, in case of liver enzymes anomalies, other causes, both non-specific and specific to pregnancy, should be ruled out, in particular those that can lead to hepatocellular failure and that require urgent treatment. It has to be emphasized that most pregnancy-related liver diseases occur in the second and third trimesters. The diagnosis of liver disease secondary to HG remains a diagnosis of exclusion. Our patient was at the end of the first trimester (week 14), we were therefore alarmed at the fall of PT ratio, fearing other pregnancy specific liver diseases.
Severe complications, fortunately rare, have also been reported in HG. Mallory-Weiss syndrome, oesophageal rupture, inhalation pneumonitis, splenic avulsion, retinal haemorrhage and vitamin deficiency due to malabsorption secondary to incoercible vomiting: Gayet-Wernicke encephalopathy and a coagulopathy secondary to vitamin K deficiency. The latter was first described in 1998 in a patient admitted for management of HG, who presented with profuse epistaxis and whose various investigations of blood haemostasis and liver function concluded that she was vitamin K deficient.

In our patient’s case, an ALI was suspected based on the significant elevation of transaminases and the low PT. We therefore performed the standard work-up. We also tested for factor V activity to be sure that liver synthetic functions were correct. Then we confirmed the diagnosis of vitamin K deficiency by determining vitamin K blood level.

Vitamin K is a fat-soluble vitamin, absorbed in the small intestine, mainly the jejunum, in the presence of bile salts. Reserves are low and are mainly in the liver. It has a key role in coagulation. Recommended intakes are usually largely covered by the diet. The aetiologies of vitamin K deficiency are diverse: lack of intake, intestinal malabsorption, liver dysfunction or the use of anti-vitamin K drugs (warfarin). In HG, vitamin K deficiency due to inadequate intake secondary to incoercible vomiting may be present in 26% of patients.

It can have serious consequences for both the mother and the foetus: vitamin K deficiency embryopathy, maternal haemorrhage and neonatal cranial haemorrhage. Vitamin K deficiency embryopathy includes Binder phenotype and chondrodysplasia punctata.

Screening for haemostasis disorders by performing a PT could allow early diagnosis and correction of the deficiency by vitamin K supplementation before the onset of these consequences.

HG management usually includes fluid and electrolyte correction, intravenous antiemetic therapy and vitamin supplementation. Indeed, vitamin B1 supplementation to prevent Wernicke’s encephalopathy is recommended and commonly practiced. Several studies suggest prophylactic vitamin K supplementation for hyperemesis gravidarum with severe malnutrition or weight loss. It remains to be proven whether early prophylactic vitamin K supplementation is safe and effective in preventing complications, especially embryopathy.

For our patient, no foetal anomalies were detected on perinatal ultrasound. PT was not performed in the context of a bleeding complication or embryopathy, but rather systematically. She did not receive initially prophylactic supplementation.

**Conclusion**

HG is generally considered as a benign condition. However, it should be kept in mind that HG could lead to coagulopathy by means of vitamin K deficiency, in order to avoid maternal and foetal complications. In this context, the disturbance of liver function tests associated with a low PT must lead to the suspicion of ALI and therefore initiate an appropriate etiological investigation. Collaboration between the hepatologist and gynaecologist is essential for better management.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Oral informed consent for publication of their clinical details and/or clinical images was obtained from the patient during her hospital stay and noted in her medical record.

**References**

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com