Journal of Biomedical Sciences | ISSN: 2960-9356
Research Article Peer-review, Open Access

Liver Dysfunction Among Women with Hyperemesis Gravidarum

Sarah Gatea Shkhair[1]

Edwar Z. Khosho[2]

Abstract

Hyperemesis gravidarum (HG) is a serious early pregnancy disorder characterized by excessive vomiting which may result in dehydration, metabolic disorders and transient liver function abnormalities. Aim to identify the occurrence and biochemical profile of liver dysfunction in pregnant women with HG. 140 pregnant women admitted with HG were included in a retrospective cross-sectional study in Basrah Maternity Hospital. Patients with liver disease were excluded. Data was collected from medical records, clinical and laboratory data. The mean age of patients was 28.5 ± 5.1 years and a majority of cases happened during the first trimester (39.3%). Most were multi-gravida (68.6%). Liver enzyme elevation was common, with mean AST 73.27 ± 10.75 IU/L and ALT 69.29 ± 8.72 IU/L. Total bilirubin averaged 1 ± 0.5 mg/dL, while direct bilirubin averaged 0.40 ± 0.15 mg/dL. Electrolyte disturbances were hypoNa^+ (Na^+ 133.2 ± 15.04 mmol/L) and hypoK (K^+ 2.97 ± 0.53 mmol/L). 57.1% of patients had severe, 25% had moderate, and 17.9% had mild vomiting. Liver dysfunction in HG is typically mild and is reversible with supportive treatment. If there is persistence or significantly elevated liver enzymes, evaluation for other causes such as acute fatty liver of pregnancy, viral hepatitis or HELLP syndrome will be necessary.

Key words: Hyperemesis Gravidarum, Liver Dysfunction, Pregnancy, Nausea and Vomiting of Pregnancy

[1] M.B.Ch.B., Iraqi Board for Medical Specializations in Obstetrics and Gynaecology, Al-Basrah Maternity Hospital, Iraq

[2] Assistant Professor, M.B.Ch.B.,D.G.O.,F.I.C.M.S., Consultant Obstetrician and Gynaecologist, College of Medicine, University of Basrah, Iraq

Correspondance: sarahgsh94@gmail.com[1], edwar.khosho@uobasrah.edu.iq[2]

Introduction

Hyperemesis gravidarum (HG) is the more serious type of NVP, and is the condition that causes continued vomiting that can result in dehydration, weight loss, ketosis, electrolyte imbalance and a decrease in daily activities [1].

It is estimated to affect 0.3 – 3% of pregnancies and is most common in the first trimester [2]. Though the underlying cause is not well understood, hormonal, genetic, metabolic and inflammatory mechanisms have been proposed and more recently, growth differentiation factor 15 (GDF15) has been implicated in the pathogenesis of this disease [3]. Women hospitalized because of HG often have biochemical abnormalities

in their liver. About 50-60% can have abnormal liver function tests, typically mild serum aminotransferase elevations [4,5].

Alanine aminotransferase (ALT) is usually more elevated than aspartate aminotransferase (AST) and bilirubin is slightly elevated but generally less than 4 mg/dl. These abnormalities typically do not persist and will correct after vomiting, hydration and nutrition improve [6,7].

The mechanisms of the liver involvement in HG remain not completely understood. Factors cited include starvation, dehydration, hypovolemia, electrolyte abnormalities, fat metabolism abnormalities, and inflammatory mediators [8,9].

It is important to make the diagnosis of these abnormalities because when liver tests are abnormal during pregnancy they have to be distinguished from viral hepatitis, drug induced liver injury, intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy and HELLP syndrome [10]. Liver dysfunction in HG is usually mild and supportive treatment is usually recommended and not specific liver therapy is usually required [11]. The purpose of the current study was to understand the frequency and pattern of liver function abnormality in women with HG and its association with clinical and laboratory characteristics.

Materials and Methods

The study was a prospective cross-sectional study carried out in Basrah Maternity Hospital from January to December 2024. One hundred and forty (140) pregnant women, who were admitted with clinical diagnosis of hyperemesis gravidarum (HG) were included. Pregnancy Unique Quantification of Emesis and Nausea (PUQE) score was used to assess diagnosis and severity of HG. Exclusion criteria were women with preexisting liver or renal disease, diabetes mellitus, HIV/AIDS, hepatitis or other chronic diseases that may have had a direct effect on the liver function tests or electrolyte levels. Women who were unable to give trustworthy clinical information due to substantial psychiatric, cognitive, communication or hearing disorders were also excluded.

The information was obtained in a prospective manner using a structured data collection form by direct interview of the patient, clinical examination and laboratory investigations. These variables were recorded as age, parity, residence, occupation, smoking status, duration of HG symptoms, severity of HG symptoms, history of medications, medical and surgical history, obstetric history, and previous episodes of HG. Blood pressure, temperature, heart and respiratory rate and pallor, jaundice, cyanosis and other relevant clinical abnormalities were recorded for all the participants following a general physical examination.

Body mass index (BMI) was calculated and classified as underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), or obese (≥30 kg/m²). Laboratory investigations consisted of urinalysis for ketonuria, albuminuria and specific gravity, complete blood count, serum electrolytes (sodium, potassium and calcium), renal function tests (serum creatinine and blood urea nitrogen) and liver function tests (serum transaminases and bilirubin). Arterial blood gas analysis was carried out as clinically indicated. Venous blood samples (5 mL) were drawn under sterile conditions, left to coagulate and the serum was analysed following standard hospital procedures.

All biochemical parameters were analyzed by an automated chemistry analyzer (Siemens EXL 200). An obstetric ultrasound was done for all of them to ensure a viable intrauterine pregnancy, ascertain gestational age, and rule out other pregnancy-related causes of severe vomiting, such as multiple gestation and molar pregnancy. When indicated, transvaginal ultrasonography was performed.

This study was approved by the Iraqi Board for Medical Specializations in Obstetrics and Gynaecology –

Institutional Ethics Committee. All participants were informed about the purpose and procedures of the study prior to its beginning and informed consent was obtained. Confidentiality and anonymity of the participants were preserved in the course of data collection, analysis and reporting.

The collected data were inputted into the microcomputer software, MS. Excel and analyzed by IBM SPSS Statistics for Windows. Normally distributed continuous variables were presented as mean ± standard deviation (SD) and non-normally distributed continuous variables were presented as median and interquartile range (IQR). The categorical variables were presented as percentages and numbers. Appropriate statistical tests were performed to examine for associations of liver function abnormalities with relevant clinical and laboratory characteristics, P value <0.05 was considered statistically significant.

Results

Table 1. Distribution of demographic data in the studied group

Demographic characteristic		Studied group N=140
Age (Mean± SD)		**28.5± 5.1**
Educational status	No-formal education	41(29.2%)
	Primary education	51(36.6%)
	Secondary education	31(22%)
	College and above	17(12.2%)
Residence	Urban	82(58.5%)
	Rural	58(41.5%)
Occupations	Housewife	76(53.7%)
	Student	10(7.3%)
	Government employee	27(19.5%)
	Others	27(19.5%)

*SD: standard deviation

This table shows the demographic characteristics of the 140 women that participated in the study. The mean age was 28.5 ± 5.1 years. The majority of the participants were primary educated, and most of them were living in urban areas. In terms of occupation housewives constituted the largest group followed by the government employees and students

Table 2. Distribution of characteristic data in the studied group.

Characteristic		Studied group N=140
Gravidity	Primigravida	44 (31.4%)
	Multigravida	96 (68.6%)
Parity	Nulliparous	24 (17.1%)
	Primiparous	102 (72.9%)
	Multiparous	14 (10%)
Gestational age in weeks (Trimesters)	1st trimester (≤13 weeks)	85 (60.7%)
	2nd trimester (14-27 weeks)	37 (26.4%)
	3rd trimester (>27	18(12.9%)

	weeks)	
Systolic blood pressure (SBP)	≤90	65 (46.4%)
mmHg	>90	75 (53.6%)
Diastolic blood pressure (DBP)	≤60	68 (48.6%)
mmHg	>60	72 (51.4%)

The clinical features of the patients studied are summarized in this table. The majority of the patients were multigravida (68.6%) and primiparous (72.9%) and the largest number were seen during the first trimester (39.3%). Most patients had a blood pressure reading of greater than 90/60 mmHg.

Table 3. Distribution of Laboratory data in the studied group.

Laboratory data	Studied group N=140	Normal values
AST (IU/L)		
Mean± SD	73.27 ± 10.75	5 – 40
ALT (IU/L)		
Mean± SD	69.29 ± 8.72	5 – 40
D. Bil (mg/dl)		
Mean± SD	0.40 ± 0.15	0 – 0.3
T. Bil (mg/dl)		
Mean± SD	1 ± 0.5	0.2 – 1.2
TP (g/dl)		
Mean± SD	8.1 ± 1.4	6.0 – 8.3
Na^+ (mmol/L)		
Mean± SD	133.2 ± 15.04	135 – 145
K^+(mmol/L)		
Mean± SD	2.97 ± 0.53	3.5 – 5.0
Cl (mmol/L)		
Mean± SD	104.16 ± 4.8	98 – 106
ALP (IU/L)		
Mean± SD	65.0 ±22	40 – 130
Alb (g/dl)		
Mean± SD	3.95 ± 0.45	3.5 – 5.0

Liver enzymes were mildly elevated, with mean AST 73.27 ± 10.75 IU/L and ALT 69.29 ± 8.72 IU/L, while the bilirubin levels were modestly raised, and the total protein (8.1 ± 1.4 g/dL) and albumin (3.95 ± 0.45 g/dL) level remained normal, suggestive of preserved liver synthetic function. It was observed that there were electrolyte disturbances, especially hyponatremia (133.2 ± 15.04 mmol/L), and hypokalemia (2.97 ± 0.53 mmol/L). The level of alkaline phosphatase (65.0 ± 22 IU/L) was within the range for early pregnancy. In general, these data indicate that biochemical abnormalities are mostly mild and short-term, as is typical in hyperemesis gravidarum.

Table 4. Distribution of Degrees of vomiting in the studied group.

Degrees of vomiting	Studied group N=140
Severe	80 (57.1%)
Moderate	35(25%)
Mild	25(17.9%)

This table shows that among the 140 patients, the majority experienced severe vomiting (57.1%), followed by moderate vomiting (25%), while mild symptoms were reported in 17.9% of cases by using PUQE Score.

Discussion

Hyperemesis gravidarum (HG) is the most severe type of nausea and vomiting in pregnancy and often complicated by dehydration, electrolyte abnormalities, ketosis, and varying degrees of hepatic dysfunction [12]. While the majority of NVP is physiological, HG is associated with a specific metabolic stress, which can cause transient aberrations in liver biochemistry.

In this study, we assessed 140 women with HG, after excluding those with known liver disease. The observed demographic pattern (mean maternal age of 28.5 ± 5.1 years and predominance of multigravida women) was similar to that of Asrade et al [13] and Adane et al [14] indicating that HG is not strongly linked to socioeconomic or demographic factors and affects a wide reproductive age group.

The majority of patients were in the first trimester, following the known temporal trend of HG with a peak between 9 and 12 weeks gestation. This phenomenon of such early trimester clusters has been documented by Kamal Ali et al. [15] and hence corroborates the trimester dependent phenotype of HG.

One aim of this study was to describe the liver dysfunction in these patients. Aminotransferases were frequently raised and the mean AST and ALT were 73.27 ± 10.75 IU/L and 69.29 ± 8.72 IU/L respectively. These levels are within the common spectrum of HG, and represent a mild hepatocellular pattern of damage. Gaba and Gaba [16] also found that over half of the HG cases had abnormal liver tests. There was also another important electrolyte abnormality, namely, hyponatremia and hypokalemia, which can be attributed to chronic vomiting, dehydration and decreased oral intake. This type of abnormality was reported by Pornchai et al. [17] and by Küçükyurt and Kolcu [18].

Significantly, there was no evidence of cholestasis (alkaline phosphatase and albumin levels were normal), which agrees with the idea that hepatic involvement is more hepatocellular rather than cholestatic in HG. This difference is consistent with the existing literature, which has recognized HG as the most common etiology of abnormal liver tests in early pregnancy, typically manifesting with mild to moderate elevation of transaminases, not with bilirubin abnormalities.

The proportion of severe (57.1%), moderate (25%) and mild (17.9%) vomiting in our cohort was similar to the proportion of severe, moderate and mild vomiting, based on the PUQE classification, reported by Worede et al. [19]. Even if not formally studied, the correlation between the severity of the symptoms and biochemical abnormalities is confirmed by several previous reports showing that as emesis worsens so does the risk of dehydration, of ketosis and of liver stress.

In general, liver dysfunction in HG is mild, transient and reversible. The biochemical abnormalities found are consistent with the metabolic effects of chronic vomiting and not with hepatic disease. These findings are consistent with the literature that indicates liver damage associated with HG is a secondary event due to hypovolemia, electrolyte imbalance and metabolic stress from starvation [20,21].

Conclusion

Hyperemesis gravidarum may, in women, be complicated by liver dysfunction which is important but generally mild and reversible, and is most commonly noted by increased liver enzymes. These biochemical abnormalities most likely are due to dehydration, electrolyte disturbances and metabolic stress that occurs when vomiting is present. Liver function will improve in most cases with supportive care, such as proper

hydration, correction of electrolyte abnormalities and nutrition. Persistent or marked liver function abnormalities should be further investigated however, to rule out other causes of hepatic dysfunction such as HELLP syndrome, acute fatty liver of pregnancy and viral hepatitis. It is crucial to identify and manage any liver abnormalities early in the course of HG in women in order to achieve the best possible maternal and fetal outcome.

References

[1] M. Erick, J. T. Cox, and K. M. Mogensen, "ACOG practice bulletin 189: Nausea and vomiting of pregnancy," *Obstetrics & Gynecology*, vol. 131, no. 5, p. 935, 2018.

[2] A. G. S. Ahmed, Y. A. E. S. Wafa, and F. A. E. A. El-Omda, "Effect of high levels of human chorionic gonadotropin and estradiol on degree of hyperemesis gravidarum," *Al-Azhar International Medical Journal*, vol. 2, no. 7, pp. 17–23, 2021.

[3] C. Liu, G. Zhao, D. Qiao, L. Wang, Y. He, M. Zhao, *et al*., "Emerging progress in nausea and vomiting of pregnancy and hyperemesis gravidarum: Challenges and opportunities," *Frontiers in Medicine*, vol. 8, Art. no. 809270, 2022.

[4] A. Joshi, G. Chadha, and P. Narayanan, "From discomfort to distress: Hyperemesis gravidarum in the emergency room," *Cureus*, vol. 15, no. 8, 2023.

[5] M. N. Niemeijer, I. J. Grooten, N. Vos, J. M. J. Bais, J. A. Van Der Post, B. W. Mol, *et al*., "Diagnostic markers for hyperemesis gravidarum," *American Journal of Obstetrics and Gynecology*, vol. 211, no. 2, pp. 150.e1–150.e7, 2014.

[6] E. Kan, E. Emektar, K. Corbacioglu, T. Safak, T. Sariaydin, and Y. Cevik, "Inflammatory markers and hyperemesis gravidarum," *American Journal of Emergency Medicine*, vol. 38, no. 2, pp. 292–295, 2020.

[7] N. Mitchell-Jones, I. Gallos, J. Farren, A. Tobias, C. Bottomley, and T. Bourne, "Psychological morbidity in hyperemesis gravidarum," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 124, no. 1, pp. 20–30, 2017.

[8] K. F. Vandraas, Å. V. Vikanes, S. Vangen, P. Magnus, N. C. Støer, and A. M. Grjibovski, "Hyperemesis gravidarum and birth outcomes," *BJOG: An International Journal of Obstetrics & Gynaecology*, vol. 120, no. 13, pp. 1654–1660, 2013.

[9] M. Nurmi, P. Rautava, M. Gissler, T. Vahlberg, and P. Polo-Kantola, "Recurrence of hyperemesis gravidarum," *American Journal of Obstetrics and Gynecology*, vol. 219, no. 5, pp. 469.e1–469.e8, 2018.

[10] C. S. García-Romero, C. Guzman, A. Cervantes, and M. Cerbón, "Liver disease in pregnancy," *Annals of Hepatology*, vol. 18, no. 4, pp. 553–562, 2019.

[11] I. Mikolasevic, T. Filipec-Kanizaj, I. Jakopcic, *et al*., "Liver disease during pregnancy," *Medical Science Monitor*, vol. 24, pp. 4080–4090, 2018.

[12] A. M. Whitfield, A. V. B. Tran Nguyen, and K. Sheikh, "Jaundice and pregnancy," *Medical Journal of Australia*, vol. 210, no. 6, pp. 255–260, 2019.

[13] P. B. Kaplan, F. Gücer, N. C. Sayin, *et al*., "Maternal serum cytokines in hyperemesis gravidarum," *Fertility and Sterility*, vol. 79, no. 3, pp. 498–502, 2003.

[14] E. K. Alexander, "ATA guidelines for thyroid disease in pregnancy," *Thyroid*, vol. 27, no. 9, p. 1212, 2017.

[15] J. E. Birkness-Gartman and K. Oshima, "Liver pathology in pregnancy," *Pathology International*, vol. 72, no. 1, pp. 1–13, 2022.

[16] Y. Sasamori, A. Tanaka, and T. Ayabe, "Liver disease in pregnancy," *Hepatology Research*, vol. 50, no. 9, pp. 1015–1023, 2020.

[17] N. A. Terrault and C. Williamson, "Pregnancy-associated liver diseases," *Gastroenterology*, vol. 163, no. 1, pp. 97–117, 2022.

[18] L. Asrade, D. Misikir, H. Alemu, *et al*., "Determinants of hyperemesis gravidarum," *BMC Women's Health*, vol. 23, no. 1, Art. no. 225, 2023.

[19] F. Kamal Ali, M. Mahmoud Hassan, and O. Abdel-Wahab Afifi, "Tailored education program in hyperemesis gravidarum," *Journal of Nursing Science Benha University*, vol. 3, no. 2, pp. 1188–1211, 2022.

[20] A. K. Küçükyurt and S. A. Kolcu, "Hyperemesis gravidarum as a predictor of intrahepatic cholestasis of pregnancy," *Clinical and Experimental Obstetrics & Gynecology*, vol. 51, no. 11, Art. no. 254, 2024.

[21] A. Worede, T. Deress, H. Wondifraw, *et al*., "Electrolyte imbalance and liver function test abnormalities in hyperemesis gravidarum," *Frontiers in Medicine*, vol. 11, Art. no. 1451036, 2024.