

# **Original Research Article**

# ALTERATIONS IN BIOCHEMICAL PARAMETERS AMONG PREGNANT WOMEN WITH HYPEREMESIS GRAVIDARUM: A HOSPITAL-BASED OBSERVATIONAL STUDY

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#### ABSTRACT

**Background:** Nausea and vomiting of pregnancy (NVP) is a common physiological condition, while hyperemesis gravidarum (HG) represents its severe form and is associated with metabolic and biochemical disturbances. Elevation of pancreatic enzymes in HG may mimic acute pancreatitis, leading to diagnostic dilemmas. Limited data are available on alterations in serum amylase and lipase among pregnant women with HG, particularly in the Indian population. **Objectives:** To evaluate biochemical alterations, with special emphasis on serum amylase and lipase levels, in pregnant women with hyperemesis gravidarum and to compare these parameters with healthy non-pregnant women.

Materials and Methods: This hospital-based observational study was conducted in the Department of Medical Biochemistry in collaboration with the Department of Obstetrics and Gynaecology, Gandhi Medical College, Bhopal, from May 2023 to May 2024. A total of 200 women were enrolled, comprising 100 healthy non-pregnant women and 100 pregnant women presenting with nausea and vomiting/hyperemesis gravidarum. Fasting blood samples were collected for estimation of serum bilirubin, liver enzymes, electrolytes, glucose, serum amylase, and lipase using a fully automated chemistry analyser. Urine samples were analysed for acetone. Data were analysed using Epi Info software. Continuous variables were expressed as mean ± standard deviation and compared using independent Student's *t*-test. A *p*-value≤0.05 was considered statistically significant.

**Results:** Pregnant women with HG showed significantly higher SGPT, SGOT, and bilirubin levels compared to non-pregnant women (p<0.001). Serum sodium and potassium levels were significantly lower in the HG group (p=0.002 and p<0.001, respectively). Serum glucose levels did not differ significantly between the groups (p=0.26) however, serum total protein significantly altered (p=0.046). Serum amylase and lipase levels were also significantly altered in the HG group (p<0.001) as compared to non-pregnant women. Ketonuria was observed exclusively among pregnant women with HG.

**Conclusions:** Hyperemesis gravidarum is associated with significant biochemical and metabolic disturbances, including alterations in liver function tests, electrolytes, and pancreatic enzymes. Elevated serum lipase levels were more frequently observed than elevated amylase levels in HG, suggesting that lipase may be a more sensitive marker of metabolic stress in these patients. Careful interpretation of pancreatic enzyme elevation is essential to avoid misdiagnosis of acute pancreatitis in pregnant women presenting with nausea and vomiting.

**Keywords**: Ketone bodies, hyperemesis gravidarum, Pregnancy, Amylase, Lipase.

# **INTRODUCTION**

Pregnancy is a physiological state lasting approximately 40 weeks, extending from the first day

of the last menstrual period to the delivery of a healthy newborn.<sup>[1]</sup> It is characterized by profound hormonal, metabolic, and biochemical adaptations that support fetal growth and maternal well-being.

These changes frequently manifest as clinical symptoms, of which nausea and vomiting are the most common, affecting up to 85% of pregnant women. [2,3] Symptoms typically begin between 4 and 6 weeks of gestation, peak between the 8th and 12th weeks, and usually resolve by the 20th week of gestation.<sup>[4]</sup> This condition, referred to as nausea and vomiting of pregnancy (NVP) or emesis gravidarum, is generally considered benign and self-limiting.<sup>[5]</sup> A subset of women with NVP, however, develop hyperemesis gravidarum (HG), the most severe form of the condition. Hyperemesis gravidarum is defined by persistent vomiting exceeding three episodes per day, associated with ketonuria and significant maternal weight loss (>3 kg or >5% of pre-pregnancy weight). [2,6,7] HG can lead to dehydration, electrolyte imbalances, nutritional deficiencies, and acid-base disturbances, including metabolic alkalosis from gastric acid loss and metabolic acidosis due to starvation. [6,7,8] As these clinical features are nonspecific, HG is considered a diagnosis of exclusion and is frequently associated with biochemical abnormalities, including elevations in liver enzymes, serum amylase, and serum lipase. [8,9]

Several risk factors have been implicated in the development of HG, including nulliparity or multiparity, obesity, metabolic disturbances, family history of HG, previous history of HG, trophoblastic disease, and psychological disorders such as anorexia nervosa and bulimia. [10,11,12] Laboratory abnormalities commonly observed in HG include mildly elevated liver transaminases (<300 U/L), serum bilirubin (<4 mg/dL), pancreatic enzymes, altered thyroid function tests, increased urinary specific gravity, and ketonuria. [2,13]

Elevation of serum amylase and lipase levels in pregnant women presenting with nausea and vomiting raises clinical suspicion for acute pancreatitis (AP).<sup>[14]</sup> Acute pancreatitis is a common inflammatory condition of the pancreas in the general population but occurs relatively infrequently during pregnancy, with an incidence ranging from 1 in 1,000 to 1 in 10,000 live births.<sup>[15]</sup> The clinical presentation of AP varies from mild, self-limiting disease to severe pancreatitis complicated by pancreatic necrosis, abscess formation, pseudocysts, and multiple organ dysfunction syndrome, posing serious risks to both maternal and fetal health.[16] The most common etiological factors for AP during pregnancy include gallstone disease and hypertriglyceridemia.[17]

Measurement of serum amylase and lipase remains the cornerstone of laboratory diagnosis of acute pancreatitis due to their wide availability, rapid turnaround time, cost-effectiveness, and diagnostic reliability. Lipase, secreted predominantly by pancreatic acinar cells, catalyses the hydrolysis of triglycerides into glycerol and free fatty acids. Serum lipase levels typically rise within 4-8 hours of symptom onset, peak at around 24 hours, and remain elevated for 8-14 days. Amylase, produced by both the pancreas and salivary glands, hydrolyses starch

and is rapidly cleared by the kidneys; hence, elevated levels may also be observed in renal dysfunction.<sup>[21]</sup> Serum amylase levels generally rise within 6-24 hours, peak at 48 hours, and normalize within 5-7 days.<sup>[22,23]</sup>

Comparative studies have demonstrated that serum lipase is more sensitive (94%) and specific (96%) for diagnosing acute pancreatitis than serum amylase, which has a sensitivity of 83% and specificity of 88%. [24] Although liver enzymes may be elevated during pancreatitis, they are not independently reliable for diagnosis. Hypertriglyceridemia is an important cause of pancreatitis in pregnancy, known as lipid-induced pancreatitis. [3,25] While triglyceride levels may physiologically rise up to 300 mg/dL during normal pregnancy, levels exceeding 750 mg/dL significantly increase the risk of pancreatitis. [26]

Nausea and vomiting are frequently considered benign symptoms of early pregnancy, leading to under-investigation of biochemical abnormalities. Elevations in serum amylase and lipase may be misattributed to hyperemesis gravidarum, potentially delaying the diagnosis of acute pancreatitis. Limited studies have systematically evaluated pancreatic enzyme alterations in pregnant women with nausea and vomiting, particularly in the Indian population. Early biochemical screening may facilitate prompt diagnosis, prevent complications, and improve prognosis. Hence, this study is undertaken to address this clinical gap.

#### **MATERIALS AND METHODS**

This hospital-based observational study was carried out in the Department of Medical Biochemistry in collaboration with the Department of Obstetrics and Gynecology, Gandhi Medical College, Bhopal from May 2023 to May 2024. 100 normal healthy nonpregnant women (hospital working female staff and female attendants/caretakers of patients who visited the hospital during the study period) and 100 pregnant women presenting nausea and vomiting or hyperemesis gravidarum attending the antenatal clinic (outpatient and inpatient department) were enrolled in this study. The inclusion criteria-was age group of 20-30 years, Singleton pregnancy, Primigravida / Multigravida. The women having any obstetric or medical complications such as anemic, hypertension, diabetes, women on intake of thyroid drugs, all other causes for electrolyte abnormalities, renal disorders, malabsorption syndrome, hepatic disorders and pancreatitis, acute intra-abdominal disorders, history of hyperemesis gravidarum during previous pregnancies and experiencing significant psychological distress were excluded from the study. A written informed consent was taken from the participants to participate in this study and ethical clearance approval was obtained from the Institutional Ethical Committee (IEC) number30697/MC/IEC/2022, dated-04/08/2022 of Gandhi Medical College, Bhopal.

**Demographic and Clinical Data**: All the detailed history was taken including the age, gravida, weight, height and Body Mass Index (BMI) calculated based on the standard formula.

**Sample collection:** Five millilitre fasting blood sample was collected in plain test tube and EDTA vial under the aseptic condition for biochemical analysis. For the separation of serum, blood was centrifuged on 3500 RPM for 15 minutes and serum was used for the analysis of biochemical parameters.

Laboratory Investigations: All the biochemical parameters such as serum SGOT, SGPT, bilirubin,

total protein, electrolytes (sodium & potassium), glucose, amylase and lipase were estimated by using fully automated chemistry analyzer. Hemoglobin was estimated by hematology analyser and urine acetone was confirmed by dipstick method. All the laboratory investigation facility was provided by Clinical Biochemistry Laboratory and Multidisciplinary Research Unit (MRU), Gandhi Medical College, Bhopal.

**Statistical Analysis:** Statistical analysis was done by using Epi-Info software. Continuous variables were expressed as mean  $\pm$  standard deviation (Mean  $\pm$ SD) and compared using independent Student's t-test. A p value  $\leq$ 0.05 was considered statistically significant.

#### RESULTS

Table 1: Demographics and Clinical Characteristics of study participants

Variable	Non-pregnant women Mean ±SD (n =100)	Pregnant women with HG Mean ±SD (n =100)	*P-Value
Age (Years)	$26.23 \pm 4.70$	$27.24 \pm 4.79$	0.134
BMI (Kg/m <sup>2</sup> )	$21.04 \pm 3.00$	$23.84 \pm 4.09$	< 0.001
Systolic BP (mmHg)	$118.28 \pm 10.0$	$114.28 \pm 11.23$	0.008
Diastolic BP (mmHg)	$74.00 \pm 8.94$	$77.00 \pm 8.50$	0.015
Haemoglobin (g/dL)	$11.45 \pm 0.81$	10.55±1.20	

Data are expressed as Mean±SD, Independent Student's t-test was used to compare the groups \*p≤0.05 was considered statistically significant

Table 1 compares the demographic and clinical characteristics of pregnant and non-pregnant women included in the study. The mean age did not differ significantly between pregnant and non-pregnant women (27.24  $\pm$  4.79 vs. 26.23  $\pm$  4.70 years; p = 0.134), indicating comparability between groups with respect to age. Body mass index was significantly higher among pregnant women compared to non-pregnant women (23.84  $\pm$  4.09 vs.

 $21.04 \pm 3.00$  Kg/m²; p<0.001). Pregnant women demonstrated a significantly lower mean systolic blood pressure (114.28  $\pm$  11.23 mmHg) compared to non-pregnant women (118.28  $\pm$  10.00 mmHg; p = 0.008). In contrast, mean diastolic blood pressure was significantly higher in pregnant women than in non-pregnant women (77.00  $\pm$  8.50 vs. 74.00  $\pm$  8.94 mmHg; p = 0.015).

Table 2: Biochemical parameters in study participants

Parameter (s)	Non-pregnant women Mean ±SD (n =100)	Pregnant women with HG Mean ±SD (n =100)	*P-Value
Serum SGPT (U/L)	$19.30 \pm 6.64$	$33.15 \pm 7.70$	< 0.001
Serum SGOT (U/L)	$18.70 \pm 7.47$	$31.63 \pm 6.44$	< 0.001
Serum Bilirubin (mg/dL)	0.69±0.03	$1.0\pm0.08$	< 0.001
Serum Total Protein (mg/dL)	$6.58 \pm 1.00$	$7.68 \pm 1.28$	0.046
Serum Glucose (mg/dL)	$99.00 \pm 14.22$	95.01±10.89	0.260
Serum Sodium (mEq/L)	$135.3 \pm 4.45$	$132.09 \pm 5.43$	0.002
Serum Potassium (mEq/L)	$5.06 \pm 1.07$	$3.43 \pm 0.58$	< 0.001
Serum Amylase (U/L)	$60.96 \pm 10.15$	89.85±11.90	< 0.001
Serum Lipase (U/L)	25.47±8.09	$40.08 \pm 7.97$	< 0.001
Urine Acetone	Negative	Positive	-

Data are expressed as Mean±SD, Independent Student's t-test was used to compare the groups \*p≤0.05 was considered statistically significant

Table 2 compares the biochemical parameters between non-pregnant women and pregnant women with hyperemesis gravidarum (HG). Pregnant women with HG showed significantly higher SGPT, SGOT, bilirubin and amylase levels compared to non-pregnant women (p<0.001), indicating hepatic and pancreatic involvement in HG. Serum sodium and potassium levels were significantly lower in the HG group (p=0.002 and p<0.001, respectively),

reflecting electrolyte imbalance due to persistent vomiting. No statistically significant difference was observed in serum glucose levels between the two groups (p=0.26). Serum lipase levels were also significantly increased in pregnant women with HG compared to non-pregnant women (p<0.001). Urine acetone positivity was observed exclusively in the HG group, indicating ketonuria and starvation state.

#### **DISCUSSION**

The findings of the present study highlight significant physiological and biochemical differences between pregnant women with hyperemesis gravidarum and non-pregnant women. As demonstrated in Table 1, pregnant women showed significant variations in body mass index and blood pressure parameters, reflecting the normal cardiovascular and metabolic adaptations that occur during pregnancy. These findings support existing evidence that pregnancy induces dynamic physiological changes, which may be further exaggerated in pathological conditions such as HG. Hyperemesis gravidarum is known to cause significant metabolic derangements, including electrolyte imbalance and hepatic dysfunction. In the present study, serum AST levels were significantly higher in women with HG compared to non-pregnant women. This observation is consistent with the findings reported by Worede et al and Tan et al, [27,28] who also documented elevated AST levels in HG cases. In contrast, studies by Alizzi et al., Agmon et al., and Gaba et al,[29,30,31] did not observe significant differences in AST levels between normal and HG pregnancies. Such discrepancies may be attributed to variations in study design, sample size, dietary patterns, lifestyle factors, and exclusion criteria adopted by different investigators.

Similarly, ALT levels were found to be significantly elevated in HG cases in the present study. These findings are in agreement with reports by Worede et al. and Agmon et al, [27,30] suggesting hepatic involvement in hyperemesis gravidarum. However, studies by Alizzi et al. and Gaba et al, [29,31] reported inconsistent ALT alterations. The variation in ALT levels across studies may reflect differences in disease severity, nutritional status, and duration of vomiting prior to biochemical evaluation.

A statistically significant elevation in total serum bilirubin was also observed in HG cases when compared to non-pregnant women. This finding aligns with observations by Worede et al., who reported increased direct bilirubin levels in HG cases and suggested that the underlying mechanism remains unclear. Possible explanations include malnutrition, intrahepatic cholestasis, dehydration, or impaired hepatic clearance resulting from prolonged vomiting and metabolic stress.<sup>[27]</sup>

The present study also demonstrated a significant increase in total protein levels in HG patients compared to non-pregnant women. A similar observation was reported by Worede et al. [27] However, other study comparing HG patients with normal pregnant women has not found significant differences. [29] The elevated total protein levels observed in this study may be attributed to hemoconcentration secondary to dehydration resulting from persistent vomiting.

No statistically significant difference in fasting serum glucose levels was observed between HG cases and non-pregnant women. Although glucose levels were marginally lower in HG patients (95.01  $\pm$  10.89 mg/dL) compared to non-pregnant women (99.00  $\pm$  14.22 mg/dL), the difference was not statistically significant (p = 0.26). Reduced caloric intake due to persistent nausea and vomiting may contribute to lower glucose levels in HG cases. These findings are supported by Watanabe et al., who reported decreased fasting blood glucose levels in women with hyperemesis gravidarum.  $^{[32]}$ 

Electrolyte imbalance is a well-recognized complication of hyperemesis gravidarum. In the present study, serum sodium and potassium levels were significantly lower in HG cases compared to non-pregnant women. These findings are consistent with studies conducted by Alizzi FJ et al, and Hussein KS et al.[29,33] which also reported hyponatremia and hypokalemia in HG patients. However, studies of Agmon N et al and Buyukkayaci Duman N et al. [30,34] did not demonstrate similar electrolyte disturbances, possibly due to differences in patient selection, hydration status at presentation, and exclusion of severe cases. One of the key objectives of this study was to evaluate pancreatic enzyme alterations in hyperemesis gravidarum. The present study demonstrated significantly elevated serum lipase levels in HG patients  $(40.08 \pm 7.97 \text{ U/L})$  compared to non-pregnant women (25.47  $\pm$  8.09 U/L) (p<0.001). Similarly, serum amylase levels were significantly higher in HG cases (89.85  $\pm$  11.90 U/L) than in nonpregnant women  $(60.96 \pm 10.15 \text{ U/L})$  (p<0.001). These findings are supported by available gastroenterology literature describing elevated pancreatic enzymes in association with hyperemesis gravidarum.[14,35,36] Johnson et al., also reported significantly increased serum lipase levels in pregnant women presenting with nausea and vomiting.<sup>[37]</sup> In contrast, Dhunga et al., reported no statistically significant difference in serum lipase levels between HG patients and non-pregnant women (p=0.086).[38] Karsenti et al., observed a decrease in serum lipase activity during the first trimester of pregnancy, although the underlying mechanism remains unclear.<sup>[39]</sup> Additionally, Dambazau et al., reported no significant alterations in serum amylase and lipase levels when comparing HG patients with normal pregnant women. [40] These conflicting findings suggest that pancreatic enzyme alterations in HG may be influenced by gestational age, severity of vomiting, nutritional status, and timing of biochemical assessment.

#### Strengths of the Study

- The study provides a comprehensive biochemical evaluation of hyperemesis gravidarum, including liver function tests, electrolytes, and pancreatic enzymes.
- Inclusion of a healthy non-pregnant control group allows clear comparison of pregnancyrelated biochemical alterations.
- The study adds valuable data from the Indian population, where limited evidence exists regarding pancreatic enzyme alterations in hyperemesis gravidarum.

#### Limitations of the Study

- The relatively small sample size limits generalizability and prevented standardization of biochemical parameters.
- The study was conducted predominantly during early pregnancy, and trimester-wise variations could not be assessed.
- Renal function tests, lipid profile, and imaging studies were not included, which may have provided additional insight into pancreatic enzyme alterations.

## **CONCLUSION**

Hyperemesis gravidarum is associated with significant biochemical disturbances, including altered liver function tests, electrolyte imbalance, and changes in pancreatic enzyme levels. In the present study, pregnant women with hyperemesis gravidarum demonstrated significantly elevated serum bilirubin, transaminases, amylase, and lipase, along with reduced sodium and potassium levels, compared to non-pregnant women. Serum lipase elevation was more frequent than amylase elevation, suggesting greater sensitivity to metabolic stress in hyperemesis gravidarum. However, pancreatic enzyme elevations should be interpreted cautiously, as they may occur in the absence of acute pancreatitis. Routine biochemical assessment may aid in early identification of metabolic derangements and guide appropriate clinical management to improve maternal outcomes.

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