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The Level of Serum Enzymes and Hormones in Patients with Miscarriage

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ABSTRACT

Background: The level of various enzymes and thyroid hormones in blood get altered during miscarriage, which can have predictive value or importance as a biomarker for the diagnosis. The aim of the present study is to validate the alteration in the level of serum enzymes and thyroid hormones in patients suffering with miscarriage in a tertiary care hospital in Nepal.

Methods: A descriptive cross-sectional study was carried out on patients suffering with miscarriage and admitted for treatment in Nobel Medical College Teaching Hospital. Demographic data were recorded in a predesigned performa. The level of various enzymes and thyroid hormones were estimated from the blood sample of patients in the department of biochemistry laboratory. Data were entered in MS excel and analyzed by statistical package for the social sciences Version version 20.0

Results: The total number of patients suffering from miscarriage and enrolled in the study was 86. The mean value of serum gamma glutamyl transferase, lactate dehydrogenase and adenosine deaminase in these patients were 22.67±8.22, 289.6±126.9 and 21.3±9.9 IU/ml respectively, which were significantly higher (p=<0.0001, 0.0004, 0.0179 respectively) when compared to healthy pregnant women. Thyroid dysfunction was noted in 15 (17.44%) patients, out of that Subclinical hypothyroidism was most common and affected 8(9.3%) individuals.

Conclusions: The mean value of serum gamma glutamyl transferase, lactate dehydrogenase and adenosine deaminase in case of miscarriage was found to be elevated significantly and thyroid dysfunction was also noted to small fraction of patients suffering from miscarriage with Subclinical hypothyroidism being the most common.

Keywords: Enzyme; hormone; miscarriage.

INTRODUCTION

A miscarriage is the unexpected end of a pregnancy and being the most frequent complication in an early pregnancy.[1] According to epidemiological research from different communities, miscarriage occurs in 8-20% of clinically diagnosed pregnancies globally, despite the fact that the women may not show any overt symptoms.[2,3] In Nepal, study revealed that 5.5% of pregnancies resulted in miscarriage.[4]

Biomarkers that are predictive of the occurrence before it happens are still lacking. Blood level of gamma-glutamyltransferase (GGT), adenosine deaminase (ADA) and lactate dehydrogenase (LDH) is found to be associated with apoptosis, maintenance of immune system and release during tissue damage and in common injuries like in case of miscarriage.[5-7] Numerous unfavorable prenatal and obstetric outcomes are also linked to thyroid disorders.[8-11]

While these biomarkers have been studied in other populations, there is limited data available on their relevance in the Nepali population. Hence, the aim of the present study is to evaluate the biochemical alterations in the serum level of various enzymes and thyroid hormones in patients having spontaneous miscarriage in a tertiary care hospital in the current setup in Nepal.

METHODS

A descriptive cross-sectional study was designed and conducted prospectively at a tertiary care Hospital,

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Nobel Medical College Teaching Hospital (NMCTH) on the patients suffering from miscarriage and admitted to Obstetrics and Gynaecology ward for the treatment during a period of 1st November 2022 to 31st October 2023. The study was conducted after receiving the ethical clearance of the study from institutional review committee, NMCTH (Ref no- 622/2022). The patients having spontaneous miscarriage and admitted to NMCTH for treatment were enrolled for the study. The patients having miscarriage because of any type of accident or intended abortion or not willing to participate in the study were excluded. The sampling technique employed for the study was convenience sampling. The sample size was calculated by using formula, $n= Z^2pq/d^2$ [where, n= minimum required sample size, Z= 1.96 at 95% Confidence Interval (CI), p= prevalence taken as 5.5%,[4] q= 1-p, d= margin of error, 5%] and was obtained as 80. The total number of sample of miscarriage enrolled and considered for the research in the study period was 86.

Demographic data (age, sex, height and weight) and other important related to pregnancy were collected in a predesigned performa. Body mass index (BMI) was calculated by the given formula, BMI= Weight in kilogram/ (Height in meter) [2]. Blood sample of the study participants were sent to laboratory of NMCTH for the estimation of various biochemical parameters as part of routine clinical care using standard laboratory protocols at our tertiary care hospital. Serum enzymes (GGT, LDH, ADA, SGOT, SGPT, ALP), hormones (free T3, free T4, TSH) and routine biochemical parameters (sugar, urea, creatinine, sodium, potassium, uric acid, total cholesterol, triglyceride, HDL, LDL) were estimated from the blood samples of participants. Serum GGT, LDH, SGOT, SGPT, ALP were estimated in fully automated BECKMAN Coulter (AU480) with the reagents supplied in the kit. The estimation of serum ADA was based on enzymatic end point reaction and carried out in a semi auto analyzer (Erba) with the reagents from BEACON company. Serum free T3, free T4 and TSH were estimated in fully automated analyzer of SIEMENS (ADVIA, Centaur XPT) company based on chemiluminescence immuno assay with the reagents supplied by the manufacturer according to the standard protocol.[12] Other biochemical parameters like serum glucose, urea, creatinine, sodium, potassium, uric acid, total cholesterol, triglyceride, HDL and LDL were estimated in a fully automated analyzer BECKMAN Coulter (AU480) using the reagents provided with the kit in the biochemistry laboratory, NMCTH. As a control group, all the required data were collected from 90 healthy pregnant women for comparision.

The data were entered in MS excel and analyzed by SPSS version 20.0. Mean and standard deviation were calculated for numerical variables whereas percentage was used to represent categorical variables. The statistical significance between two mean values with standard deviation was calculated by one sample t test. The data was considered as significant if the value of $p<0.05$ at 95% confidence interval.

RESULTS

The total number of study participants, admitted in wards with miscarriage, and enrolled in the study was 86.The mean age of the participants was 28.27±7.27 years. The maximum number of cases of miscarriage was observed in age group 20-30, in which 47 (54.65%) cases were noted followed by 20 (23.26%) cases in 31-40 age groups of patients. The mean value of body mass index (BMI) among participants was 22.4±3.2 kg/m^2. The maximum number of miscarriage cases was reported among patients having normal (18.5-24.9) BMI. The total number of miscarriage cases in multigravida patients was 58 (67.44%), whereas only 28 (32.56%) cases were reported in primigravida patients as shown in Table 1.

Table 1. Baseline characteristics of study participants with miscarriage (n=86)

Characteristics	Number	Percentage
Age in year (Mean ± SD)	28.27±7.27	
Miscarriage in different age group		
<20	11	12.79
20-30	47	54.65
31-40	20	23.26
>40	8	9.30
BMI in Kg/meter^2	22.4±3.2	
<18.5	15	17.44
18.5-24.9	54	62.79
25-30	17	19.77
>30	0	0
Number of Pregnancy		
Primigravida	28	32.56
Multigravida	58	67.44

Table 2. Mean value of serum enzymes among patients with miscarriage.

Serum enzymes	Miscarriage patients (Mean±SD) n=86	Healthy pregnant individuals (Mean±SD) n=90	p-Value
GGT (U/L)	22.67±8.22	16.19±6.81	<0.0001
LDH (U/L)	289.6±126.9	226.14±103.44	0.0004
ADA (U/L)	21.3±9.9	18.37±5.96	0.0179
SGPT (U/L)	30.11±6.48	29.05±5.31	0.2359
SGOT (U/L)	27.91±5.43	26.73±6.22	0.1826
ALP (U/L)	113.57±54.88	105.84±46.49	0.314

The mean serum GGT value among miscarriage participants was 22.67±8.22 U/l, which was considerably (p=<0.0001) higher than the mean serum GGT value among pregnant women in good health. Similarly, the mean value of serum LDH (289.6±126.9 U/l) and ADA (21.3±9.9 U/l) was significantly (p=0.0004, p=0.0179 respectively) increased among miscarriage patients when compared with healthy pregnant individuals. The mean value of serum SGPT, SGOT and ALP was non-significantly increased in study participants than among healthy individuals as shown in Table 2.

While analyzing thyroid function test among the study participants, it was observed that 15 (17.44%) patients were suffering with thyroid hormone abnormality. Out of 86 patients with miscarriage, 8 (9.3%) patients were having subclinical hypothyroidism followed by hypothyroidism in 5 (5.81%). Only 2 (2.33%) patients were found to have hyperthyroidism as shown in Table 3.

Table 3. Status of thyroid among patients with miscarriage.

Thyroid status	Number	Percentage
Subclinical Hypothyroidism	8	9.30
Hypothyroidism	5	5.81
Hyperthyroidism	2	2.33
Euthyroidism	71	82.56

Table 4. Mean value of thyroid hormones in miscarriage patients with different thyroid status.

Thyroid status	T3 (pg/ml)	T4 (ng/dl)	TSH (µIU/ml)
Subclinical Hypothyroidism	3.78±0.36	0.99±0.09	7.48±1.66
Hypothyroidism	2.15±0.22	0.80±0.03	16.01±6.69
Hyperthyroidism	15.40±4.14	6.15±0.35	0.19±0.03
Euthyroidism	3.43±0.43	0.99±0.18	2.93±1.36
Reference range	2.5-4.16	0.89-1.76	0.34-5.12

The mean value of serum TSH among patients with miscarriage and suffering from subclinical hypothyroidism, hypothyroidism, hyperthyroidism and euthyroidism in µIU/ml were 7.48±1.66, 16.01±6.69, 0.19±0.03 and 2.93±1.36 respectively. Similarly, The mean value of serum free T_3 among participants with subclinical hypothyroidism, hypothyroidism, hyperthyroidism and euthyroidism in pg/ml were 3.78±0.36, 2.15±0.22, 15.40±4.14 and 3.43±0.43 respectively, where asthe mean value of serum free T_4 in ng/dl were 0.99±0.09, 0.80±0.03, 6.15±0.35 and 0.99±0.18 respectively in those same group of participants as shown in Table 4.

Table 5. Mean Value of serum biochemical parameters in miscarriage patients.

Biochemical Parameters	Miscarriage patients (Mean±SD) n=86	Healthy individual (Mean±SD) n=90	p-Value
Sugar (mg/dl)	87.45±13.41	90.33±17.52	0.21
Urea (mg/dl)	23.76±8.32	25.74±7.16	0.07
Creatinine (mg/dl)	0.7±0.2	0.9±0.3	0.06
Sodium (mmol/l)	139.4±5.1	140.21±4.23	0.23
Potassium (mmol/l)	3.9±0.3	3.7±0.3	0.06
Uric acid (mg/dl)	4.78±1.47	5.04±1.2	0.17
Total cholesterol (mg/dl)	177.13±13.39	180.01±10.38	0.09
Triglyceride (mg/dl)	112.96±18.44	116.71±12.63	0.08
HDL (mg/dl)	43.21±6.12	42.79±5.77	0.6
LDL (mg/dl)	93.86±10.34	96.59±12.74	0.1

The level of other serum biochemical parameters were also analyzed and it was noted that the mean value of serum glucose (87.45±13.41 mg/dl), urea (23.76±8.32 mg/dl), creatinine (0.7±0.2mg/dl), sodium (139.4±5.1 mmol/l), uric acid (4.78±1.47 mg/dl), total cholesterol (177.13±13.39 mg/dl), triglyceride (112.96±18.44 mg/dl) and LDL (93.86±10.34 mg/dl) was non-significantly decreased among patients with miscarriage than healthy pregnant individuals, whereas the mean value of serum potassium (3.9±0.3 mmol/l) and HDL (43.21±6.12 mg/dl) was found to be non-significantly increased in miscarriage patients as shown in Table 5.

DISCUSSION

Pregnancy is a fruitful event but unfortunately it also ends up with complication like miscarriage in many cases. In the current study, the patients attending hospital with the case of miscarriage are taken into consideration. The mean age of the patients is 28.27±7.27 years. The maximum cases (47, 54.65%) of miscarriage were reported among patients in age group 20-30. A study conducted in western Nepal reported that the maximum number of cases of stillbirth was observed in age group 30-39, which was 200 (40.98%) in number. [4] Another study from china revealed that the maximum cases, i.e. 431 (54.21%), of miscarriage was noted in 28-38 age group of patients. [13] A study from Netherlands reported 36.9% of stillbirth was noted in 30-34 year of age group. [14] In the current study, it was noted that the maximum number (54, 62.79%) of miscarriage was seen in those women, who had normal BMI (18.5-24.9) and 67.44% of miscarriage was seen in mutigravida cases whereas 32.56% was in primigravida. Similarly, Nijkamp JW*et. al*. had reported in his study that the maximum cases, 36.9% of stillbirth was seen in women having normal range BMI (18.5-24.9) but adversely 52.45% of stillbirth was seen in case of primigravida and 47.54% in mutigravida. [14]

The mean value of serum enzymes like GGT, LDH and ADA in patients with miscarriage was noted as 22.67±8.22, 289.6±126.9 and 21.3±9.9 U/l respectively, which was significantly elevated (p=<0.0001, 0.0004 and 0.0179 respectively) than the healthy pregnant control. Similarly, the mean value of SGPT (30.11±6.48 U/l), SGOT (27.91±5.43 U/l) and ALP (113.57±54.88 U/l) in the blood of patients with miscarriage was non-significantly elevated than healthy pregnant women. Similar finding was reported by Fang J in a study conducted among women with missed abortion, which revealed that the serum mean value of GGT among them was noted to be 17.68±9.85 U/l and found to be significantly (p=<.0001) elevated than healthy control. In the same way, the mean value of serum ADA (6.05±3.94 U/l)) in them was observed to be significantly (p=.0459) higher when compared to healthy control, whereas the mean value of LDH (148.05±30.46 U/l) was non-significantly (p=0.3951) elevated.[13] The observed elevations in serum GGT, LDH, and ADA suggest that biochemical markers could serve as potential indicators for early identification of women at risk of miscarriage. Regular monitoring of these biomarkers in pregnant women, especially those with a history of pregnancy loss, could aid in early detection and timely intervention.

While analyzing the thyroid status among the participants with miscarriage, it was noted that subclinical hypothyroidism was seen in 8 (9.3%) patients followed by hypothyroidism in 5 (5.81%) and hyperthyroidism in 2 (2.33%) patients. Euthyroidism was seen in 71 (82.54%) of participants. In a study carried out

in India, it was reported that among the patients with miscarriage in a hospital, 7.84% of them was suffering from overt hypothyroidism followed by subclinical hypothyroidism in 3.92%. Overt hyperthyroidism and subclinical hyperthyroidism was observed in 1.96% of patients with miscarriage for each case, whereas euthyroidism was noted in 84.31%.[15] Another nationwide multicenter prospective cohort research, that included 1025 women who had stillbirths, revealed that 3.90%of patients had subclinical hypothyroidism followed by overt hypothyroidism and subclinical hyperthyroidism in 1.36% and 1.26% of patients respectively.[14] Benhadi N *et. al*. concluded in his study that more maternal TSH levels were associated with an increased chance of child loss.[16]

The high prevalence of subclinical hypothyroidism in our study underscores the importance of routine thyroid function screening during early pregnancy. Early diagnosis and appropriate thyroid hormone supplementation could potentially reduce the risk of miscarriage.

In the present study, the mean value of serum TSH (μIU/ml) in cases of miscarriage with subclinical hypothyroidism, hypothyroidism and hyperthyroidism was reported to be 7.48±1.66, 16.01±6.69 and 0.19±0.03 respectively. A study from USA reported that women with serum TSH >6 mU/l had a significant increased risk for stillbirth [OR 4.40 (95% CI: 1.9-9.5)].[9] Conversely, a study from Bethesda Maryland, USA reported that neither high TSH nor low TSH was found to be associated with risk of miscarriage.[17]A report from United Kingdom revealed that Women with TSH levels between 4.51 and 10 mU/L had a higher chance of miscarriage.[18] Women with hyperthyroidism having low serum TSH level were more likely to experience both early pregnancy loss and late pregnancy stillbirth.[19]

Future research should focus on developing predictive models incorporating these biochemical parameters to enhance risk assessment and guide clinical decision-making.

While comparing other biochemical parameters of patients with miscarriages with healthy pregnant women, it was observed that the mean value of serum glucose, urea, creatinine, sodium, uric acid, total cholesterol, triglyceride and LDL was non-significantly decreased whereas the mean value of serum potassium and HDL was non-significantly increased.

We acknowledge that a confounder analysis was not conducted in this study, which is a limitation. Future studies should incorporate multivariate analyses to account for potential confounding variables such as maternal age, gestational age, and underlying medical conditions that may influence serum enzyme and hormone levels in miscarriage patients.

The data of patients suffering from miscarriages and admitted to a tertiary care hospital is taken from only one center of Nepal, which is also the limitation of the current study. Hence the study should be expanded to a larger cohort with an independent group of participants to validate our findings which requires future studies with a larger sample size and diverse population to strengthen the generalizability of our results.

CONCLUSIONS

The current study showed that the mean value of serum enzymes like GGT, LDH and ADA was significantly elevated whereas the mean value of serum enzymes like SGOT, SGPT and ALP were non-significantly elevated in patients having miscarriage than the healthy pregnant women. A small group of these patients suffering from miscarriage were having alteration in thyroid hormone level, in which the commonest thyroid abnormality was subclinical hypothyroidism followed by hypothyroidism and then hyperthyroidism. There was no significant alteration observed in the mean value of other biochemical parameters in study participants when compared to healthy pregnant individuals.

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CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

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