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Original Research Article

## Prevalence of dual endocrinopathy: hypothyroidism and gestational diabetes mellitus in patients of preeclampsia

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### ABSTRACT

**Background:** Hypertension associated with proteinuria greater than 0.3g/L in a 24-hour urine collection or 1+ by qualitative urine examination, after 20 weeks of gestation is preeclampsia. The present study was conducted to evaluate prevalence of dual endocrinopathy (hypothyroidism and gestational diabetes mellitus) in patients of preeclampsia.

**Methods:** The observational study was conducted within a period of one year from November 2015 to October 2016 in the Department of Obstetrics and Gynaecology SMGS Hospital, GMC, Jammu. A total of 400 patients of preeclampsia were included in the study and underwent serum TSH and oral glucose tolerance test.

**Results:** In this study 32.5% of the preeclampsia patients (130 out of 400) had hypothyroidism, 15.25% patients (61 out of 400 preeclampsia) had gestational diabetes mellitus, 9.75 % patients of preeclampsia had dual endocrinopathy (both hypothyroidism and gestational diabetes mellitus).

**Conclusions:** The current study concluded that dual endocrinopathy (both hypothyroidism and gestational diabetes mellitus) has substantially higher prevalence (9.75%) in the patients of preeclampsia.

**Keywords:** Dual endocrinopathy, Gestational diabetes mellitus, Hypothyroidism, Preeclampsia

### INTRODUCTION

Preeclampsia is identified in 3.9 percent of all pregnancies.<sup>1</sup> The World Health Organization systematically reviews maternal mortality worldwide, and in developed countries, 16 percent of maternal deaths were reported to be due to hypertensive disorders.<sup>2</sup> Importantly more than half of these hypertension related deaths were preventable.<sup>3</sup>

The prevalence of preeclampsia varies in different populations and in different ethnic groups.<sup>4</sup> African American, Native American, Asian, and Hispanic women are at higher risk for gestational diabetes compared with white women.<sup>5</sup> Diabetes is the most common medical

complication of pregnancy. The incidence of diabetes complicating pregnancy increased approximately 40 percent between 1989 and 2004.<sup>6</sup>

Endothelial dysfunction, an early marker of macrovascular disease, is present in pregnancy complicated by impaired glucose tolerance and gestational diabetes mellitus. This could explain, the increased risk for concurrent hypertensive disorders during pregnancy in diabetic women.<sup>7</sup> These patients also have increased neonatal morbidity including fetal demise, neonatal hypoglycemia, jaundice, polycythemia and hypocalcemia.<sup>8</sup> Moreover, maternal diabetes is associated with long term implications on the fetus including increase incidence of future obesity and type II diabetes.

Hypothyroidism is the second most common endocrinopathy during pregnancy, and its incidence range from 2% to 5%. Autoimmune thyroiditis (also known as Hashimoto's thyroiditis) and iatrogenic thyroid gland destruction are the most common etiologies for this endocrinopathy in pregnant women.<sup>9</sup>

Thyroid function is very intimately related to the reproductive performance of women. Pregnant women with hypothyroidism experience a higher rate of first trimester abortions, anemia, post-partum hemorrhage, gestational hypertension and placental abruption.<sup>10</sup>

The pathophysiology correlating hypothyroidism and preeclampsia is not clear. Thyroid hormones seem to be important in placentation and regulation of early pregnancy, partly explaining the association between hypothyroidism and preeclampsia.<sup>11</sup>

It was postulated that effect of preeclampsia on thyroid function during pregnancy is mediated by antiangiogenic factor soluble fms like tyrosine kinase (sFlt-1) which is elevated in patients with preeclampsia.<sup>12</sup>

In utero exposure to maternal hypothyroidism increases the risk for miscarriage, intrauterine death and developmental disorders and lower than average IQ later on in life. Fetuses of pregnant women with uncontrolled hypothyroidism are at a greater risk to develop multinodular goiter and have a higher tendency to be small for gestational age.<sup>13,14</sup>

A better understanding of the association between these conditions may lead to more effective strategies for prenatal care and may ultimately lead to better understanding of their pathophysiology. Thus the present study was conducted to evaluate the prevalence of dual endocrinopathy (hypothyroidism and gestational diabetes mellitus) in patients of preeclampsia.

## METHODS

The present cross sectional observational study was conducted within a period of one year from November 2015 to October 2016 in the Department of Obstetrics and Gynaecology SMGS Hospital, GMC Jammu. Total 400 patients diagnosed with preeclampsia (both inpatient and outpatient) were included in the study. Informed consent was obtained from all women.

### Inclusion criteria

- Age 18-45 years
- Patient with two blood pressure readings of atleast 140 mmHg systolic and/or 90 mmHg diastolic, atleast 6 hours apart after 20<sup>th</sup> week of gestation with proteinuria  $\geq$  1+ by qualitative urine examination or  $\geq$  0.3g/l in a 24-hour urine collection after 20 weeks of gestation.

### Exclusion criteria

- Pregnancy with gestational hypertension, eclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension
- All women with history of renal disease, metabolic disorders and other chronic illnesses during pregnancy
- Multiple pregnancy
- Molar gestation.

### Sample collection

All samples were collected prior to delivery and were sent to hospital laboratory.

Serum TSH levels were measured by chemiluminescence immunoassay (CLIA). The TSH CLIA is based on the principle of a solid phase enzyme linked immunosorbent assay. The following reference ranges of TSH were taken (as recommended by American Thyroid Association 2011).

- First trimester - 0.1 to 2.5 mIU/L
- Second trimester - 0.2 to 3.0 mIU/L
- Third trimester - 0.3 to 3.0 mIU/L.

In all subjects, Oral Glucose Tolerance Test (OGTT) was done with 75 grams anhydrous glucose and plasma glucose was measured as fasting (after an overnight fast of atleast 8 hours), one and two hours. The diagnosis of gestational diabetes mellitus was made when any of the following plasma glucose values were as follows:

- Fasting blood glucose  $\geq$ 92 mg/dl
- Post 1 hr  $\geq$ 180 mg/dl
- Post 2 hr  $\geq$ 153 mg/dl

For the collection of 24 hr urinary sample, the patients were instructed to void the first morning sample and then start collecting urine in a special container for the next 24 hours and the next morning sample was also collected. Patients were advised to avoid dehydration and strenuous exercise.

The study subjects underwent basic investigations including blood group, CBC, RFTs, LFTs, Blood Sugar and special investigations including Urine for Albumin, 24 hour urinary protein, serum TSH and OGTT.

Prior to urine collection all women were carefully instructed on the procedure of collection. Urine for albumin was sent and 24-hour urine collection was started on the first morning after admission to hospital.

### Statistical methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data

editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and Categorical variables were expressed as percentages. Frequency distribution tables and bar charts were used for data presentation. Chi-square test was employed to determine association of dual endocrinopathy with severity of preeclampsia. p-value less than 0.05 was considered statistically significant.

## RESULTS

**Table 1: Age distribution of study patients.**

Age (years)	Number of patients	%
18-24	94	23.50
25-29	180	45.00
30-34	98	24.50
≥ 35	28	7.00
<b>Total</b>	<b>400</b>	<b>100</b>

Mean age of patients was Mean±SD = 27.4±4.21 years.

**Table 2: Distribution of study patients as per gravidity.**

Gravidity	Number of patients	%
Primigravida	247	61.75
Multigravida	153	38.25
<b>Total</b>	<b>400</b>	<b>100</b>

According to the study and Table 2 showing distribution of study patients as per gravidity, majority of the patients 61.25% (247 out of 400) in the study were primigravida, followed by 38.25% (153 out of 400) were multigravida.

**Table 3: Gestational age (weeks) at diagnosis of preeclampsia among study patients.**

Gestational age (weeks)	Number of patients	%
< 32	37	9.25
32-36	122	30.50
> 36	241	60.25
<b>Total</b>	<b>400</b>	<b>100</b>

Mean ± SD (weeks) = 36.7±3.95 weeks

Table 3 shows gestational age (weeks) at diagnosis of preeclampsia among study patients. In our study we divided the patients into 3 groups according to period of gestation, <32 weeks, 32-36 weeks, >36 weeks. According to the above table showing gestational age (weeks), majority of the patients 60.25% (241 out of 400) were more than 36 weeks period of gestation followed by 30.50% (122 out of 400) of the patients in the 32-36 week group. Only 9.25% of patients (37 out of 400) were in the < 32 week group.

Table 4 shows distribution of study patients as per systolic blood pressure. In present study majority of the patients, 40.25% (161 out of 400) had systolic BP 140-149 mmHg, followed by 35.50 % (142 out of 400) had

Systolic BP 150-160 mmHg. Least number of patients 24.25% (97 out of 400) had systolic BP 150-160 mmHg.

Mean systolic BP of patients in present study was 153.9 mmHg with SD of 10.76 mmHg.

**Table 4: Distribution of study patients as per systolic blood pressure.**

Systolic BP (mmHg)	Number of patients	%
140-149	161	40.25
150-160	142	35.50
> 160	97	24.25
<b>Total</b>	<b>400</b>	<b>100</b>

Mean ±SD (mmHg) = 153.9±10.76

**Table 5: Distribution of study patients as per diastolic blood pressure.**

Diastolic BP (mmHg)	Number of patients	%
90-99	110	27.50
100-110	249	62.25
> 110	41	10.25
<b>Total</b>	<b>400</b>	<b>100</b>

Mean±SD = 103.7±8.04

Table 5 shows distribution of study patients as per diastolic blood pressure, majority of the patients, 62.25% (249 out of 400) had Diastolic BP 100 - 110 mmHg, followed by 27.50% (110 out of 400) had Diastolic BP 90-99 mmHg. While only 10.25% (41 out of 400) had Diastolic BP > 110 mmHg.

Mean diastolic BP of patients was 103.7 mmHg with SD of 8.04 mmHg.

**Table 6: Prevalence of hypothyroidism in study patients.**

Hypothyroidism	Number of patients	%
Present	130	32.50
Absent	270	67.50
<b>Total</b>	<b>400</b>	<b>100</b>

Table 6 shows the prevalence of hypothyroidism in study patients. In the study, 32.5% (130 out of 400) had hypothyroidism while 67.50% (270 out of 400) did not have hypothyroidism. According to the study, mean serum TSH was 2.54±2.27 mIU/L.

**Table 7: Prevalence of GDM in study patients.**

Gestational diabetes mellitus (interpreted by positive OGTT)	Number of patients	%
Present	61	15.25
Absent	339	84.75
<b>Total</b>	<b>400</b>	<b>100</b>

According to Table 9, showing prevalence of GDM in study patients, 15.25% (61 out of 400) patients had gestational diabetes mellitus and 84.75% (339 out of 400) did not have gestational diabetes mellitus.

**Table 8: Prevalence of dual endocrinopathy (hypothyroidism and gestational diabetes mellitus) in study patients.**

Dual endocrinopathy	Number of patients	%
Present	39	9.75
Absent	361	90.25
<b>Total</b>	<b>400</b>	<b>100</b>

According to Table 8, 9.75% (39 out of 400) patients had dual endocrinopathy (both hypothyroidism and gestational diabetes mellitus) while 90.25% (361 out of 400) did not have dual endocrinopathy (both hypothyroidism and gestational diabetes mellitus).

## DISCUSSION

Preeclampsia is a multiorgan disorder of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. Predisposing factors for this deadly disorder are nulliparity, black race, younger age, low socioeconomic status, obesity, diabetes. Although there are no reliable, valid and economic screening tests available for predicting this pregnancy related disease, some studies have shown association between the levels of thyroid hormones and development of preeclampsia. Preeclampsia women show high incidence of hypothyroidism that might correlate with the severity of preeclampsia.<sup>15</sup> Different studies have shown that mean serum TSH were significantly elevated in preeclampsia women.<sup>16</sup> Some studies showed that serum levels of serum TSH were increased in women with severe preeclampsia when compared to mild preeclampsia.<sup>17</sup>

Gestational diabetes and preeclampsia have been postulated to be an early expression of metabolic syndrome. Wendland EM et al in 2008 conducted a study according to which gestational diabetes and preeclampsia have a similar profile of risk factors.<sup>18</sup> Taking into account that the global prevalence of Gestational Diabetes Mellitus has increased over the past decades this would certainly result in increased number of pregnant women with diabetes.

There is a need to focus on the combined morbidity of hypothyroidism and gestational diabetes mellitus in the patients of preeclampsia Therefore the early identification and treatment of hypothyroidism and gestational diabetes mellitus may affect the occurrence and severity of the morbidity and mortality associated with preeclampsia.

Strength of the study was that it was an observational cross sectional study, and sample size was good (n=400) while limitations of the study was that no controls were taken in the study and the study could not establish the

correlation between dual endocrinopathy and preeclampsia due to lack of controls.

## CONCLUSION

The current study concluded that dual endocrinopathy (both hypothyroidism and gestational diabetes mellitus) has substantially higher prevalence (9.75%) in the patients of preeclampsia. Therefore, the current study emphasises to manage preeclampsia pregnancies with extra care. Early identification and appropriate measures might affect the occurrence and severity of morbidity associated with preeclampsia.

The study is of a novel kind which has laid down a strong basis to look for dual endocrinopathy in patients of preeclampsia.

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