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Original Article

An Analytical Study on Biochemical Values in Women with First Trimester Pregnancy

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Abstract

Background: Routine serum biochemical and ultrasound examinations are performed in women in the first trimester of pregnancy. In addition, antenatal diagnosis is usually based on clinical risk factors, previous placenta previa, previous cesarean delivery or uterine surgery, previous uterine curettage, advanced maternal age, and associated ultrasound findings.

Aim of the Study: This study aims to analyze the results of routine serum biochemical tests and ultrasound examination during the first trimester, in the diagnosis of paternal, placental, and fetal abnormalities.

Materials and Methods: A total of 384 women in the first trimester pregnancy with gestational age between 11 and 14 weeks biochemical and ultrasound examination. The collected was analyzed to find the abnormalities of maternal, placental, and fetal diseases.

Observations: 384 antenatal women of OBG department were included. Age groups were 20–40 years with a mean age of 26.74 ± 3.8. The mean height was 157 ± 4.7 cm. The mean weight was 59.30 ± 4.50 kg. The mean BMI was 22.1 ± 1.40. Pap–HPV test was normal in 99/104 (95.19%) of the women. The mean FBS was 84.60 ± 4.60. The mean glycated Hb1Ac value was 04.32 ± 0.46. TSH values were in the range of 0.56–4.9.

Discussion: women in first trimester pregnancy undergo a battery of biochemical tests, serological tests which are directed to diagnose certain chromosomal disorders, abnormalities in the fetus, placenta, and maternal diseases. In the present study, BMI was high >25 kg/m^2 in 52 patients (13.4%) and one of the patients developed complications during pregnancy. The Institute of Medicine published recommended weight gains by pre-pregnancy BMI which have been the standard for subsequent research.[11] The recommendations are for BMI < 19.8 kg/m^2 total weight gain between 12.5 and 18 kg; BMI = 19.8–26.0 kg/m^2 total weight gain between 11.5 and 16 kg; BMI > 26.0–29.0 kg/m^2 total weight gain between 7.0 and 11.5 kg, and for BMI > 29.0 kg/m^2.

Conclusions: Screening antenatal women with biochemical tests during first-trimester combined with screening at 11 weeks of pregnancy is beneficial to the mother and the infant as both step wise sequential screening and fully integrated screening have high rates of detection of various endocrine, cardiovascular diseases and renal of the mother and and congenital diseases of the fetus. Even though there is always possibility of false positive test results it outweighs the benfit.

Key words: Fetal, Human chorionic gonadotropin, Maternal, Placenta, Pregnancy, Ultrasound

INTRODUCTION

Serum biochemical markers are used to assess maternal, placental, and fetal health. They help to diagnose and monitor maternal conditions such as gestational diabetes and pre-eclampsia, trophoblastic diseases, and fetal chromosomal abnormalities such as Down's syndrome. These biochemical and hormonal tests constitute only one aspect of obstetric care. They should be used together with clinical findings and imaging, particularly ultrasonography.[1] The most common problems of pregnancy that should be excluded at this gestational age is gestational diabetes and pre-eclampsia.[2] The prevalence of gestational diabetes mellitus ranges from 1 to 14% depending on the populations studied.[1] Regular screening for gestational diabetes mellitus during first trimester enables early intervention which results in significant improvements in both fetal and maternal outcomes.[3] Pre-eclampsia occurs typically in the third

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trimester and affects 4–8% of pregnancies.[4] Placental health could be assessed by ultrasound examination, serum human chorionic gonadotropin (HCG) levels, beta-HCG (β-HCG) levels, and urinary HCG levels.[5] In assessing the fetal health during pregnancy, especially in the first and second trimesters to identify neural tube defects ultrasound examination is useful. In addition, estimation of β-HCG, alpha-fetoprotein (AFP), pregnancy-associated plasma protein-A (PAPP-A), and assessment of nuchal thickness of the fetus helps in the diagnosis of Down's syndrome.[6] The nuchal thickness is increased in Down's syndrome which can be detected in approximately 70% of cases by ultrasound in experienced centers.[7] In combination with biochemical markers, the detection rate increases to 85–90%.[8] Abnormal results can be followed up with direct karyotyping using chorionic villus sampling, but this carries a 0.5–1.0% risk of pregnancy loss in the first trimester. Recent advances show that using maternal growth hormone and insulin-like growth factor levels during the first and second trimester of pregnancy as predictors of fetal outcome is possible, but these are yet to be of routine clinical use.[9] With this background, the present study was conducted in a tertiary teaching hospital to identify the prevalence of abnormalities of placenta, fetus, and maternal diseases.

Aim of the Study

This study aims to analyze the results of routine serum biochemical tests and ultrasound examination during the first trimester, in the diagnosis of paternal, placental, and fetal abnormalities.

Institute of Study

The study was conducted at Kannur Medical College, Anjarakandy, Kannur, Kerala.

Period of Study

The period of study was from May 2014 to April 2016.

MATERIALS AND METHODS

A total of 384 women who were attending for antenatal checkups with the gestational age range of 11–14 weeks were included in the study. An Ethical Committee clearance was obtained from the Institutional Ethical Committee and standard pro forma approved by the ethical committee was used in the study. All the women were elicited about their clinical history followed by clinical examination. The presence of maternal or fetal abnormalities was noted. The following maternal serum biochemical tests were done: Pregnancy test (HCG), blood typing and red blood cells antibody screen, Pap test and human papillomavirus (HPV) testing, urine screen for glucose and/or protein, blood glucose, and hemoglobin A1c (HbAlc) test - for women at risk of Type 2 diabetes, thyroid-stimulating hormone (TSH) - for women with a history of thyroid disease, human immunodeficiency virus screening, gonorrhea, chlamydia, and syphilis tests, hepatitis b and hepatitis c screening, and varicella zoster virus testing - to check for immunity to chickenpox; less routine, maternal serum free β-HCG, and PAPP-A. AFP is done women who have previous stillbirths. Demographic data were collected. All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

A total of 384 women attending the Department of Obstetrics and Gynecology of a tertiary teaching hospital were included in the study. The women belonged to the age groups of 20–40 years with a mean age of 26.74 ± 3.8. The mean height was 157 ± 4.7 cm. The mean weight was 59.30 ± 4.50 kg. 87/384 (22.65%) belonged to high-income group, 178 (46.35%) belonged to middle-income group, and 119/384 (30.98%) belonged to low-income group. 344/384 (89.58%) were educated above 12th standard and the remaining 40 were (11.42%) below 12th standard [Table 1].

The laboratory data and ultrasound findings are tabulated in Table 2. The mean body mass index (BMI) value was 22.1 ± 1.40 with a range of 20.2–46.2 kg/m^2. All the patients in this study had a positive pregnancy test [Table 2]. The distribution of blood groups and Rh typing is tabulated in Table 2. The Pap–HPV test was done in 104 patients and showed normal in 99/104 (95.19%) of the women. Urine for sugar and proteins was abnormal in 43/384 (11.19%) and 68/384 (17.70%) patients. The mean fasting blood sugar (FBS) value was 84.60 ± 4.60 with a range of 72–110. Among the women who showed abnormal FBS levels, 52/384 (13.54%) further tests were done to exclude Type 2 diabetes mellitus and none of them had diabetes. The mean glycated Hb1Ac value in this study was 04.32 ± 0.46 with a range of 4.9–5.9. As the incidence of gestational diabetes, during pregnancy period is less likely if the Hb1Ac value is <5.3 in this study, it was taken as a cut off value.[10] The TSH values were in the range of 0.56–4.9, with a mean value of 2.65 ± 1.10.

Table 1: The demographic data in the study (*n*=384)

Observation	Mean values	Percentage
Age (years)	26.74±3.8	100
Below 35	25.10±1.30	75.26
Above 35	33.50±2.60	24.73
Height (cm)	157±4.7	-
Weight (kg)	59.30±4.50	-
Low income	87	22.65
Middle income	178	46.35
High income	119	3.98
Above 12th Std.	344	89.58
Below 12th Std.	40	11.42

Table 2: The ultrasound and biochemical test values (*n*=384)

Serum biochemical tests number performed	Range mean±SD	Number of normal tests (%)	Number of abnormal tests (%)
BMI- kg.m^2	20.2–46.2 kg/m^2, 22.1±1.40	332–86.45	52–13.54
Pregnancy test-HCG	--	positive in 100	-
Blood group Rh type-384 (%)			
A	186–48.43		
B	121–31.51		
AB	21–05.46	--	--
O	56–14.58		
Rh+ve	96.87		
Rh– ve	03.21		
Pap-HPV test-104	--	99–95.19	05–04.8
Urine- sugar- 384	--	341–88.80	43–11.19
Urine- proteins- 384	--	316–82.29	68–17.70
Fasting blood glucose-384	72–110, 84.60±4.60	332–86.45	52–13.54
HbA1c-255	4.9–5.9, 04.32–0.46		
<5.3	5.3–.9, 5.5±0.42	238–93.33	17–6.66
>5.3	5.3–6.10, 5.8±0.48		
TSH-384	0.56–4.9, 2.65±1.10		
<5.3	1.2–3.6, 2.45±0.06	361–94.01	23–5.98
more than 5.3	5.3–6.9, 5.7±0.1.10		
CBC-384	--	294–76.56	90–23.43
HIV-384	--	379–98.69	05–1.3
Hepatitis B- 316	--	306–96.83	10–3.16
Hepatitis C	--	382–99.47	02–0.52
VDRL-384	--	379–98.60	05–1.30
Gonorrhea-192	--	187–97.39	05–2.60
Rubella-124	--	118–95.16	06–04.8
CMV-96	--	92–95.83	04.16
β-HCG-265			
0.05–2.0 MOM-254	0.05–2.0, 0.16±0.07	95.84	04.15
>2.0 MOM-11	2.0–7.18, 2.92±0.75		
PAPP-A-172			
<0.05 MOM- 12	0.042–0.05, 0.43±0.03	160–93.02	12–06.97
≥0.05 MOM- 160	0.05–0.062, 0.55±0.04		
AFP-183			
0.05–2.0 MOM-176	0.05–0.20, 0.14±0.50	176–96.17	07–3.82
>2.0 MOM-07	2.0–4.8, 2.70±1.10		

TSH: Thyroid-stimulating hormone, HIV: Human Immunodeficiency Virus, CMV: Cytomegalovirus, CRL: Crown-rump length, PAPP-A: Pregnancy-associated plasma protein-A, HbA1c: Hemoglobin A1c, HPV: Human papillomavirus, SD: Standard deviation, AFP: Alpha-fetoprotein, β-HCG: Beta-human chorionic gonadotropin, VDRL: Veneriological diseases research Laboratory

DISCUSSION

Women in first trimester pregnancy undergo a battery of biochemical tests, serological tests which are directed to diagnose certain chromosomal disorders, abnormalities in the fetus, placenta, and maternal diseases. In the present study, BMI was high >25 kg/m^2 in 52 patients (13.4%) and one of the patients developed complications during pregnancy. The Institute of Medicine published recommended weight gains by pre-pregnancy BMI which have been the standard for subsequent research.[11] The recommendations are for BMI < 19.8 kg/m^2 total weight gain between 12.5 and 18 kg; BMI = 19.8–26.0 kg/m^2 total weight gain between 11.5 and 16 kg; BMI > 26.0–29.0 kg/m^2 total weight gain between 7.0 and 11.5 kg, and for BMI > 29.0 kg/m^2 total weight gain of 7.0 kg. In the present study, BMI was >26.0–29.0 kg/m^2 total weight gain between 7.0 and 11.5 kg. Pregnancy tests were positive in all the women. Pap test was positive in 5/384 (04.8%) and the tests were a false negative test as the Pap tests were negative after delivery. The mean FBS value in this study was 84.60 ± 0.46 with a range of 71–110 mg%. Abnormal FBS levels of more than 110 mg% were noted in 53/384 (13.54%) patients and their corresponding Hb1Ac levels were normal in 34/52 (65.38%) of the women of <5.3. The remaining 19 women had normal delivery and no fetal abnormalities in the study. The mean Hb1Ac value was 04.32 ± 0.46 with a range of 4.9–5.9 in this study. Review of literature shows that glucose variability, characterized by extreme glucose excursions, may overlap with HbA1c levels giving rise to a risk of diabetes-related complications.[12,13] Patil *et al.* postulated an association between maternal hyperglycemia-induced oxygen free radical overproduction and fetal abnormalities, with the onset of diabetes-related embryopathy.[14] In addition to FBS, HbA1c is a useful parameter in assessing the metabolic regulation in pregnant women.[15] Thus, supplementation with HbA1c, as is common outside pregnancy, seems appropriate. The TSH values were in the range of 0.56–4.9, with a mean value of

2.65 ± 1.10. <3.5 mIU/L was seen 94.01% of the women and >3.5 mIU/L was observed in 23/384 (05.98%) women. The median levels of TSH during gestational weeks of 7–12 mean (1.47 mIU/L) were significantly than that of gestational weeks 4–6 values; (2.15 mIU/L).[16] The values of PAPP-A more than or equal to 0.5 MOM is considered normal, while levels <0.5 MOM are marked as low. In this study, the PAPP-A levels are ≥0.05 MOM - 160 in 160/172 women. There were 12/172 women who had undergone PAPP-A showing <0.05 MOM. Low maternal serum PAPP-A, at 11–13 weeks of gestation, is associated with stillbirth, infant death, intrauterine growth restriction, preterm birth, and pre-eclampsia in chromosomally normal fetuses, while a raised nuchal translucency is associated with specific structural abnormalities and genetic syndromes.[17] There are possibilities of these tests being false positive but the prevalence of false positive nature falls with the increasing maternal age.[18] Basically, PAPP-A is a large glycoprotein produced by the placenta and decidua having many functions including prevention of recognition of the fetus by the maternal immune system, matrix mineralization, and angiogenesis. Hence, a low PAPP-A is may lead to poor early placentation resulting in complications such as fetal growth restriction, fetal demise, preterm birth, and pre-eclampsia in the third trimester.[19] In a study b Morssink *et al.*,[20] 35% of the pregnant women with unexplained increased AFP level had at least one adverse perinatal outcome.[21] In the present study, there were seven abnormal test results in AFP values with mean value of 2.70 ± 1.10 and among them two patients had stillbirths [Table 2]. The adverse perinatal outcomes may be due to placental function disorders in patients with unexplained increase of maternal serum markers. Elevation of AFP was related to increased transition from fetomaternal circulation due to the placental fetomaternal surface damage.[22] Abnormal increased HCG levels were observed in 11 patients in this study with a mean value of 2.92 ± 0.75 [Table 2] which are thought to be due to decreased placental perfusion related to low oxidation stemming, cytotrophoblasts abnormal placentation induced by hypoxia were shown in the histological studies conducted by Liu *et al.*;[23] Studies also show low birth weight in infants born to mothers with high level of AFP.[23]

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