Open Access

Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study

Haymanot Tewabe^{1*}, Mistire Wolde¹

¹Department of medical laboratory Sciences, Collage of Health Science, Addis Ababa University, Ethiopia

*Corresponding Author: Haymanot Tewabe, Department of medical laboratory Sciences, Collage of Health Science, Addis Ababa University, Ethiopia, Email: haymanottewabe@gmail.com

Received Date: 28-04-2020, Accepted Date: 04-09-2020, Published Date: 11-09-2020

Copyright© 2020 by Tewabe H, et al. All rights reserved under CC BY-NC-ND. This is an open access article distributed under the terms of the Creative Commons Attribution License, which provides freedom to read, share, copy and redistribution of material in any of the medium, provided with the original author and source are credited.

Abstract

Background: Pregnancy-induced hypertension has remained a significant global public health threat in both developed and developing countries. Therefore, this study aimed to assess renal function tests and serum total protein among pregnant women with pregnancy-induced hypertension.

Methods: A case-control study was done on 200 pregnant women, 100 with pregnancy-induced hypertension (case group) and 100 normotensives (control group) at Asrade Zewudie Memorable Primary hospital Gojjam, Ethiopia, from January 24, 2020 to April 30, 2020. 5 ml of venous blood was collected on the SST test tube and analysed for serum lipid profile, renal function test, and serum total protein. The analysis was done by using SPSS software (version 20.0). The level significance was set at a 95% confidence interval (p-value is less than 0.05 was considered clinically significant).

Results: There was a significant increase in blood urea, and serum creatinine ($p < 0.05$) in case groups as compared to normal groups ($p < 0.05$). The elevation of serum total protein was not significant ($p > 0.05$). The outcome of the final multiple logistic regression model indicated that factors like Body Mass Index (BMI), habits of doing scheduled exercise, habit of drinking

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. Jour Clin Med Res. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

alcohol, habit of fruit consumption, trimester and gravidity were having significant association with high blood urea, and serum creatinine results of the study participants.

Conclusion: It might be better, if clinicians to use renal function tests as screening test than requesting other costly tests. Further studies in different areas of the country by considering life style variation also recommended.

Keywords

Serum Total Protein, Renal Function Test, PIH, Ethiopia, Gestational Hypertension

Abbreviations

AOR: Adjusted Odd Ratio, BMI: Body Mass Index, CDC: Center of Disease Control Center, DBP: Diastolic Blood Pressure, HDL: High-Density Lipoprotein, HDP: Hypertension Disorder of Pregnancy, IQC: Internal Quality Control, LDL: Low-Density Lipoprotein, PIH: Pregnancy Induced Hypertension, SBP: Systolic Blood Pressure, SOP: Standard Operating Procedures, SST: Serum Separated Tube, TC: Total Cholesterol, TG: Triglyceride, WHO: World Health Organization

Introduction

Pregnancy-Induced Hypertension (PIH) also referred to as Gestational Hypertension (GH), is a multifactorial condition occurring during pregnancy, usually appears after the 20th week of gestation and characterized by high blood pressure (over 140/90) present during pregnancy [1,2]. PIH can lead to more serious maternal complications called preeclampsia, which is characterized by a hypertensive state, systemic vascular disturbances, and reduced blood flow to multiple organs both for mothers and babies. If left untreated can prevent the placenta from getting enough blood and this limit the baby from getting enough oxygen and food [3-7].

Pregnancy-induced hypertension is classified into three main classes. The first one is Chronic Hypertension which is defined by women who have high blood pressure (over 140/90) before pregnancy, early in pregnancy (before 20 weeks), or persisting longer than 12 weeks after delivery. The second class is Gestational Hypertension characterized by a woman with high blood pressure that develops after 20 weeks' gestation in pregnancy and goes away after delivery. In addition, the third one Preeclampsia which is defined both by chronic and gestational hypertension can lead to this severe condition after 20 weeks of pregnancy [3,4].

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. Jour Clin Med Res. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

Pre-eclampsia is a theory of complication during pregnancy, where the exact etiology is still unknown [8-18]. Serum total protein is important in regulating blood volume by maintaining the oncotic pressure (colloid osmotic pressure) of the blood compartment. So alteration level of total protein can be identified as an early sign in developing preeclampsia, and many clinicians consider serum protein level as one of the important laboratory findings in the treatment of hypertensive disorders in pregnancy [19]. During physiological pregnancy, in most women's urinary protein excretion normally increases from its normal value because of increased GFR, the permeability of the glomerular basement membrane and reduction of tubular reabsorption of filtered protein, but if it exceeds 300 mg/24 hours, it is abnormal [20,21].

Proteinuria in pregnancy can indicate primary preeclampsia, renal disease, or renal disease secondary to systemic disorders, such as diabetes or primary hypertension [20,22]. Additional information on pregnancy-related changes in renal function and the urinary tract can be found separately [23]. During the assessment of a pregnant woman with proteinuria, determination of the time of onset and quantity of proteinuria should be considered and if the onset of proteinuria is also continuing for more than 20 weeks after gestation, preeclampsia is likely [24]. On the other hand, if the onset of proteinuria is before 20 weeks gestation, the cause may be due to primary or secondary renal disease [25]. In women with chronic hypertension, even mild proteinuria (50 to 300 mg/day) is associated with adverse pregnancy outcomes. Urinary protein excretion >3 g/day can be seen in preeclampsia [24,26]. With the dramatic hormonal and hemodynamic changes of pregnancy, renal function is altered and these changes must be considered when assessing renal function in pregnancy and the choice of medications provided through parturition. Renal function and filtration are also affected in preeclampsia, and recent advances have greatly expanded our understanding of the pathophysiological mechanisms of this pregnancy-related renal syndrome [27].

Hypertensive disorders of pregnancy are a global public health concern both in developed and developing countries. However, evidence regarding the risk factors of hypertensive disorders of pregnancy is limited particularly in Ethiopia. As many studies indicated, in Ethiopia the incidence of PIH is rapidly increased from time to time and increase the medical complication both on the mortality of mother and fetus [28-41]. But most of the studies done in Africa especially in Ethiopia mainly focuses on the prevalence of pregnancy induced hypertension. Therefore, the main aim of the present study was to assess renal function, and serum total protein among pregnant women with pregnancy-induced hypertension attending in Asrade Zewudie Memorable hospital (ASZMPH), Gojjam, Ethiopia: Case-control study, 2020 [42-48].

Materials and Methods

Study Area/ Setting

The study was conducted at Asrade Zewudie Memorable Primary Hospital, the governmental hospital located in Burie town, west Gojjam (Mirab Gojjam), Amhara, Ethiopia. The town is found 400 km North-west of Addis Ababa, the capital city of Ethiopia and 148 km south-west of the Amhara Regional State capital, Bahir Dar.

Study Design and Period

The study was a prospective case-control study from January 24, 2020, to March 26, 2020 and analysis was done in the period between March 29, 2020 to April 30, 2020.

Population

Source Population

The study population was all pregnant mothers attending the maternity centers of Asrade Zewudie Memorable Primary Hospital (AZMPH), Gojjam, Ethiopia during the study period.

Study Population

The study population was consisting of a total of 200 pregnant women with a gestational period of greater than 20 weeks (100 for each group) divided into two groups. Ages ranged from 18-to-45 years. Obstetricians classify the gestational weeks into three trimesters which were first trimester (<12 weeks), second trimester (12-24 weeks) and third trimester (24-42 weeks). A case group was pregnant mothers with PIH ($> 140/90$ mmHg) and a control group was pregnant woman in the maternity wards of the hospital and who did not have a diagnosis of hypertensive disorders (BP $< 140/90$ mmHg).

Inclusion and Exclusion Criteria

Inclusion Criteria

All pregnant women in the maternity ward with a gestational age greater than 20 weeks were prepared for the two groups.

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. Jour Clin Med Res. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

Exclusion Criteria

Pregnant women with a gestational age of fewer than 20 weeks, having a history of chronic hypertension before pregnancy, with complicated problems and unable to take a blood sample, mothers with previously or currently renal disorders, with the previous history of a liver disorder, cardiac disease, with a history of dyslipidemia, who are on treatment of lipidemic drugs, with a previous or current history of HIV, who are obesity, below 18 years old and mothers greater than 45 years old, who were not voluntary to give blood samples and who have smoking were excluded from the study [49,50].

Study Variables

Dependent Variables

Lipid profile and PIH

Independent Variables

Age, drinking alcohol, nutritional status, residence, educational status, occupation, income status, week of gestation, BMI, parity, gravidity, pregnancy status, gestational age, and trimester.

Sample Size Calculation and Sampling Method

Sample Size Calculation

The sample size was calculated using a 95% confidence interval with 0.05 precision. Different previous studies which are focusing on the assessment of lipid profile with PIH, serum total protein with PIH and prevalence of PIH in Ethiopia was carefully assessed and a systematic study conducted on the aim of identification risk factor and prevalence of pregnancy-induced hypertension, entitled with a prevalence of hypertensive disorders of pregnancy in Ethiopia was used to calculate the minimum required sample size for this study. The systematic study reported that the overall prevalence of PIH in Ethiopia was 6.29 % [48].

The sample size was calculated based on the comparison of proportions for matched case-control study using $n = Z^2 P(1-P)/d^2$. $n = 90.58 = 91$ then $n = 100$

Sampling Method

A prospective convenient sampling method was used for this study. The data was collected until the required sample size was achieved.

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. Jour Clin Med Res. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

Measurement and Data Collection

Data Collection Procedure

The data was collected by using a pre-tested structured questionnaire. A detailed history of present pregnancy, history of diabetes, renal disorders, cardiac disorder, thyroid disorders and family history regarding preeclampsia was taken by the physician before enrolling patients for the study. The BMI was calculated in the maternity ward and those who are obese were excluded from the study. The actual data was collected by face to face interviews, measurements and reviewing medical records of the mother using a pretested structured questionnaire by trained data collectors. The participants were allowed to sit and rest for about 5 minutes [51-54]. The blood pressure reading was taken while the woman seated in the upright position and supine position using a mercury sphygmomanometer apparatus and for referred women, BP was taken from referral form. Elevated blood pressure was repeated after at least 4 hours.

General Sample Collection Procedures

Following written informed consent, 4-5 ml of blood sample from pregnant mothers who have eaten food within two hours was collected after a minimum of 3 hours fasting. The whole blood sample was stored at room temperature for 10-20 minutes until it is coagulated. Then the blood sample was transported to the laboratory department and centrifuged at 3,000 revolutions per minute for 5 minutes to separate the serum from the red cells. After centrifugation, the sample was immediately analysed by the principal investigator in the laboratory department of the clinical chemistry section at AZMPH.

Data Quality Assurance

Data Quality Control Measures

The quality of the data was assured by using a validated and pretested questionnaire. Before the actual data collection, pre-testing was done on 5% of the total study subjects. SOPS was used for each test. All the three analytical phases was carefully checked.

Data Analysis and Interpretation

Data was analyzed using SPSS version 20.0. Categorical variables were analysed using the chi-square and continuous variables were analyzed with multiple logistic regression. Pearson's

correlation was used to find a correlation between RFT with PIH, and serum total protein with PIH. The level of statistical significance was set at a 95% confidence interval. A p-value of less than 0.05 was considered statistically clinically significant. Finally, the result was presented using tables and other narrative form.

Ethical Considerations

The study was conducted after ethical approval was obtained from the Research and Ethics Institutional Review Board of Addis Ababa University College of Health Science, Department of Medical Laboratory Science. Informed written consent was also obtained from each study participant before the actual data collection.

Dissemination of the Result

The result is submitted to Addis Ababa University, College of Health Science, Department of Medical Laboratory Science. Identification of association was one basic thing for physicians who care for pregnant women for the management of PIH easily by using analysis of these analytes rather than requesting other costly and complicated tests. In addition, the result of the study finding may be used as baseline information for further studies.

Results

A total of 200 pregnant women were participated in the study. The study participants were classifying into two as case and control groups. Control groups were pregnant women without PIH, whereas case groups were pregnant women with PIH. Each group contains 100 study participants. Out of 200 study participants, 140 (70 %) were from antenatal clinics and the rest 60 (30 %) were from other maternity wards like a delivery ward, postnatal care ward, and high-risk maternity wards. Demographic data related to the studied population was noted and tabulated in Table 1.

The age range of total pregnant women who participated in this study was from 18-41 years with a mean of 29.07 ± 5.29 years. The mean age of pregnant women with PIH and pregnant women without PIH was 28.23 ± 5.39 years and 29.9 ± 5.07 years respectively. Most of the study participants of both the control and case group found in the age range 25-29.9 years with a percentage of 34 % and 43% respectively. The percentage of pregnant women in the age group > 40 years contained the lowest percentage which is 4 % in each group. From a total of 200 pregnant women participated in this study, 142 (71 %) were from urban, 142 (71 %) were literate, 151 (75.5%) husbands were literate, 104 (52%) of them were economically in the

middle-income class, 83 (41.5%) were governmental employers (Table 1), most of the study participants were multiparous (55%), 193 (96.5 %) were married, 110 (77.5%) of them were in the third trimester, and 125 (62.5%) were had a gestational week of from 20 to 37 weeks (Table 2, 3).

Both case and control groups had almost similar age distribution which aids the study to compare other factors variations in the two groups by maintaining nearly similar parties between groups (SD 5.07 and 5.4 respectively). Blood pressure is the main variable for this study to classify groups and parameters. In this study the distribution of diastolic and systolic blood pressure in control groups was less disperse than that of the case groups (70.0 ± 8.8 and 115.0 ± 9.03 and 104.7 ± 15.2 and 154.0 ± 15.6 respectively) (Table 1).

Parameters		Control	Cases	Total	p-value
Age range of participants (in years)	< 25 years	22	16		0.068
	25- 29.9 years	43	34		
	30- 34.9 years	20	28		
	35- 39.9 years	11	18		
	> 40 years	4	4		
BMI	< 17.3 kg/m ²	9	8		0.001
	18.5- 24.9 kg/m ²	91	72		
	25- 29.9 kg/m ²	0	20		
DBP in mmHg (mean + SD)		70.0 ± 8.8	104.7 ± 15.2	< .001	
SBP in mmHg (mean + SD)		115.0 ±9.0	154.0 ± 15.6	< .001	
Resident	Urban	69 (69 %)	73 (73 %)	142 (71 %)	0.533
	Rural	31 (31 %)	27 (27 %)	58 (29 %)	
Educational status of participants	Illiterate	25 (25%)	33 (33 %)	58 (29 %)	0.009
	Up to 12 th	24 (24 %)	7 (7%)	31 (15.5%)	
	Diploma	17 (14 %)	24 (24 %)	41 (20.5%)	
	Degree and above	34 (34 %)	36 (36 %)	70 (35 %)	
Occupational status of mothers	House wife	29 (29 %)	26 (26 %)	55 (22.5 %)	0.680
	Governmental	43 (43 %)	40 (40 %)	83 (41.5 %)	
	NGO	12 (12 %)	18 (18 %)	30 (15 %)	
	Farmer	16 (16 %)	16 (16 %)	32 (16 %)	
Monthly income of study participants	Low level (< 793)	18 (18%)	19 (19%)	37 (37%)	0.010
	Middle (793 -2805)	39 (39%)	20 (20%)	59 (59%)	
	High income (>2805)	43 (43%)	61 (61%)	104 (52%)	
BMI = Body Mass Index, DBP= Diastolic Blood Pressure, NGO= Nongovernmental Organization, PIH= Pregnancy Induced Hypertension, SD = Standard Deviation, SBP = Systolic Blood Pressure					

Table1: Blood pressure results and demographic factor distribution of study participants both control and case groups.

Most of the study participants in both groups were from an urban resident (69 % and 73 %), were degree and above holders (34 % and 26 %), and were governmental employers (43 % and 40 %). The highest percentage of the educational status of the husbands of the pregnant women was degree and above holders in both case and control groups (50 % and 52 %: respectively) and 51% out of the total participants. Changes in demographic factors like income status and educational status in case groups were significant as compared to controls (P-value < 0.05), and changes like occupation and residence were not significant as compared to controls (P-value >0.05) (Table 1). So depends on this study finding, pregnant women's with higher income level have greater chance to develop PIH (P-value = 0.010) (Table 1).

Mean BP (both SBP and DBP) was significantly increased in hypertensive pregnant women as compared to that in normotensive pregnant women (104.70/154.00 mmHg and 74.75/ 112.75 mmHg, respectively). The consistency of high SBP/DBP was maintained throughout the whole pregnancy period in pregnant women with PIH when directly compared to SBP/DBP of normotensive pregnant women. The finding shows that the distribution blood pressure (both DBP and SBP) was more dispersed in the case group than the normal group with a standard deviation of 15.2/8.8 and 15.6/9.03 respectively (Table 1). Most of the study participants were within normal weight in both control (91%) and case groups (73%). But the percentage of overweight is higher in the case group than the normal group (19 % and 2 % respectively). In this study BMI was significantly high in case groups relative to control groups (p- value < 0.001) and the result indicated that pregnant women's with BMI > 25 Kg/m² had high chance to develop PIH than those of with normal (p- value < 0.001) (Table 1).

From a total of 200 study participants, 49.5% of the respondents did not have a habit of scheduled physical exercise (39% control and 60% of case groups) and of which only 5.5% (8 % of control and 3% cases) have done always scheduled exercise. Also from a total of pregnant women participated in this study, 47.5% were alcohol drinkers (3.5% drinks always and 44% drinks sometimes), 94 % were have a habit of fruit consumption (3.5% eat fruit always, 26.5 % eat fruit once a week and 64 % eat fruit sometimes) (Table 2).

Parameters		Blood pressure		Total	P-value
		Control	Case		
Have you do scheduled physical exercise?	Yes, always	8 (8%)	3 (3 %)	11(5.5%)	0.005
	Yes, 2-3 times a week	26 (26%)	19 (19 %)	45(22.5%)	
	Yes, once a weeks	10 (10%)	4 (4 %)	14(7 %)	
	Yes, irregularly	17 (17%)	14 (14 %)	31(15.5%)	

	Not at all	39 (39%)	60 (60 %)	99(49.5%)	
Are you an alcohol drinker	Yes, always	1 (1%)	6 (6 %)	7 (3.5%)	0.007
	Yes, sometimes	38 (38%)	50 (50 %)	88 (44%)	
	Not at all	61 (61%)	44 (44 %)	105(52.5%)	
Habits of fruit consumption	Always	4 (4%)	3 (3 %)	7 (3.5%)	0.083
	Sometimes	68 (68%)	60 (60 %)	128 (64%)	
	Once a week	25 (25%)	28 (28 %)	53 (26.5%)	
	Never at all	3 (3%)	9 (9 %)	12 (8%)	
P-value ≤ 0.05 considered as statistically significant					

Table 2: Activity related findings of participants and its association with the dependent variable.

According to the finding of this study change in habit of taking alcohol and doing scheduled exercise was significantly associated with blood pressure (p- value <0.05), whereas a change in habit of fruit consumption was not significantly associated with blood pressure (p- value >0.083) (Table 2).

In the present study, finding of maternity-related factors were almost similar between the control group and the case group. From a total of 200 pregnant women participated in this study, 68 % of the study participants were not have a history of partner change, 96.5% were married once, almost half (51.5 %) of the study participants are multigravida, 87.5 % were wanted their pregnancy and 55% were with parity range of 1-4. The gestational weeks of the pregnant women range from 20 weeks to 42 weeks with a higher percentage in the third trimester (> 24 weeks) both in the control and case groups which accounts 78 % and 77 % respectively, and the rest were in the second trimester (22 % and 23 % respectively). Most of the study participants in both case and control groups are with a gestational week of from 20 to 37 weeks (64 % and 61%, respectively) and this indicates that the gestational weeks of most pregnant women's included in this study are in the range between 20 weeks to 37 weeks (Table 3).

Parameter		Blood Pressure		Total	P-value
		Control	Case		
Partner change	Yes	30(30%)	34 (34%)	64 (32%)	0.544
	No	70 (70%)	66 (66%)	136 (68%)	
Trimester	Second	22 (22%)	23 (23%)	45 (22.5%)	0.866
	Third	78 (78%)	77 (77%)	155 (77.5%)	
Marital status	Married	98 (98%)	95 (95%)	193 (96.5%)	0.381
	Single	2 (2%)	5 (5 %)	7 (3.5 %)	
Gravidity	Primigravida	50 (50%)	47 (47%)	97 (48.5%)	0.68
	Multigravidia	50 (50%)	53 (53%)	103 (51.5%)	
Pregnancy status	Wanted	94 (94%)	94 (94%)	175 (87.5%)	0.987
	Unwanted	6 (6%)	6 (6%)	25 (12.5%)	
Parity	Uniparous	43 (43%)	41 (41%)	84 (42%)	0.604
	Multiparous	57 (57%)	59 (55%)	116 (58%)	
Gestational age	20 -37 weeks	61 (61%)	64 (64%)	125 (62.5%)	0.007
	37- 42 weeks	29 (29%)	14 (22%)	43 (21.5%)	
	> 42 weeks	10 (10%)	22 (22%)	32 (16%)	
Gestational Diabetic Mellitus	Yes	1 (1%)	8 (8%)	9 (4.5%)	NA
	No	99(99%)	92 (92%)	191 (95.5%)	
Family history of chronic hypertension	Yes	6 (6%)	13 (13%)	19 (9.5%)	0.146
	No	94 (94%)	87 (87%)	181 (90.5%)	
Family history of diabetes	Yes	3 (3%)	13 (13%)	16 (7.5%)	0.001
	No	98 (98%)	87 (87%)	185 (92.5%)	
Have you sense of Headache	Yes	14 (14%)	40 (40%)	54 (27%)	0.015*
	No	86 (86%)	60 (60%)	146 (73%)	

Table 3: Maternity related factors and previous clinical history records distribution and their association with blood pressure results of the study participants.

As shown in Table 3, change in gestational weeks, family history of diabetes and sense of headache were significantly associated with blood pressure results of the study participants ($P < 0.05$) and other maternity factors like partner change, marital status, trimester, party, gravidity, family history of diabetes, gestational diabetes mellitus were not show significant association with blood pressure ($P\text{-value} > 0.005$). According to the present study finding, concentration of blood urea were more dispersed and higher in case pregnant women's relative with control pregnant women (44.86 ± 35.96 for case groups and 29.51 ± 17.79 for control groups). But the level of serum creatinine and serum total protein was relatively less dispersed between the two groups, even if some higher results are seen in case groups relative with control groups (1.00 ± 0.45 for case groups and $0.79 \pm .196$ for control groups, 5.60 ± 1.53 for case groups and 5.47 ± 1.52 for control groups, respectively) (Table 4).

Parameters	Group	Mean $\pm$ 1SD	Range	Maximum	Minimum
Serum urea (mg/dl)	Control	29.51 $\pm$ 17.79	84.64	96.03	11.39
	Case	44.86 $\pm$ 35.96	202.9	214.3	11.4
Serum creatinine (mg/dl)	Control	0.79 $\pm$ 0.196	1.32	1.8	0.48
	Case	1.00 $\pm$ 0.450	2.22	2.7	0.48
Serum total protein (g/dl)	Control	5.47 $\pm$ 1.52	8.39	12.32	3.93
	Case	5.60 $\pm$ 1.53	10.88	13.9	3.02

mg/dl= Milligram Per Deciliter, SD= Standard Deviation

Table 4: Comparison of renal function, and total protein concentration between control and case groups of pregnant women.

In the present study the relatively high percentage of abnormal level of serum creatinine and blood urea level were seen in pregnant women with PIH compared with pregnant women without PIH. The level of serum total protein was nearly similar between the two groups. Abnormal result of RFT were seen in case groups compared with the control groups (serum creatinine level 40 % in case groups and 20% in control groups and blood urea nitrogen level 62 % in case groups and 40% in control groups, respectively) (Table 5).

		Blood pressure		Total	P-value
		Control	Case		
TP	Decreased (< 5.6 g/dl)	69 (69 %)	57 (57 %)	126 (63%)	0.282
	Normal (5.6 - 6.7 g/dl)	17 (17 %)	30 (30 %)	47 (23.5%)	
	Increased (> 6.7 g/dl)	14 (14 %)	13 (13 %)	27 (13.5%)	
Cr	Normal (0.4 - 0.9mg/dl)	80 (80 %)	60 (60 %)	140 (70 %)	0.002
	Increased (> 0.9 mg/dl)	20 (20 %)	40 (40 %)	60 (30 %)	
BUN	Normal (3 -11mg/dl)	60 (60 %)	39 (39 %)	99 (49 %)	0.002
	Increased (> 11mg/dl)	40 (40 %)	62 (62 %)	102 (51 %)	

Cr = Serum Creatinine, TP = Serum Total Protein, BUN= Blood Urea Nitrogen, g/dl= Gram Per Deciliter, mg/dl= Milligram Per Deciliter

Table 5: Biochemical test finding and its association with the blood pressure of the study participants.

RFTs in case groups were significantly higher than the control groups ($P < 0.05$). But the change of serum total protein did not show a significant association with BP (P -value = 0.282) (Table 5). A multivariate approach was also applied to determine which factor best explained and predict the outcome of RFT and serum total protein results in both groups. And the multiple logistic regression model indicate that factors like BMI and gravidity were have significant association with blood urea nitrogen and serum creatinine test results of both groups.

A multivariable analysis revealed that pregnant women with BMI greater than 24.9 kg/m² were have greater chance to develop abnormally increased level of BUN level (AOR: 2.935, 95% CI: 0.614-13.700, P= .027 in case groups and AOR: 1.850, 95% CI: 0.629-5.573, P= 0.011 in control groups) and serum creatinine level (not significant in case groups and AOR: 6.507, 95% CI: 1.475-28.698, P= 0.013 in control groups) compared with study participants with normal BMI. Pregnant mothers with multigravida also have high chance to had increased level of serum creatinine (AOR: 2.352, 95% CI: 0.942-5.874, P= 0.007, in case groups and AOR: 2.027, 95% CI: 0.702-5.858, P= 0.012 in control groups) and blood urea level (AOR: 1.856, 95% CI: 0.754-4.566, P= 0.018 in case groups and AOR: 2.288, 95% CI: 0.971-5.390, P= 0.045 in control groups) compared with pregnant women's with pri-gravidia (Table 6).

Multiple logistic regression analysis also indicated that pregnant women who were in the third trimester were have significantly more chance to had abnormally low serum total protein result compared with pregnant women in the second trimester in both groups (AOR: 1.254, 95% CI: 0.503-3.126, P= 0.028, in case groups and AOR: 1.693, 95% CI: 0.750-3.825, P= 0.025 in control groups) (Table 6).

Parameters		Control Groups				Case Groups			
		P-value	AOR	95% C.I		P-value	AOR	95% C.I	
				Lower	Upper			Lower	Upper
BUN	BMI >25kg/m ²	0.011	1.85	0.629	5.573	0.027	2.935	0.614	13.7
	Multigravida	0.045	2.288	0.971	5.39	0.018	1.856	0.754	4.566
TP	Not take Fruit	0.242	3.711	0.412	33.443	0.165	2.137	0.731	6.249
	3 rd Trimester	0.025	1.693	0.75	3.825	0.028	1.254	0.503	3.126
CR	BMI>25kg/m ²	0.013	6.507	1.475	28.698	0.449	1.523	0.513	4.526
	Not did Exercise	0.018	1.464	0.147	1.461	0.021	1.825	0.706	4.713
	Multigravidia	0.012	2.027	0.702	5.858	0.0067	2.352	0.942	5.874
BMI = Body Mass Index, CR = Serum Creatinine, TP = Serum Total Protein, BUN= Blood Urea Nitrogen									

Table 6: Association between different risk factors of PIH with lipid profile, RFT and serum total protein test results of the study participants.

As we have seen in the above table (Table 6), the reference groups for pregnant women with BMI >25 kgm², in multigravida, not consume enough amount of fruit in their diet, in the third trimester, and not did scheduled exercise were pregnant women with normal BMI (BMI 8.5-24.9 kg/m²), with a gravid of prigravidia, who consumes enough fruits in their diet and those

who have habits of doing scheduled physical exercise. So, Table 6 focuses on comparison of these contemporary groups.

Discussion

Overall in the present study, a significant increase results of serum creatinine and blood urea nitrogen were seen in pregnant mothers with PIH compared with pregnant women without PIH ($P < 0.001$). But in the present study incensement of serum total protein in case groups was not significant compared with control groups ($P > 0.05$). The current finding was consistent with different previously published studies [38,54-56]. But all of these previous studies indicated that the elevation of serum total protein in case groups was significant. The present finding provides evidence for physicians and policymakers for control and prevention of complications that happened due to PIH by regularly monitoring abnormal lipid profile tests.

In the present study pregnant mothers with multigravida, history of preeclampsia on prior pregnancy, multiple pregnancies, not receiving nutritional counselling during pregnancy, drinking alcohol during pregnancy, not consuming fruit, with $BMI > 25 \text{ Kg/m}^2$, with gestational weeks of greater than 37 weeks, have a family history of diabetes mellitus and age > 35 years were have greater significant chance to develop pregnancy-induced hypertension ($P < 0.05$). These risk factors in our study are in agreement with already published reports [57, 58]. Also in the present study, pregnant mothers from Urban resident have greater chance to develop PIH than pregnant mothers from Rural resident, which is opposite with the previously published study done in Tigray, Ethiopia which reported that mothers with rural residents were at greater odds of suffering to hypertensive disorders ($OR = 3.7$, 95% CI, 1.9, 7.1) and this variation may be due to lifestyle and nutritional variation between the two study participants [58].

According to the present study finding the mean blood urea level in preeclampsia was $44.86 \pm 35.96 \text{ mg/dl}$ and normal pregnancy was $29.51 \pm 17.79 \text{ mg/dl}$ and the mean serum creatinine level in pregnant women with PIH was $1.00 \pm 0.45 \text{ mg/dl}$ and normal pregnancy was $0.79 \pm 0.196 \text{ mg/dl}$. Serum creatinine and blood urea level were increased in preeclampsia when compared to normal pregnancy, and the change was statistically significant ($P < 0.05$). And this was similar with the finding of different previously published studies which all reported that a significant alternation of blood urea and serum creatinine was found with pregnant women who have PIH compared with pregnant women without PIH ($P < 0.05$) [34,54,55].

According to the finding of the present study nearly all of the study participants (in both groups) were has decreased level of serum total protein. The cause for this decreasing value may be due to life style and nutritional based problems. The mean serum total protein level in pregnant women with PIH was $5.60 \pm 1.53 \text{ g/dl}$ and in women with normal pregnancy was $5.47 \pm 1.52 \text{ g/dl}$. The level of serum total protein was somewhat high in case groups relative with control

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. Jour Clin Med Res. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

groups but the change was not significantly low in case groups relative with the control groups ($P > 0.05$) which is similar with the finding of different previous studies which indicated that pregnant women with PIH have increased level compared with pregnant women's without PIH and the change in serum total protein level was significantly ($p < 0.001$), even if, the change in this study was not significant ($P > 0.05$) [54-56]. On the contemporary, the finding of the current study was in opposite with finding of different previously published studies [33,38,50,53]. All reported that there was statistically significant decreasing in the level of total protein ($p < 0.05$). This difference may be happened due to different variation of study participants like a nutritional habit, ethnicity, and follow up care during ANC, exercise and other factors, which have a greater effect on the protein level of study participants.

A multiple logistic regression analysis indicate that factors like BMI and gravidity were have significant association with RFT and factors like exercise and trimester were have significant association with serum total protein result of the study participants (Table 6).

Pregnant women with BMI $> 24.9 \text{ kg/m}^2$ have greater chance to develop abnormally increased level of BUN level (AOR: 2.935, 95% CI: 0.614-13.700, $P = .027$ in case groups and AOR: 1.850, 95% CI: 0.629-5.573, $P = 0.011$ in control groups) and serum creatinine level (AOR: 6.507, 95% CI: 1.475-28.698, $P = 0.013$ in control groups) (Table 6).

Pregnant mothers in the third trimester were have higher chance to have abnormally low serum total protein (AOR: 1.254, 95% CI: 0.503-3.126, $P = 0.028$, in case groups and AOR: 1.693, 95% CI: 0.750-3.825, $P = 0.025$ in control groups) compared to those in the 2nd trimester. Multigravida was also the other factor to increased level serum creatinine (AOR: 2.352, 95% CI: 0.942-5.874, $P = 0.007$, in case groups and AOR: 2.027, 95% CI: 0.702-5.858, $P = 0.012$ in control groups) and BUN (AOR: 1.856, 95% CI: 0.754-4.566, $P = 0.018$ in case groups and AOR: 12.288, 95% CI: 0.971-5.390, $P = 0.045$ in control groups), compared with primigravida women (Table 6).

As general the present study finding indicated that pregnant women with PIH were have significantly increased level of RFT compared with pregnant women without PIH [59,60]. The study finding also indicates that pregnant mothers with multigravida, history of preeclampsia, multiple pregnancies, not receiving nutritional counselling during pregnancy, drinking alcohol during pregnancy, not consuming fruit, with BMI $> 25 \text{ Kg/m}^2$, gestational weeks greater than 37 weeks, have a family history of diabetes mellitus and age > 35 years were have greater significant chance to develop pregnancy-induced hypertension ($P < 0.05$). Factors like BMI, schedule physical exercise, drinking alcohol fruit consumption, trimester and gravidity were have significant association with abnormal RFT result of the study participants (Table 6) [61].

Conclusion

Elevation of renal function tests were seen among pregnant women with pregnancy-induced hypertension when compared with pregnant women without pregnancy-induced hypertension. To conclude, the findings of the present study suggest that abnormal levels of renal function test may contribute to the promotion of hypertension in pregnant women. In the present study the level of RFT were significantly higher in case groups relative the control groups. This association may help to investigate the underlying pathological process of hypertension in pregnancy. Level of serum total protein was somewhat increased in case groups relative with the control groups, but the change was not significant (P- value= 0.282).

So early detection of altered renal function test in preeclampsia, the incidence of complications can be decreased, which in turn reduces the maternofetal morbidity and mortality. Therefore, renal function tests must be continuously monitored throughout the whole pregnancy period for early detection and/or developing the strategies to prevent any obstetric-associated complication during PIH and/or at the time of delivery.

Recommendation

Estimating renal function test and serum total protein can improve the fetomaternal outcome by early detection of high-risk patients.

So depending the present study finding the following ways are recommend:

- Different studies have to been done in different area of our country
- Other studies have to been done by including different clusters with consideration lifestyle, attitude and nutritional variation
- Clinicians who follow pregnant women advised to use lipid profiles and RFT tests as screening purposes for PIH before requesting other costly and complicated tests

Acknowledgment

We would like to thanks Addis Ababa University, College of Health Science, Department of Medical Laboratory Science for granting me to do the research. Our deepest gratitude and heartfelt thanks go to for all Midwife professionals, Laboratory professionals in AZMPH for their support during data collection and sample analysis. Here also, we would like to address our heart full thanks to Doctor Tebikew (Radiologist specialist) for his constructive advice and professional support during data collection.

References

1. Van Balen VAL, Spaan JJ, Ghossein-Doha C, van Kuijk SM, Spaanderman ME, Peeters LL. Early pregnancy circulatory adaptation and recurrent hypertensive disease. *Vascular and Renal Adjustments*. 2018;95.
2. Topel ML, Duncan EM, Krishna I, Badell ML, Vaccarino V, Quyyumi AA. Estimated impact of the 2017 American college of cardiology/American heart association blood pressure guidelines on reproductive-aged women. *Hypertension*. 2018;72(4):39-42.
3. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, et al. Hypertensive disorders of pregnancy:ISSHP classification, diagnosis, and management recommendations for international practice. *Hypertension*. 2018;72(1):24-43.
4. Pauli JM, Repke JT. Pitfalls with the New American College of obstetricians and gynaecologists task force on hypertension in pregnancy. *Clinical Obstetrics Gynecol*. 2017;60(1):141-52.
5. Mol BW, Roberts CT, Thangaratinam S, Magee LA, De Groot CJ, Hofmeyr GJ. Pre-eclampsia. *The Lancet*. 2016;387(10022):999-1011.
6. Bibbins-Domingo K, Grossman DC, Curry SJ, Barry MJ, Davidson KW, Doubeni CA, et al. Screening for preeclampsia:US preventive services task force recommendation statement. *JAMA*. 2017;317(16):1661-7.
7. Sroussi HY, Epstein JB, Bensadoun RJ, Saunders DP, Lalla RV, Migliorati CA, et al. Common oral complications of head and neck cancer radiation therapy:mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med*. 2017;6(12):2918-31.
8. Ghodke B, Pusukuru R, Mehta V. Association of lipid profile in pregnancy with preeclampsia, gestational diabetes mellitus, and preterm delivery. *Cureus*. 2017;9(7).
9. English FA, Kenny LC, McCarthy FP. Risk factors and effective management of preeclampsia. *Integrated Blood Pressure Control*. 2015;8:7.
10. Kar K, Sinha S. Role of lipids, ionized calcium, and alkaline phosphatase in progress of pregnancy-induced hypertension-A prospective study in Kolkata. *Int Arch Integrated Med*. 2016;3(2):129-35.
11. Soma-Pillay P, Catherine NP, Tolppanen H, Mebazaa A, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovas J Africa*. 2016;27(2):89.
12. Gupta S, Agarwal A, Sharma RK. The role of placental oxidative stress and lipid peroxidation in preeclampsia. *Obstetrical Gynecol Survey*. 2005;60(12):807-16.
13. Serrano NC, Guio-Mahecha E, Quintero-Lesmes DC, Becerra-Bayona S, Paez MC, Beltran M, et al. Lipid profile, plasma apolipoproteins, and pre-eclampsia risk in the GenPE case-control study. *Atherosclerosis*. 2018;276:189-94.
14. Gao Q, Tang J, Li N, Liu B, Zhang M, Sun M, et al. What is precise pathophysiology in the development of hypertension in pregnancy? Precision medicine requires precise physiology and pathophysiology. *Drug Discovery Today*. 2018;23(2):286-99.
15. Yadav S, Agrawal M, Hariharan C, Dewani D, Vadera K, Krishna N. A comparative study of the serum lipid profile of women with preeclampsia and normotensive pregnancy. *J Datta Meghe Int Med Sci Uni*. 2018;13(2):83.
16. Singh M, Pathak MS, Paul A. A study on atherogenic indices of pregnancy-induced hypertension patients as compared to normal pregnant women. *Journal of clinical and diagnostic research*. *JCDR*. 2015;9(7):BC05.
17. Wild R, Weedin EA, Wilson D. Dyslipidemia in pregnancy. *Cardiology Clin*. 2015;33(2):209-15.
18. Ngene NC, Moodley J. Role of angiogenic factors in the pathogenesis and management of pre-eclampsia. *Int J Gynecol Obstetrics*. 2018;141(1):5-13.
19. Al Ghazali B, Al-Taie AA-H, Hameed RJ. Study of the clinical significance of serum albumin level in preeclampsia and in the detection of its severity. *Am J BioMed*. 2014;2:964-74.
20. Thadhani RI, Maynard SE. Proteinuria in pregnancy:Evaluation and management. *Monografia Glasscock*. 2015:1-150.
21. Phillips JK, McBride CA, Hale SA, Solomon RJ, Badger GJ, Bernstein IM. Examination of prepregnancy and pregnancy urinary protein levels in healthy nulliparous women. *Reproduct Sci*. 2017;24(3):407-12.

Tewabe H | Volume 1, Issue 3 (2020) | JCMR-1(3)-016 | Research Article

Citation: Tewabe H, et al. Assessment of Renal Function Tests and Serum Total Protein among Pregnant Women with Pregnancy-Induced Hypertension Attending in Asrade Zewudie Memorable Hospital (ASZMPH), Gojjam, Ethiopia: Case-Control Study. *Jour Clin Med Res*. 2020,1(3):1-19.

DOI: <http://dx.doi.org/10.46889/JCMR.2020.1301>

22. Hong DSC, Oh IH, Park J-S, Lee CH, Kang CM, Kim G-H. Evaluation of urinary indices for albuminuria and proteinuria in patients with chronic kidney disease. *Kidney and Blood Pressure Res.* 2016;41(3):258-66.
23. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Practice & Res Clin Obstetrics Gynecol.* 2013;27(6):791-802.
24. August P, Sibai BM. Preeclampsia: Clinical features and diagnosis. 2017;22.
25. Hladunewich MA, Melamad N, Bramham K. Pregnancy across the spectrum of chronic kidney disease. *Kidney Int.* 2016;89(5):995-1007.
26. Aziz MM, Kulkarni A, Shah L, Lashley S, Oyelese Y. Physiologic proteinuria in labor and postpartum: The results of the postpartum proteinuria trial (PoPPy). *Pregnancy Hypertension.* 2018;13:22-4.
27. Osungbade KO, Ige OK. Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. *J Pregnancy.* 2011;2011.
28. Gaym A, Bailey P, Pearson L, Admasu K, Gebrehiwot Y, Team ENEA. Disease burden due to pre-eclampsia/eclampsia and the Ethiopian health system's response. *Int J Gynecol Obstetrics.* 2011;115(1):112-6.
29. Abdella A. Maternal mortality trend in Ethiopia. *Ethiopian J Health Develop.* 2010;24(1).
30. Wolde Z, Segni H, Woldie M. Hypertensive disorders of pregnancy in Jimma University specialized hospital. *Ethiopian J Health Sci.* 2011;21(3).
31. Nugteren JJ, Snijder CA, Hofman A, Jaddoe VW, Steegers EA, Burdorf A. Work-related maternal risk factors and the risk of pregnancy-induced hypertension and preeclampsia during pregnancy. The Generation R Study. *PloS One.* 2012;7(6):e39263.
32. Organization WHO. WHO recommendation: calcium supplementation during pregnancy for the prevention of pre-eclampsia and its complications. 2018.
33. Villar J, Abdel-Aleem H, Merialdi M, Mathai M, Ali MM, Zavaleta N, et al. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. *Am J Obstetrics Gynecol.* 2006;194(3):639-49.
34. Ladouceur M, Benoit L, Radojevic J, Basquin A, Dauphin C, Hascoet S, et al. Pregnancy outcomes in patients with pulmonary arterial hypertension associated with congenital heart disease. *Heart.* 2017;103(4):287-92.
35. Organization WH, UNICEF. Trends in maternal mortality: 1990-2015: estimates from WHO, UNICEF, UNFPA, World Bank Group, and the United Nations Population Division. 2015.
36. Obstetricians ACo, Gynecologists. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' task force on hypertension in pregnancy. *Obstetrics and Gynecol.* 2013;122(5):1122.
37. Asamoah BO, Moussa KM, Stafström M, Musinguzi G. Distribution of causes of maternal mortality among different socio-demographic groups in Ghana; a descriptive study. *BMC Public Health.* 2011;11(1):159.
38. Awoke A, Awoke T, Alemu S, Megabiaw B. Prevalence and associated factors of hypertension among adults in Gondar, Northwest Ethiopia: a community based cross-sectional study. *BMC Cardiovascular Disorders.* 2012;12(1):113.
39. Teklu S, Gaym A. Prevalence and clinical correlates of the hypertensive disorders of pregnancy at Tikur Anbessa Hospital, Addis Ababa, Ethiopia. *Ethiopian Med J.* 2006;44(1):17-26.
40. Seyom E, Abera M, Tesfaye M, Fentahun N. Maternal and fetal outcome of pregnancy-related hypertension in Mettu Karl Referral Hospital, Ethiopia. *J Ovarian Res.* 2015;8(1):10.
41. Berhan Y, Berhan A. Causes of maternal mortality in Ethiopia: a significant decline in abortion related death. *Ethiopian J Health Sci.* 2014;24:15-28.
42. Gudeta TA, Regassa TM. Pregnancy induced hypertension and associated factors among women attending delivery service at mizan-tepi university teaching hospital, Tepi General Hospital and Gebretsadik Shawo Hospital, Southwest, Ethiopia. *Ethiopian J Health Sci.* 2019;29(1).
43. Tessema GA, Laurence CO, Melaku YA, Misganaw A, Woldie SA, Hiruye A, et al. Trends and causes of maternal mortality in Ethiopia during 1990-2013: findings from the Global Burden of Diseases study 2013. *BMC Public Health.* 2017;17(1):160.

44. Seong WJ, Chong GO, Hong DG, Lee TH, Lee YS, Cho YL, et al. Clinical significance of serum albumin level in pregnancy-related hypertension. *J Obstetrics Gynaecol Res.* 2010;36(6):1165-73.
45. Roohi S, Khan J, Rosaline M, Anees S, Kazi H, Kaleemullah M, et al. Evaluation of lipid profile, calcium and alkaline phosphatase in pregnancy induced hypertension women. *UK J Pharma Biosciences.* 2015;3(2):24-8.
46. Pusukuru R, Shenoi AS, Kyada PK, Ghodke B, Mehta V, Bhuta K, et al. Evaluation of lipid profile in the second and third trimester of pregnancy. *JCDR.* 2016;10(3):QC12.
47. Olalere Fd. A Comparative study of serum lipid profile in pre-eclamptic and normotensive pregnant women at the Lagos University Teaching Hospital (LUTH). Faculty of Obstetrics and Gynaecol. 2016.
48. Von Dadelszen P, Ayres de Campos D, Barivalala W. Classification of hypertensive disorders of pregnancy. The FIGO textbook of pregnancy hypertension:an evidence-based guide to monitoring, prevention and management London. Global Library of Women's Med. 2016:33-61.
49. Poalelungi C, Ceausu I. Hypertension in pregnancy. *J Hypertension Res.* 2018;4(2):53-9.
50. Chen H, Tao F, Fang X, Wang X. Association of hypoproteinemia in preeclampsia with maternal and perinatal outcomes:A retrospective analysis of high-risk women. *Journal of research in medical sciences. J Isfahan Uni of Med Sci.* 2016;21.
51. Chopra S, Bedi P, Mahajan M. study of maternal serum lipids and lipoproteins in pregnancy induced hypertension. *Ind Obstetrics and Gynaecol.* 2017;7(3).
52. Rabia A, Nureen Z, Kanwal R, Rabail A, Asia P, Muhammad T, et al. Comparative analysis of serum lipid profile between normotensive and hypertensive Pakistani pregnant women. *J Molecular and Genetic Med.* 2013;7(2).
53. Ali R, Farheen S, Zaheer A, Adnan B. Assessment of lipid profile & serum total protein in patients with hypertension. *Ann Pak Inst Med Sci.* 2017;23(8).
54. Ahmad MA, Ellahi E, Taqi-Ul-Jawad SM. Pregnancy Hypertensive Disorders Frequency and Obstetric Outcome. *Pak J Med Health Sci.* 2018;12(1):85-8.
55. Maputle S, Khoza L, Lebesse R. Knowledge towards Pregnancy-induced hypertension among pregnant women in Vhembe District, Limpopo Province. *J Human Ecol.* 2015;51(1-2):47-54.
56. Begum Ja, Sultana R, Naher S. serum levels of total protein, albumin and globulin in woman with hyperemesis gravidarum. *J Dhaka Med Coll.* 2010;19(1):8-60.
57. Grum T, Seifu A, Abay M, Angesom T, Tsegay L. Determinants of pre-eclampsia/Eclampsia among women attending delivery Services in Selected Public Hospitals of Addis Ababa, Ethiopia:a case control study. *BMC Pregnancy and Childbirth.* 2017;17(1):307.
58. Kahsay HB, Gashe FE, Ayele WM. Risk factors for hypertensive disorders of pregnancy among mothers in Tigray region, Ethiopia:matched case-control study. *BMC Pregnancy and Childbirth.* 2018;18(1):482.
59. Ramsay M, James D, Steer PJ, Weiner C, Gonik B. Normal values in pregnancy:WB Saunders London. 2000.
60. Berhe AK, Kassa GM, Fekadu GA, Muche AA. Prevalence of hypertensive disorders of pregnancy in Ethiopia:a systemic review and meta-analysis. *BMC Pregnancy and Childbirth.* 2018;18(1):34.
61. Campbell OM, Graham WJ;Lancet Maternal Survival Series steering group. Strategies for reducing maternal mortality:getting on with what works. *Lancet.* 2006;368(9543):1284-99.