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CORRELATION OF SERUM ALBUMIN, A; G RATIO AND THYRIOD FUNCTION TESTS IN NORMAL PREGNANT WOMEN AND PREECLAMPTIC WOMEN.

Physiology

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ABSTRACT

Aim: The study was done to find out correlation between serum albumin, A;G ratio and thyroid function tests in normal pregnant women and preeclamptic women.

Material and Methods: The present study was done in the Department of Physiology, Government Medical College Jammu on 100 pregnant women in second and third trimester of pregnancy. Of the 100 subjects, 50 were preeclamptic women as cases i.e. diseased group (Group I) and 50 normal pregnant women were taken as controls i.e. control group (Group II), w.e.f. November 2014 to October 2015. Total proteins, Serum total Tri-iodothyronine (T3), Tetraiodothyronine (T4), Thyroid Stimulating Hormone (TSH) and serum albumin ,A;G ratio were estimated in both groups.

Results: Our study shows that Serum TSH is increased significantly while T3 and T4 are decreased significantly in preeclampsia as compared to normal pregnancy. Serum albumin is also decreased in preeclamptic women in comparison to normal pregnant women significantly .Also it is seen that relation of serum globulin in preeclamptic and normal pregnant women is not significant ($p>0.05$). However, total protein and A;G(albumin; globulin) ratio is decreased significantly in preeclamptic women in comparison to normal pregnant women. Hence the correlation of serum albumin with T_3 is significant and direct while with TSH it is significant but inverse.

KEYWORDS

preeclampsia, serum albumin, A;G ratio(Albumin ;Globulin ratio), TSH

INTRODUCTION

Normal pregnancy is characterized by increased levels of circulating steroids, numerous metabolic alterations and presence of rapidly developing and apparently well tolerated allograft i.e. the fetus. These changes are expected to produce alterations in serum protein pattern of mother.[1]Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, hematological and immunological processes. If these changes are exaggerated, they can lead to complications during pregnancy. Several complex physiological changes take place during pregnancy, which together tend to modify the economy of the thyroid and have a variable impact at different time periods during gestation.[2] The women who develop preeclampsia are more likely to have lower normal limits of thyroid function during the final weeks of their pregnancies.[3]

Hypertensive disease in pregnancy is a major cause of maternal and fetal morbidity and mortality. Preeclampsia adversely affects the maternal and fetal outcome, due to its widespread multi-organ involvement. Preeclampsia is a complication in approximately 5% of all pregnancies. The incidence in primigravida is about 10% and in multigravida 5%. Preeclampsia is one of the most common causes of perinatal morbidity and mortality, resulting in estimated 35~300 deaths per 1000 births, depending on neonatal support. Preeclampsia usually occurs in women in both extremes of reproductive age, however, the risk of preeclampsia is greatest in women younger than 20 years.[4]

Albumin is lower in women with preeclampsia than in healthy pregnant women**.** This is explained by an increase in plasma and interstitial volume and possibly by an increase in albumin metabolism . [5] The albumin synthesis is significantly greater in preeclampsia than in normal pregnancy, probably because of diminished estrogen production by foetoplacental unit or simply because the hypoalbuminemia of preeclampsia is a greater stimulus to albumin synthesis by liver. This lower concentration of serum albumin is claimed to be the result of proteinuria and hypercatabolism of albumin, with no detectable loss of albumin in interstitial fluid or gut .[6]

Arbogast *et al.*, (1994)[7] proposed that the pathophysiology of preeclampsia is related to concentration of free very low density lipoproteins (VLDL) and the albumin protects against VLDL induced injury. The findings of **Studd *et al.*, (1970)**[8] showed different serum protein levels in severe preeclampsia, as compared to normal pregnancy, and these changes are to some degree dependent upon the molecular weight of serum proteins. **Gojnic *et al.*, (2004)**[9] proposed that hypoalbuminemia in preeclampsia is the result of reduced hepatic blood flow which is secondary to hypovolemia created by higher filtration pressure in the capillaries. The glomerular injury of preeclampsia manifests as a clinical triad, namely, hypertension, albuminuria, and a loss of intrinsic filtration capacity that lowers the GFR.[10]

In 2000, the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy published a report with revisions to preeclampsia-eclampsia classification criteria. Preeclampsia is currently classified as a pregnancy-specific syndrome, characterized by the presence of new-onset hypertension in a previously normotensive woman after 20 weeks gestation with proteinuria. Blood pressure (BP) criteria include a systolic BP > 140 mm Hg or a diastolic BP > 90 mm Hg. Proteinuria is defined as urinary excretion of ≥ 0.3 grams of protein in a 24-hour specimen, which correlates with a random ≥ 1+ urine dipstick in the absence of a urinary tract infection. The presence of edema was dropped from the diagnostic criteria because many pregnant women with normal pregnancies develop edema. Furthermore, eclampsia is classified as the presence of seizures, non-attributable to other causes, in a woman diagnosed with preeclampsia.[11]

From a clinical practice viewpoint, it should be mentioned that both hypothyroidism and hyperthyroidism are accompanied by remarkable alterations in the metabolism of water and electrolyte, as well as in cardiovascular function. All these effects generate changes in water and electrolyte kidney management. Moreover, the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism and elimination of thyroid hormone.[12]In preeclampsia there is loss of albumin in urine so hormones bound to albumin are also lost in urine. This may lead low serum T3 and T4 levels. This suggests a strong relationship between loss of albumin with low serum T3 and T4 levels in preeclamptic women.[13,14,15]

AIMS AND OBJECTIVES

To study the correlation between serum albumin, A;G rations and thyroid function tests normal pregnant and preeclamptic women.

MATERIAL AND METHODS

The present study was done in the Department of Physiology, Government Medical College **Jammu** on 100 pregnant women in second and third trimester of pregnancy. Of the 100 subjects, 50 were preeclamptic women as cases i.e diseased group (Group I) and 50 normal pregnant women were taken as controls i.e control group (Group II) , *w.e.f.* November, 2014 to October, 2015

Subjects were selected from outpatient Department of Obstetrics and Gynecology, SMGS Hospital, Government Medical College, Jammu. After detailing the purpose and methodology of the study, all eligible subjects were requested to participate in the study.

INCLUSION CRITERIA

- Singleton pregnancy, 20 to 40 years of age, and who were not on any medication during pregnancy (except, iron and calcium).
- Previously healthy normotensive women were considered to have preeclampsia when their blood pressure after 20 weeks of gestation was raised to 140/90 mmHg or more(on two occasions 6 hrs apart) and proteinuria of more than 300mg/day or 100mg/dl.
- 50 women with normal pregnancy in their second and third trimester were matched on an individual basis for the same parameters and were taken as controls.

EXCLUSION CRITERIA

- Associated renal, hepatic, cardiac disease, metabolic disorder like diabetes mellitus, known thyroid disorder and past history of hypertension.

Blood pressure was measured by auscultatory method with a sphygmomanometer (mercury manometer). Thyroid function tests were performed by chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of thyroid hormones (Total T_3, Total T_4 and TSH) in human serum and plasma.[16,17]

Albumin estimation: The albumin method based on the dimension clinical chemistry system is an *in vitro* diagnostic test intended for the quantitative determination of albumin in human serum or plasma.
The albumin method is an adaptation of the bromocresol purple (BCP) dye-binding method.[18,19] Because of an enhanced specificity of bromocresol for albumin, this method is not subject to globulin interference. In the presence of a solubilising agent, BCP binds to albumin at pH 4.9. The amount of albumin-BCP complex is directly proportional to the albumin concentration. The complex absorbs at 600nm and was measured using a polychromatic (600nm, 540nm and 700nm) endpoint technique. Samples were collected and kept at room temperature. Samples remain stable for 2 days at 2-8^{0}C.

Serum globulin estimation: The globulin is measured by taking the difference between total proteins and albumin .[20]

Total protein estimation: The TP method used on the Dimension clinical chemistry system is an in vitro diagnostic test for the quantitative determination of total protein in human serum and heparinized plasma. The total protein method is a modification of the biuret reaction, modified by Henry.[21]

RESULTS;

Table 1:-- T_3, T_4, TSH and serum albumin values in Disease Group and Control Group.

	Disease Group (n=50)		Control Group (n=50)		p-value
	Mean ± SD	Range	Mean ± SD	Range	
T_3	0.92±0.38	0.13-1.79	1.41±0.29	0.37-1.98	<0.001
T_4	5.29±2.16	2.10-12.66	9.46±1.96	5.30-14.07	<0.001
TSH	6.19±2.32	2.34-13.10	2.22±0.84	0.16-3.70	<0.001
Serum Albumin	2.70±0.55	1.4-3.6	3.84±0.33	3.1-4.4	<0.001

Table 1 (Fig.1) shows the values of thyroid functions in preeclamptic women and normal pregnant women. Serum TSH is increased significantly while T3 and T4 are decreased significantly in preeclampsia as compared to normal pregnancy. Serum albumin is also decreased significantly in preeclamptic women in comparison to normal pregnant women.

Table 2:--Serum globulin, total Protein, A:G (Albumin : Globulin) Ratio values in Disease Group and Control Group.

	Disease Group (n=50)		Control Group (n=50)		p-value
	Mean±SD	Range	Mean±SD	Range	
Serum Globulin	2.932±0.42	2.2-4.0	2.73±0.34	2.0-3.2	0.567
Total Protein	6.15±0.57	5-7	6.61±0.46	6-7	<0.001
A:G Ratio	0.80±0.23	0.36-1.45	1.43±0.23	1.00-2.10	<0.001

Table 2 (Fig.2) shows the comparison of serum globulin, total protein and A:G ratio in preeclamptic women and normal pregnant women. It is seen that relation of serum globulin in preeclamptic and normal pregnant women is not significant (p>0.05). However, total protein is decreased significantly in preeclamptic women in comparison to normal pregnant women. Similarly A:G ratio is decreased significantly in preeclamptic women in comparison to normal pregnant women.

Table 3: Correlation of serum albumin with T_3, T_4, TSH and A:G Ratio.

		T_3	T_4	TSH	A:G Ratio	Serum Albumin
T_3	R	1.000	.808**	-.733**	.577**	.563**
	p value		<0.001	<0.001	<0.001	<0.001
T_4	R	.808**	1.000	-.737**	.695**	.643**
	p value	<0.001		<0.001	<0.001	<0.001
TSH	R	-.733**	-.737**	1.000	-.674**	-.673**
	p value	<0.001	<0.001		<0.001	<0.001
A:G Ratio	R	.577**	.695**	-.674**	1.000	.891**
	p value	<0.001	<0.001	<0.001		<0.001
Serum albumin	R	.563**	.643**	-.673**	.891**	1.000
	p value	<0.001	<0.001	<0.001	<0.001	

Table 3 (Fig.4) shows co-efficient of correlation between various variable among preeclamptic women. It is seen that the correlation of serum albumin with T_3 is significant and direct while with TSH it is significant but inverse.

DISCUSSION

Our study showed that with increase in mean arterial pressure, TSH levels increased significantly in preeclamptics (Disease group) while T_3 and T_4 levels decreased significantly. Severe preeclamptics have significantly higher TSH levels (7.28 ± 2.06) as compared to milder cases (4.04 ± 0.90). Our findings are in agreement with those of **Khaliq *et al*., (1999)** and **Kharb *et al*., (2013)[22,23].**

In our study, serum concentration of total protein in control group (mean ± standard deviation) 6.61 ± 0.46 g/dL reduced to 6.15 ± 0.57 g/dL in disease group, which was significant (p<.05). Similarly serum albumin in control group 3.84 ± 0.33 decreased to 2.70 ± 0.55 in disease group, which was significant (p<.05). Further it was observed that A:G ratio decreased from 1.43 ± 0.23 in control group to 0.80 ± 0.23 in disease group. The changes in level of globulin in control group 2.73 ± 0.34 and in disease group 2.932 ± 0.42 were not significant .Similar findings were reported by **Studd *et al.,* (1970)[8]; Hofmeyr *et al.*[24], (1991); Sazina *et al.*,[25] (2014); Durga *et al.*, (2014).[26]**

This is because the electrophoretic distribution of serum proteins in preeclampsia is similar to that occurring in nephrotic syndrome.[27] In both situations, there is proteinuria, edema, a decrease in albumin and an increase in alpha 2-macroglobulin.[5] In nephrotic syndrome, the elevation of 3-lipoprotein and alpha 2-macroglobulin is the result of nonspecific synthesis of proteins after loss of protein in urine. There is loss of proteins of intermediate molecular weight, such as albumin (MW 69,000), hemopexin (MW 80,000) and transferrin (MW 90,000), and retention of large proteins such as alpha 2-macroglobulin (MW 820,000) and 3-lipoproteins (MW 3.2 x 106) which are too large to pass the defective glomerular basement membrane.[28]

Olooto *et al.,* (2013)[29] and **Arinola *et al*., (2006)[30]** showed that total protein and serum albumin levels were significantly decreased while urinary protein was significantly increased in preeclamptics as compared to normal pregnant women.

Studies have demonstrated that there is significant proteinuria in

women with gestational hypertension. In preeclampsia there is marked hypofiltration due to reduction in renal plasma flow and GFR. There is a loss of glomerular barrier charge and size selectivity which normalizes after delivery .[31]

Hypoalbuminemia is explained by an increase in plasma and interstitial volume and possibly by an increase in albumin metabolism. Increase in capillary permeability secondary to endothelial damage seems to be partly responsible for this findings .[32] **Mukherjee and Goven (1950)**[33] showed that the mean protein content of 0.24 gm/100 ml of oedema fluid of preeclampsia was no different from the concentration in the tissue fluid of normal pregnancy. They also found that A:G ratio was much higher in oedema fluid than in plasma. Present study demonstrates that the considerable change in serum proteins that occur in preeclampsia can be a result of heavy proteinuria. These observations indicate that total proteins, albumin and A:G ratio was found to be decreased, while there was no change in levels of globulins with preeclampsia as compared to normal pregnancy.

A highly significant positive correlation was observed between serum albumin and T_3 and T_4 levels in preeclampsia ($r = 0.563$ & $r = 0.643$ respectively, $p<0.01$), while there was a significant negative correlation between serum albumin levels and TSH levels ($r = -.673$, $p<.001$) in preeclampsia. Similar results were shown by **Sardana *et al.*, (2009)**[14] and **Lao *et al.*, (1990).**[34]

A similar positive correlation was seen between A:G ratio and serum albumin ($r = .89$, $p<.01$) by **Tolino *et al.*, (1985)**.[35]

Farah *et al*., (1999)[36] reported same findings but found that correlation of albumin and T_4 was not significant. The difference in T_3 and T_4 can be because of different degree of saturation with thyroid binding globulins.

The correlation between TSH and albumin is significant and inverse because the preeclamptic patients are in a state of hypothyroidism.[34]

CONCLUSION

- A highly significant positive correlation was found between T_3, T_4, TSH, A:G ratio and serum albumin with the severity of blood pressure.
- There is a significant increase in TSH level in preeclamptic group while as T_3 and T_4 were decreased significantly.
- Total protein, serum albumin and A:G ratio decreased significantly in preeclamptic group as compared to normal pregnancy.
- There was no significant change in serum globulin between the two groups.

REFERENCE

1) Mack HC. Plasma proteins of pregnancy. Clinical Obstetrics and Gynaecology 1960; 3-336.
2) Glinoer D. Thyroid disease during pregnancy. In: Braverman L, Utiger R, eds. Werner's and Ingbar's the thyroid: a fundamental and clinical text. 9th ed. Philadelphia: Lippincott Williams & Wilkins 2005; 1086-108.
3) Raoofi Z, Jalilian A, Shabani Zanjani M, Parvar SP and Parvar SP. Comparison of thyroid hormone levels between normal and preeclamptic pregnancies. Med J Islam Repub Iran 2014; 28: 1.
4) Khanam M and Ilias M. Pregnancy and preeclampsia. Medicine today. 2013; 25(2): 63-6.
5) Horne CH, Howie PW and Goudie RB. Serum-alpha2-macroglobulin, transferrin, albumin, and IgG levels in preeclampsia. J Clin Pathol 1970; 23: 514-6.
6) Honger PE. Protein changes in preeclampsia-eclampsia syndrome. Scandinavian Journal of clinical and Laboratory Investigation 1968; 22: 177-84.
7) Arbogast BW, Leeper SC, Merrick RD, Olive KE and Taylor RN. Which plasma factors bring about disturbance of endothelial function in pre-eclampsia? Lancet 1994; 343: 340-1.
8) Studd JWW, Blainey JD and Bailey DE. Serum protein changes in the preeclampsia-eclampsia syndrome. J Obstet Gynaecol Br Common W 1970; 77: 796-802.
9) Gojnic M, Petkovic S, Papic M, Mostic T, Jeremic K, Vilendecic Z and Djordjevic S. Institute of Gynecology and Obstetrics, Clinical Center of Serbia, University of Belgrade (Serbia). Clinical and Experimental Obstetrics & Gynecology 2004; 31(3): 209-0.
10) Hladunewich MA, Myers BD, Derby GC, Blouch KL, Druzin ML, Deen WM, Naimark DM and Lafayette RA. American Journal of Physiology - Renal Physiology 2008; 294(3): 614-20.
11) National Heart, Lung, and Blood Institute, National High Blood Pressure Education Program. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. American Journal of Obstetrics and Gynecology 2000; 183(1):
12) Katz AI and Lindheimer MD. Actions of hormones on the kidney. Annual Review of Physiology 1977; 39: 97-133.
13) Kaya E, Sahin Y, Ozkceci Z, Pasaoglu H. Relation between birth weight and thyroid function in preeclampsia. Gynecol Obstet Invest. 1994;37(1):30–3.
14) Sardana D, Nanda S, Kharb S. Thyroid hormones in pregnancy and preeclampsia. J Turkish Ger Gynecol Assoc. 2009;10(3):168–71.
15) Osathanondh R, Tulchinsky D, Chopra IJ. Total and free thyroxine and triiodothyronine in normal and complicated pregnancy. J Clin Endocrinol Metab. 1976;42(1):98–104)
16) Patel YC, Alford FP and Burger HG. The 24-Hour Plasma Thyrotropin Profile. Clin Sci 1972; 43:71-7.
17) Sterling K and Lazarus JH. The Thyroid and its control. Annu Rev Physiol 1977; 39: 349-71.
18) Carter P. Utramicroestimation of human serum albumin; binding cationic dye 5.5'dibromo –o cresolsulfonphthalein, Microchem 1970; 15: 531-9.
19) Louderback A, Measley EH and Taylor NA. A new dye-binder technique using bromocresol purple for determination of albumin in serum, Clin Chem 1968; 14: 793-4.
20) Jha Jagarati. A Clinical Biochemistry Laboratory. Training module for technicians 2004; 53-5.
21) Henry RJ. Clinical chemistry, Principles and Technique, Harper and Row, New York, NY 1974; 407-21.
22) Khaliq F, Singhal U, Arshad Z and Hossain MM. Thyroid functions in pre-eclampsia and its correlation with maternal age, parity, severity of blood pressure and serum albumin. Indian J Physiol Pharmacol 1999; 43: 193-8. 23)Kharb S and Singh GP. Hyperuricemia, Oxidative stress in preeclampsia. Clin Chim Acta 2001; 305: 201-3.
24) Hofmeyr G T, William T and Redman C. C4 and plasma protein in hypertension during pregnancy with and without proteinuria. B.H.J. 1991; 302-18.
25) Sazina M, Khalid U and Ali N. Comparison of serum protein in Preeclamptic women. European Journal of Biomedical and Pharmaceutical sciences ISSN 2014; 1(2): 165-70.
26) Durga P, Shabana S, Ramana G V and Shalini G. Assessment of Copper, Ceruloplasmin, Total Proteins and Albumin in Gestational Hypertension. IOSR Journal of Dental and Medical Sciences Ver 2014; 13(4): 101-4.
27) de Alvarez R R, Alfonso J F, and Sher- RARD D J. Serum protein fractionation in normal pregnancy. Amer. J. Obstet. Gynec 1961; 82: 1096-111.
28) Studd JWW and Blainey JD. Pregnancy and the Nephrotic Syndrome. British Medical Journal. 1969; 276-80.
29) Olooto WE, Amballi AA, Mosuro, Adeleye AA and Banjo TA. Assessment of total protein, albumin, creatinine and aspartate transaminase level in toxaemia of pregnancy. J.med sci. 2013; 13(8):791-796.
30) Arinola G, Arowojolu A, Bamgboye A, Akinwale A and Adeniyi A. Serum concentrations of immunoglobulins and acute phase proteins in Nigerian women with preeclampsia Reprod Biol 2006; 6(3): 265-74.
31) Moran P, Baylis PH, Lindheimer MD and Davison JM. Glomerular ultrafiltration in normal and preeclamptic pregnancy. J Am Soc Nephrol 2003; 14: 648-52.
32) Homer CS, Brown MA, Mangos G and Davis Gk. Non- proteinuric preeclampsia: a novel risk indicator in women with gestational hypertension. J. Hypertens 2008; 26: 295-02.
33) Mukherjee CL and Goven ADT. The nature of the tissue fluid in the oedema of toxaemia of pregnancy. Journal of Clinical Pathology 1950; 3: 274.
34) Lao T, Chin R and Swaminathan R. Maternal Thyroid Hormones and Outcome of Pre-eclamptic Pregnancies. Br. J. Obstet. Gynaecol 1990; (97): 71-4.
35) Tolino A, De Conciliis B and Montemagno U. Thyroid hormones in human pregnancy. Acta Obstet Gynecol Scan 1985; 64: 557-9.
36) Farah Khaliq, Usha Singhal, Zakia Arshad and Mobarak Hossain M. Thyroid functions in preeclampsia and its correlation with maternal age, parity, severity of blood pressure and Serum albumin. Indian J Physiol Pharmacol 1999; 43(2): 193-8.