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Serum Ceruloplasmin Levels In Pregnant Women

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Abstract: ***Pregnancy is a state of altered, but normal, physiologic process. [1] The pregnancy related hepatic and G.I disorders may affect uniquely in pregnancy hence the physician should have safe diagnostic tools which would help in medication. This study was conducted to estimate the levels of serum Ceruloplasmin, and LFT like Total Proteins, Albumin, Globulin, A/G Ratio, Alkaline phosphatase, Alanine amino transferase and Aspartate amino transferase in normal healthy pregnant women and to compare them with normal healthy non pregnant women.***

The present study was conducted in the Department of Biochemistry, Osmania General Hospital and Medical College, Koti, Hyderabad-AP. The study was conducted on 85 women {50 Pregnant and 35 Nonpregnant} attending ANC clinic GMH Hyderabad and Area Hospital, Golconda Forte, Hyderabad were divided into 2 groups. The mean value of CP stastistically increases in all cases which is highly significant.

The mean value of TP, Globulins and A: G ratio stastistically decreased in all cases which is highly significant. The statistically significant increase in ALP values in all cases, which is highly significant. The statistically significant decrease in ALT values in all cases, which is highly significant. Statistically there is not much change in AST value. As shown by several studies elevation of serum CP and ALP, decrease in TP, Globulins and A: G ratio of the normal pregnant women. The present study suggested the same; this would also indicate Nutritional status of the mother.

Keywords: Serum Ceruloplasmin, Total Proteins, Albumin, Globulin

1. Introduction

Pregnancy is a state of altered, but normal, physiologic process. [1] The pregnancy related hepatic and G.I disorders may affect uniquely in pregnancy hence the physician should have safe diagnostic tools which would help in medication.

Pregnancy is an acute phase reaction. [2] The level of acute phase protein is moderately elevated, but the gamma glutamyl transpeptidase (GGTP) level is normal but only minimally elevated.

The levels of serum amino transferase are also elevated, occasionally to values of 1000 U/L or higher. Hence, distinguishing cholestasis of pregnancy from hepatitis is difficult. [3]

In normal pregnancy as early as 4-6th week of gestation, the levels of copper and ceruloplasmin start rising.

This study was conducted to estimate the levels of serum ceruloplasmin, and some LFT like total proteins, albumin, globulin, A/G ratio, alkaline phosphatase, alanine amino transferase and aspartate amino transferase in normal healthy pregnant women and to compare them with normal healthy non pregnant women.

2. MATERIALS AND METHODS:

The present study was conducted in the department of Biochemistry, Osmania General Hospital and Medical College, Koti, Hyderabad-AP.

The study was conducted on 85 women attending ANC clinic GMH Hyderabad and Area Hospital, Golconda Forte, Hyderabad were divided into 2 groups.

Group I: Non pregnant healthy women n=35 (healthy non diabetic and non-hypertensive (screened for DM and HTN), non reactive for HIV. These are mostly attendants accompanying pregnant women in age between 18-38 yrs serve as Controls.

Group II: Normal pregnancy consisting of 50 healthy normal pregnant women attending ANC including 1^{st,} 2nd and 3rd trimester of pregnancy.This group served as tests (cases) (Screened for DM, HTN HIV, anemia, total proteins).

The levels of serum ceruloplasmin, TP, Albumin, Globulin, A:G ratio, ALP, ALT (SGPT), and AST(SGOT) were estimated in 50 cases and the values were compared with 35 controls.

Serum CP was estimated by O-dianisidine method of Schosinsky et al. [4] The value was expressed in IU/L.

Sr.TP was estimated by Biuret method. Albumin by Bromocresol Green dye binding method. Globulin was obtained by calculating the difference between TP and AIb and all three values were expressed in gm/dl. Albumin: Globulin ratio was also calculated.

ALT and AST was estimated by Reitman Frankel method. Both the above values are expressed in the IU/dl. ALP was estimated by King Armstrong Method. This value was expressed the KA units/ dl.

Inclusion Criteria:
Normal healthy pregnant women
Age group: 18yrs-38yrs
Including primi, Gravida II, Gravida III; Non Diabetic, Non Hypertensive normal Hb & Non reactive for HIV

Exclusion Criteria:
Diabetes Mellitus
Primary renal disorders ,Hypertension
Anaemia
HIV +ve cases

After fulfilling the inclusion and exclusion criteria and obtaining prior written informed consent from all study participants both cases and controls the samples were collected.

Sample collection: Venous blood 6ml was collected under aseptic conditions in a sterile plain bottle. Serum was separated within 2 hours of collection of blood. Care was taken to prevent the hemolysis of the sample. Icteric and Lipemic sera were not used.

Investigations:
Serum ceruloplasmin
LFT : Total proteins
Albumin
Globulin {Calculated}
A: G ratio{Calculated}
Alkaline phosphatase,
Alanine amino transferase
Aspartate amino transferase

3. RESULTS

The study of the levels of various parameters in 50 normal healthy pregnant women who were non diabetic, non hypertensive not anaemic, non reactive for HIV were carried out in the Department of Biochemistry, Osmania General Hospital. They were all in the age group of 18yrs to 38 yrs and their informed written consent was obtained.

The patients are from all socio economic and religious backgrounds. The parameters were estimated and compared in these patients with those obtained in 35 normal healthy women who were non diabetic, non hypertensive, not anaemic, non reactive for HIV in the same age group.

Table 1: Comparison of mean values between pregnant and non pregnant women

Parameter	N=35 Controls Mean±SD	N=50 Cases Mean±SD	t value	p value
CP	99.8±12.73	179.31±45.82	9.9836	0.0001
TP	7.03±0.717	6.36±0.56	4.8327	0.0001
ALB	3.64±0.36	3.06±0.27	8.4882	0.0001
GLOB *	3.38±0.36	3.29±0.30	1.253	0.2137
A : G	1.07±0.04	0.93±0.03	18.44	0.0001
ALP *	8.42±2.69	24.52±7.36	12.358	0.0001
ALT (SGPT)	51.42±13.09	35.0±11.41	6.144	0.0001
AST (SGOT)	42.05±4.53	44.04±12.74	0.8845	0.379

Table 2: Comparision of T test and p value of controls compared with 2nd Trimester

Parameter	N=35 controls	N=25 2nd trimester	t test	p value
CP	99.8±12.73	155.24±14.75	-11.319	0
TP	7.03±0.717	6.24±0.62	4.422	0
ALB	3.64±0.36	3.02±0.29	7.08	0
GLOB *	3.38±0.36	3.24±14.8	2.088	0.041
A : G	1.07±0.04	0.94±0.48	-14.742	0
ALP *	8.42±2.69	23.39±3.97	-17.385	0
ALT (SGPT)	51.42±13.09	34.32±12.9	5.018	0
AST (SGOT)	42.05±4.53	37.28±11.8	2.185	0.033

Table 3: Comparision of T test and p value of controls compared with 3rd Trimester

Parameter	N=35 controls	N=20 3rd trimester	t test	p value
CP	99.8±12.73	228.65±11.07	-22.443	0
TP	7.03±0.717	6.38±0.49	3.6	0.001
ALB	3.64±0.36	3.04±0.23	6.579	0
GLOB *	3.38±0.36	3.33±0.28	0.508	0.614
A : G	1.07±0.04	0.91±0.03	-14.29	0
ALP *	8.42±2.69	29.24±6.95	-15.826	0
ALT (SGPT)	51.42±13.09	34.7±8.51	5.118	0

The mean value of CP stastistically increases in all cases which is highly significant. The mean value of TP,Albumin, A:G Ratio, ALT, AST stastistically decreased in all cases which is highly significant.

The statistically significant decrease in value of Globulins is not significant. The statistically significant decrease in value of A: G ratio, which is highly significant.

The statistically significant increase in ALP values in all cases, which is highly significant. Statistically there is not much change in AST value.

4. DISCUSSION:

The present study was aimed to estimate the serum levels of ceruloplasimin (CP) in normal healthy pregnant women in the age group of 18yrs to 38yrs of total n=50 cases including 1st, 2nd,3rd trimester of cases compared with the same age group controls (18yrs to 38yrs) normal healthy women n=35. Controls and cases are non diabetic, non hypertensive, not anaemic and non-reactive for HIV.

In the present study serum CP level were found to be elevated 2-3 fold in normal pregnant group when compared with control group, which is statistically significant ($p< 0.000$).

The serum levels of CP were highest in the 3rd Trimester. The present study is in comparison with results obtained by Roopam Kalra VB et al. [5]

A raise in serum CP levels is observed in 2nd and 3rd trimester of normal pregnancy. This is in concurence with numerous other studies that have demonstrated increase in levels of CP in II & II trimester of pregnancy similar to previous observations of Friedman et al [6] and Singhal et al. [7]

In the present study the serum levels of CP were increased in 1st trimester when compared to controls with p value 0.899,Non significant since the number n is less hence it is affecting the t and p values, the increased CP levels in the 2nd and 3rd trimester when compared to controls with p value < 0.000.

The serum CP levels increase as a result of an acute phase reaction (APR). [2] Ceruloplasmin is a weak, late reacting Acute phase protein (APP). Levels are increased significantly by estrogens as in cases of pregnancy and in oral contraception.

The present study of serum total proteins were found to be decreased in pregnant group cases when compared with controls group which is statistically significant with ($p < 0.000$) which is highly significant. [3]

In the present study serum albumin was found to be decreased in pregnant group cases when compared with control group which is statistically not significant ($p < 0.440$).

The present study was in comparison with results obtained by Mendanhall. [8]

The present study of serum globulin were found to be elevated in pregnancy group cases when compared with control group which is statistically significant $p < 1.131$. [8]

The present study of serum A:G ratio was decreased in pregnant group cases when compared with control group which is statistically highly significant ($p <0.000$).

Divalent copper ion is known to bind to and active the estrogen receptor. The copper ions present in CP may activate estrogen receptors and thus play a role in increasing CP in pregnancy. The increase of copper level is also a sensitivity indicator of normal pregnancy.

Based on this study it can be proposed, that CP determination can be made as a routine marker in pregnancy to assess the fetal status and also avoid high risk pregnancy.

Hence, this study is an Endeavour to evaluate new markers in the assessment of pregnancy. Early intervention and appropriate diagnosis by estimation of serum copper and ceruloplasmin can substantially reduce morbidity and mortality associated with hepatic derangements of pregnancy.

Studies have shown that during pregnancy serum ALP levels increased which was highest in 3rd trimester, hence it has been extensively investigated.

Higher serum ALP levels and a correlation with the controls have been observed in present study ($P < 0.000$) which is highly significant. Hence, distinguishing cholestasis of pregnancy from hepatitis is difficult. [3] Hence, study of ALP isoenzyme pattern would help in evaluation of normal pregnancy.

Decrease in ALT and AST serum levels are not much reported in literature. However decrease in serum AST and ALT levels are seen in southern India in normal pregnancy by Loganathan G et al. [9]

Serum ALT levels of cases in the present study were significantly decreased when compared to the control group ($P < 0.000$). The lower value obtained for ALT concentration is in accordance with the study conducted by MAKU YANA D et al. [10] They have observed a lower concentration in pregnant women when compared to control group.

The serum AST levels were lower in pregnant women when compared to the control group Present study also showed that serum AST levels were correlated with the control ($P < 0.000$) which is highly significant. [10]

On the basis of the obtained results as well as the available literature, the increased serum levels of CP, ALP and decreased A:G ratio are the best markers of the pregnancy; The total proteins have not shown much significance. Probably this decrease in the total proteins must have been masked by the nutritional status.

In the first trimester the numbers of cases are only 5, this number is very less hence affecting the t-test and P value 0.895, when compared to controls, but there is an increase in CP levels in 2nd and 3rd trimester when compared to controls with P value < 0.000 which is highly significant.

Hence, it is also the best marker of the pregnancy. In the present study serum levels of ALT and AST were found to decreased in cases group when compared to control group.

Hepatic diseases complicate 3% of all pregnancy, the increase in ALP levels can not be differentiated from normal pregnancy. Hence to differentiate other parameters should be done such as Total Bilirubin, Types of bilirubin and gamma glutamyl transpeptidase GGTP could help in pregnancy coincidental hepatic disease because the gamma GGTP levels is normal or minimally elevated in pregnancy; Hence this can be estimated. [11]

Early detection and appropriate diagnosis by estimation of serum copper, CP and ALP can subsequently reduce morbidty and mortality associated with hepatic disorders of pregnancy.. These are economical, cost effective, easily estimated and not cumbersome and can be done routinely..

5. CONCLUSION:

Pregnancy is a normal physiological process of healthy women. Increased serum levels of CP and ALP were observed during normal pregnancy.

TP and A : G ratio of the normal pregnant women was decreased during normal pregnancy which indicates nutritional status of the mother.

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