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Original Article

Physiology Section

Effect of Ageing and Sex on the Caeruloplasmin (Cp) and the Plasma Protein Levels

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ABSTRACT

Introduction: Ageing is characterized by a failure to maintain homeostasis under conditions of physiological stress and this failure is associated with a decrease in the viability and an increase in the vulnerability of an individual. Because proteins are of critical importance to all the living organisms, there has been a great deal of interest on how ageing affects the synthesis and the turnover of proteins. Most of the plasma proteins, except immunoglobulins, are synthesized by the liver and they are also catabolized by it. So, the effect of ageing on the plasma proteins could also give a clue about the liver function and integrity in ageing in the 2 sexes

Objective: To study the effect of ageing and sex on the caeruloplasmin and the plasma protein levels.

Method: This study was done on individuals who were aged between 21 years and 90 years, of both sexes, who were selected from the medicine and the geriatric outpatient departments. Their anthropometric assessments were done and a dietary recall was obtained to assess their nutritional status. Their samples were subjected to blood test for the estimation of haemoglobin, ESR, blood sugar, serum creatinine, liver function tests and caeruloplasmin values.

Result: The effect of ageing on the serum levels of caeruloplasmin, albumin, globulin and total protein was assessed and it was found to be negative in both the sexes in all the progressive decades of life. However, a significant gender difference was observed in the serum levels of Cp and albumin. The observed increase in the Cp levels in females was probably due to the greater levels of circulating oestrogen in their bodies. Going by the literature, the lower levels of albumin in females may be inferred to be due to the lower rate of hepatic protein synthesis in the fairer sex.

Conclusion: This study convincingly proved that there was no adverse effect of ageing on either the liver integrity or on its over all functional ability to meet the metabolic demands. This however did not rule out that there was a decrease in the functional reserves of the ageing liver.

Key Words: Caeruloplasmin, Albumin, Globulin, Ageing

INTRODUCTION

Ageing is characterized by a failure to maintain homeostasis under conditions of physiological stress and this failure is associated with a decrease in the viability and an increase in the vulnerability of an individual. Because proteins are of critical importance to all living organisms, there has been a great deal of interest on how ageing affects the synthesis and the turnover of proteins. The changes in the protein metabolism could be a major result of the age associated differences in the gene expression and most of the plasma proteins except immunoglobulins are synthesized by the liver and are also catabolized by it. So, the effect of ageing on the plasma proteins could also give a clue about the liver function and integrity in ageing in the two sexes.

The rate of the hepatic regeneration declines with increasing age, but whether this is related to the lower circulating levels of the hepatotrophic factors, is not clear. Somatic mutations which include gene rearrangements increase with age and they are more frequent in the liver than in the brain [1].

In the studies of Fleming JE et al [2]. and Johnson TE et al [3] the hepatic synthesis of most of the proteins appeared to decrease with age, but it was found to vary with the individual proteins.

Prothro J [4] studied the protein and amino acid requirements of the elderly. This paper reviewed the changes in the body composition and the protein metabolism that are associated with ageing. The levels of the total plasma proteins, albumin, pre-albumin, transferrin and caeruloplasmin decline with age, and in the case of the albumin levels, the decline continues when the young-old are compared with the old-old.

Tokunaga K et al [5] studied the lipid peroxides and the antioxidants in the elderly. In their study, they determined the serum concentrations of the lipid peroxides and the antioxidants as the biomarkers for ageing. The lipid peroxides in the elderly group were significantly higher than those in the younger group.

Monod J and Jacob F [6] demonstrated an increased synthesis of caeruloplasmin which accompanied elevated oestrogen levels. In contrast, the decreased oestrogen levels did not alter the serum Cp levels. These results indicated that the Cp synthesis was not dependent on the oestrogen production and that it was independent of the hepatic copper status. These results confirmed that oestrogens may act as inducers for the synthesis of the Cp RNA templates, thus causing a subsequent increase in the caeruloplasmin protein levels.

OBJECTIVES

This study is done, (1) To study the effect of ageing on the metabolism of caeruloplasmin and other plasma proteins. (2) To correlate the plasma caeruloplasmin levels with advancing age in

the two sexes. (3) To study the changes in the levels of plasma albumin and globulin, the albumin / globulin ratio and total proteins which were caused by ageing in both the sexes.

PURPOSE

To study the effect of ageing on the liver integrity and function.

MATERIALS AND METHODS

Study Groups

120 healthy individuals of ages between 21 years and 90 years, of both the sexes, from the medicine and geriatric outpatient departments of the Government General Hospital, Park Town, Chennai-3, India were selected and divided into seven groups, decade wise. Those who had normal blood pressure and a normal body mass index and who were having a balanced diet were included in the study.

Illnesses like Diabetes mellitus, a history of recent surgery, trauma and infection and a past history of Diabetes mellitus, bronchial asthma, pulmonary tuberculosis, chronic infection or any disease which pertained to a chronic protein loss were excluded. Chronic smokers and alcoholics were also excluded from the study, as they could interfere with the liver function. Blood samples were taken from the groups in the morning after obtaining a written informed consent from the subjects. A careful history about the inclusion and exclusion criteria was elicited. Their anthropometric assessment was done and a dietary recall was obtained to assess their nutritional status. The samples were subjected to blood tests for the estimation of haemoglobin, ESR, blood sugar, serum creatinine, liver function tests and the caeruloplasmin values.

METHODS

- Haemoglobin estimation by the acid haematin method by using Sahli's haemoglobinometer.
- Assessment of the erythrocyte sedimentation rate by using Westergren's method.
- Blood glucose estimation by using an autoanalyser by the glucose oxidase and the perioxidase methods (Trinder's method).
- Assessment of serum creatinine by using the alkaline picrate method and an autoanalyser.
- Liver function tests were done in an autoanalyser by using reagent kits.
- Caeruloplasmin: Manual method (the P-Phenylene diamine oxidase method) [7]

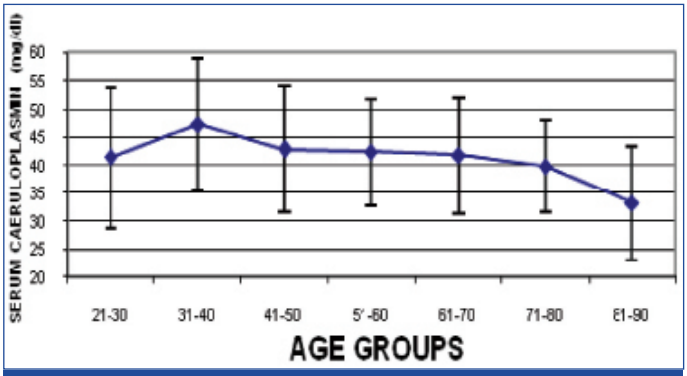
RESULTS AND ANALYSIS

120 individuals were included in the study. They were classified into seven groups depending on their ages. They were once again classified according to their sex and their menopausal status. The haematological statistical parameters which were assessed in this study are given in [Table/Fig-1].

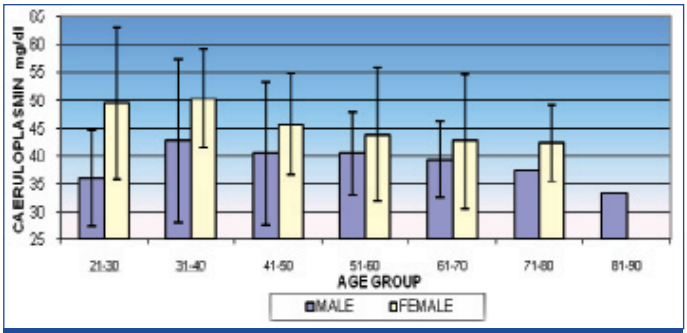
The mean caeruloplasmin levels gradually decreased with age from 41.4 mg/dl in the 21-30 years age group to 33.26 mg./dl in the age group of 81-90, years, peaking in the 31-40 years age group, with a mean value of 47.225mg/dl. The p value was > 0.05. The results were not statistically significant, though they showed a decreasing trend in the mean values with increasing age. The p value was obtained by correlating the caeruloplasmin values between the age groups [Table/Fig-2].

Parameters	Subjects	Mean	SD
Age	120	50.98	17.36
BMI kg/m^2	120	22.86	2.01
Hb g/dl	120	11.48	1.17
ESR_30	120	9.13	5.22
ESR_60	120	26.95	15.97
RBS mg/dl	120	104.18	21.92
Serum Creatinine mg/dl	120	.97	.26
Serum Bilirubin mg/dl	120	.74	.68
SGOT IU/L	120	22.78	5.18
SGPT IU/L	120	20.26	6.14
ALP IU/L	120	140.43	49.26
Total-protein g/dl	120	7.03	.43
Albumin g/dl	120	3.90	.40
Globulin g/dl	120	3.12	.52
Caeruloplasmin mg/dl	120	42.62	10.80

[Table/Fig-1]: Statistical Haematological Parameters of the Study Group



[Table/Fig-2]: Distribution of Caeruloplasmin in Different Age Groups

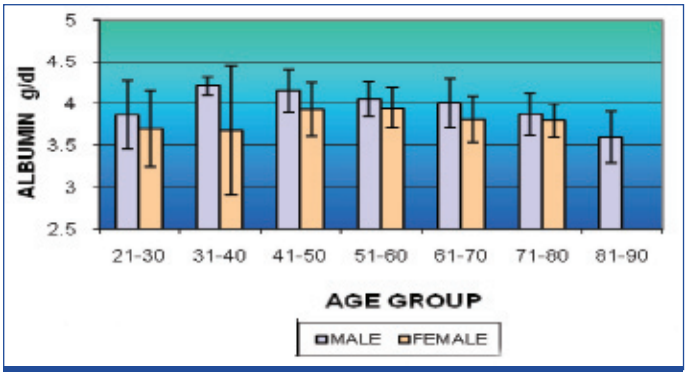


[Table/Fig-3]: Age & Sex-wise Distribution of Caeruloplasmin

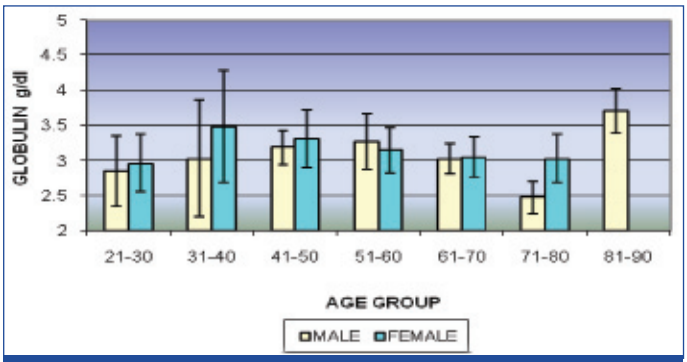
The mean serum caeruloplasmin levels in the females were higher in all the age groups as compared to those in the males, in this study, with a p value < 0.05, which is statistically significant [Table/Fig-3]. The age and sex wise comparison of the mean serum albumin levels showed lower levels in the females than in the males in all the age groups . The p value was < 0.05 sexwise. The results were statistically significant [Table/Fig-4].

Their levels almost intersected in both the sexes. There was no sexwise difference in the mean values. The p value was more than 0.05, which showed that the sexwise difference in the levels was not statistically significant [Table/Fig-5].

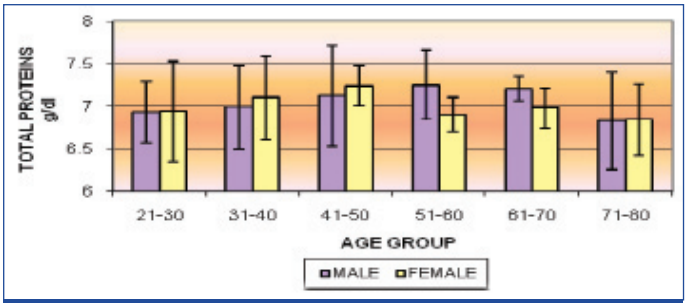
The mean total protein levels sex wise in the different age groups of both the sexes are shown. There was an increase in the mean level after the age of 50 years in males and there was a decrease in the mean value after the age of 50 years in females, which was



[Table/Fig-4]: Age & Sex-wise Distribution of Albumin



[Table/Fig-5]: Age & Sex-wise Distribution of Globulin



[Table/Fig-6]: Age & Sex-wise Distribution of Total Proteins

not statistically significant. The sexwise p value was > 0.05, which showed no statistically significant difference between the sexes [Table/Fig-6].

DISCUSSION

In the present study, the serum levels of caeruloplasmin, albumin, globulin and total proteins were compared between the different age groups in both the sexes, to study the effect of age and sex on these levels. Various haematological parameters were measured to rule out Diabetes mellitus, renal disorders, etc. Liver function tests were done to assess the liver integrity and function.

CAERULOPLASMIN

The mean Cp level in the total study group was 42.62 mg/dl; in the male group, it was 39.42 mg/dl and in the female group, it was 45.83 mg/dl. The mean Cp level in the third decade of life was 41.4 mg/dl, which increased further in the next decade to 47.225 mg/dl. The mean values gradually decreased as the age advanced, till it reached 33.26 mg/dl in the oldest age group. As the p value was > 0.05, this study showed that there was no significant change in the serum Cp levels as the age advanced. The mean serum caeruloplasmin levels in the females were higher in all the age groups as compared to those in the males in the study, with a p value of < 0.05, which was statistically significant. The mean values of serum Cp, depending on the menopausal status, did not show a significant difference. The present study showed no change in the serum Cp levels with advancing age and there was a significant higher range of serum Cp in the females than in the males. The reason for this sex difference may be the direct effect of oestrogen in the females. As was studied by Mond. J. [6], oestrogen could act as an inducer for the synthesis of the CpRNA templates, thus causing a subsequent increase in the Cp protein levels since the increase in independent of hepatic copper levels. These results are in consonance with that hypothesis. Johnson E et al. [8] have shown increased serum Cp levels in females who were on oral contraceptives.

ALBUMIN

The mean serum albumin levels in all the age groups fell within the range of 3.6 to 4.006 g/dl and the p value for the variation, t was> 0.05, which was not statistically significant. This showed that there was no effect of age on the serum albumin levels. This was similar to the findings of Oyeyinka Go et al. [9], who saw no change in the albumin levels as the age advanced, although 70% of the other studies showed lower albumin levels with advancing age. The serum albumin levels were lower in females than in males in all the age groups, which was similar to the finding of Wintered et al. They compared the rate of the protein synthesis in females and males. They proposed that the protein synthesis was lower in the female subjects, but it should be kept in mind that the low values could also be caused by an increase in the rate of degradation.

The difference in the mean values in females, as was shown by their menopausal status, did not show any statistical significance and there was no change in the levels, based on the menopausal status in females.

GLOBULIN AND TOTAL PROTEINS

The mean serum globulin and total proteins levels, based on the age, sex and the menopausal status, did not show any statistical insignificance. This showed that there was no effect of age and sex on these levels. The globulin levels do not depend only on the protein synthesis, but they are altered by the immunoglobulin levels, as a result of which the globulin levels in ageing and sex cannot be explained by the protein metabolism. In the same way, total protein depends on the globulin levels and for the same reason, cannot indicate protein metabolism in ageing.

THE A/G RATIO

There was no change in the A/G ratio in both the sexes in all the age groups which were studied, except the oldest group.

The serum caeruloplasmin and the albumin levels did not show any change with advancing age in the present study. Many studies have suggested that the protein synthesis decreases with increasing age. Some studies have also shown the effect of age on the specific steps in protein synthesis, which causes the decline in the protein synthesis. In the same way, there also are studies which suggest that the protein degradation also decreases with increasing age. Thus, the protein turnover in decreased, but the concentration remains the same. The above evidence may substantiate our finding that there was no effect of age on the serum Cp and the albumin levels.

On comparison of the degree of fall between the Cp and the albumin levels, they were seen to run parallel in the males as well as in the females with advancing age, but this finding was statistically

insignificant. However, in the pre menopausal females, there was no fall in the levels of Cp and albumin . The consistent higher levels of Cp in the pre menopausal women may be attributed to the effect of oestrogen.

SGOT/SGPT/ALP

The mean values of the liver enzymes which were examined in this study were found to be within the normal range in both sexes in all the age groups .This indicated that ageing had not compromised the liver integrity and function. However, the effect on the anatomical and functional reserve capacity of the liver remains to be investigated.

SUMMARY AND CONCLUSION

120 subjects who consisted of 60 males and 60 females were divided according to their age, decade wise, into seven groups. The effect of ageing on the serum levels of caeruloplasmin, albumin, globulin and total protein was assessed and it was found to be negative in both the sexes in all the progressive decades of life.

However, a significant gender difference was observed in the serum levels of Cp and albumin. There were significantly higher levels of Cp in females, not only in the reproductive age group, but also after the climacteric. On the other hand, the serum albumin levels were significantly lower in the females in all the age groups.

The observed increase in the Cp levels in females was probably due to the greater levels of circulating oestrogen.

Going by the literature, the lower levels of albumin in females may be inferred to be due to a lower rate of hepatic protein synthesis in the fairer sex.

No age or gender difference was detected in this study with regards to the serum globulin and the total protein concentration as well as in the A/G ratio.

Comparison of the Cp and albumin levels in the males and females revealed a similar trend in males and postmenopausal females. The difference in the premenopausal women may be due to the hormonal influence.

This study convincingly proved that there was no adverse effect of ageing on either the liver integrity or on its overall functional ability to meet the ordinary metabolic demands. This however, does not rule out, that there was a decrease in the functional reserve of the ageing liver.

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