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Effect of Systemic Lupus Erythematosus on some Biochemical Parameters in Female Patients

Eman G.E Helal*, Medhat El- Shafaey, Hala Rahoma** and Mervat Abdel- Rahman*****

*Zoology Department, Faculty of Science, Al- Azhar University (Girls).** Clinical Immunology and Allergy Department, Faculty of Medicine, Ain- Shams University. ***Clinical Pathology Lab., Student Hospital, Cairo University.

Abstract:

It has been noticed that there is an increase in the number of women suffering from SLE. Most studies confirmed that serum DHEA (dehydroepiandrosterone) and DHEA sulphate are lower among patients with SLE than among controls even- during phases of inactive disease so we performed this study to detect the level of DHEA-S in the female patients with SLE. The overall results confirm that DHEA treatment was well- tolerated, significantly reduced the number of SLE flares, and improved patient's global assessment of disease activity. Some serum parameters like liver and kidney functions were detected. Biochemical analysis showed that there is a significant increase of total lipids, cholestrol, triglycerides. But insignificant change in serum glucose, urea nitrogen and uric acid levels were recorded. From the present study three things were concluded. Firstly, there is a strong relationship between level of DHEA and the progression of SLE. Secondly, liver activity and kidney functions were not affected by SLE disease.Thirdly, DHEA treatment has a beneficial effect on female patients. So this study recommended to follow up DHEAS in female patients and use it in a proper dosage. In addition, further study must be done.

Key Words: SLE, DHEA, Liver functions, Kidney functions.

Introduction:

Systemic lupus erthematosus (SLE) is an autoimmune disease that causes a characterisitic rash associated with inflam-mation of connective tissues, particularly joints, throughout the body. In autoimmune diseases, the immune system attacks the body instead of protecting it. Renal, pulmonary and vascular damage are potential problems resulting from SLE (Kardestuncer and Frumkin, 1997).

DHEA (dehydroepiandrosterone) is the most abundant steroid in the bloodstream produced mainly in the adrenal glands. It is a prohormone that produces other hormones. DHEA converts to estrogens, testosterone, progesterone, cortisone and many other steroid hormones. Possible therapeutic applications of DHEA supplementation include the prevention and\or treatment of heart disease, diabetes, obesity, osteoporosis and arthritis (Barrett-conner *et al*., 1986).

Several studies have documented that serum levels of DHEA and DHEA sulphate are lower among patients with SLE than among controls even during phases of inactive disease and that these lower levels are not explained by corticosteroid therapy (Jungers *et al*., 1982 and Lahita *et al*., 1987). The decline in circulating DHEA levels occuring with aging has been linked to the

gradually increasing prevalence of atherosclerosis, obesity and diabetes in elderly individuals*(Perrini et al., 2004)*. DHEA shows promise as a new therapeutic agent for the treatment of mild to moderate SLE. Further studies of DHEA in the treatment of SLE are warranted (Van vollenhoven, 1994).

The present study was therefore designed to examine the leuels of DHEA in the Egyptian female patients with SLE and study the effect of SLE on some serum parameters including liver and kidney functions, lipid and protein profile, where their relation to DHEA level is still unclear.

Material and Methods:

Patients:

This study comprised thirty premenopausal females which were selected from the Out patient Clinic of Internal Medicine Departement of Ain- Shams Universtiy hospital. Their ages ranged from 18-45 years. They were classified into the three following groups:

Group A (normal): include ten women without SLE.

Group B (patient 1): include ten women with SLE, disease duration less than three years.

Group C (patient 2): include ten women with SLE, disease duration more than three years.

SLE Disease Index (SLEDAI):

SLEDAI is a valid model of experienced physicians global assessment of disease activity in lupus. It experts in the field of lupus research. They selected the 24 "most important" descriptors of disease activity in SLE and exclude some rare manifestations of disease activity (Bombardier et al., 1992). We selected SLEDAI over other disease activity measures such as the systemic lupus measures, the British isles lupus activity index because it could be scored retrospectively and had been demonstrated to be at all least sensitive to changes in clinical status as other indices (Esadaile *et al*., 1996).

Biochemical Assessment:

Laboratory investigation included serum glucose level, total protein, albumin concentration, total lipid, cholesterol level, triglyceride level, aspartate transaminase (AST), alanine transaminase (ALT), total bilirubin levels, urea nitrogen level, uric acid and serum DHEA-S. Clotted blood samples were centrifuged for 10 min at 5000 rpm and separated for analysis. Glucose determination was based on the enzymatic colourimetric method by Trinder (1969). Serum total protein was estimated using protein kits according to Doumas (1975). Albumin concentration has been determined according to the method of (Doumas *et al*., 1971). Total lipid concentration in serum was done according to the method of (Knight *et al*., 1972). Serum cholesterol level has been determined according to the method of (Allain *et al*., 1974). Also triglyceride concentration has been measured according to the method of Wahlefeld (1974). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) activities in serum were measured according to Reitmon and Framkel (1957). The determination of total bilirubin in serum was carried out using the method of (Wooton, 1964). Serum urea nitrogen was estimated according to the method of Beale and Croft (1961). Measurement of serum DHEA-S has been determined by using ELISA kit (Gordon *et al*., 2002).

Statistical Analysis:

The method of t-test (Snedcor,1982) was used for the comparison between the means obtained for the different measured parameters in control and each of the experimental groups. The level of significance accepted was $p<0.05$.

Results

Assessment of the disease activity:

Using SLE disease activity index SLEDAI (Bombardier *et al*., 1992). The disease was active in 30% of patients of group B (disease duration less than 3 years)

and it was inactive in 70% of patients of the same group. While in group C (disease duration more than 3 years), the disease was active in 40% patients, and inactive in 60% of patients of the same group (results were summarized in table 1).

Serum DHEA–S level:

Statistical analysis showed significant decrease ($P < 0.05$) in SLE patients of both group B and group C (fig.1) .

Fasting serum glucose level:

In the present study serum glucose level showedan insignificant change in SLE patients in both group B and group C as compared with normal women (fig.2) .

Serum AST and ALT activity:

Concerning serum AST and ALT activities , the present study showed non significant change in SLE patients in both group B and group C as compared with normal women (fig. 3,4) .

Serum total bilirubin level:

Mean serum total bilirubin level in group B was found to be 1.003 mg/dl ± 0.106, while in control group was 0.171 mg/dl ± 0.053. Mean serum total bilirubin level in SLE women of group C was found to be 1.04 mg/dl ± 0.063 . So statistical analysis showed no significant change when compared with control women (fig.5) .

Kidney Functions:

Serum urea nitrogen levels:

Serum urea nitrogen level had an insignificant change on SLE women of both group B and group C when compared to normal women (fig.6).

Serum Uric acid

In the present study the level of serum uric acid had an insignificant change on SLE women (group B and group C) when compared with normal women (fig. 7).

Proteins Profile:

Serum total protein level:

In the present study the level of serum total protein was insignificant change in SLE patients of group B and group C of adult women as compare to normal women (fig.8).

Serum albumin level:

Concerning Serum albumin level, an insignificant change was recorded in both group B and group C compared with normal women. Results were summarized in (fig.9).

Serum globulin level:

In this study Serum globulin level showed insignificant change in SLE patients of both group B(disease duration less than 3 years) and group C (disease duration more than 3 years) compared with normal women (fig.10).

A/G ratio:

Statistical analysis of A/G ratio showed insignificant change in SLE women (group B and group C) as compare to normal one (fig.11).

Lipids profile:

Total lipids level:

In the present study serum total lipids level recorded highly significant increase ($P<0.05$) in patients complaining from SLE in both group B and group C as compared to normal women as shown in (fig.12).

Serum cholesterol level:

Mean serum cholesterol level in group B was found to be 169.2 mg/dl ± 1.899 , and in group C was found to be 171.7 mg/dl ± 1.48 , while in normal group was 154.5 ± 1.29. Statistical analysis showed highly significant increase ($P<0.01$) of cholesterol level in both group B and group C (fig.13).

Serum triglyceride level:

It is clearly in the present data that both group B and group C had a highly significant increase ($P<0.01$) in serum triglyceride level as compared with control women (fig.14).

Table (1): Disease activity of SLE patients:

Groups	Group B (Time of disease less than 3 years)		Group C (time of disease more than 3 years)	
Disease activity	Active disease	Inactive disease	Active disease	Inactive disease
% patients	(30%)	(70%)	(40%)	(60%)
Activity score	(6-10)	(0-3)	(6-18)	(0-3)

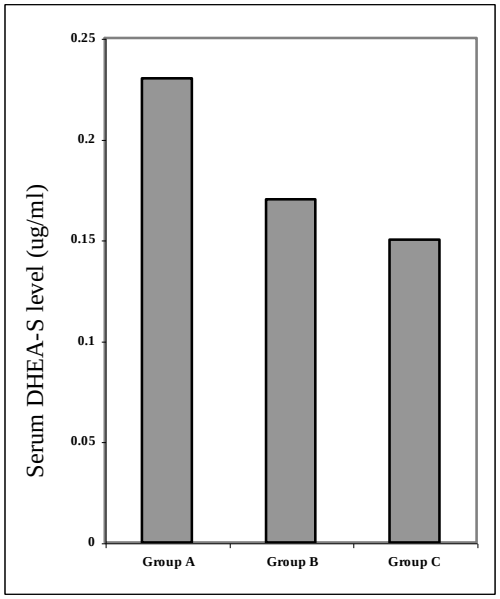
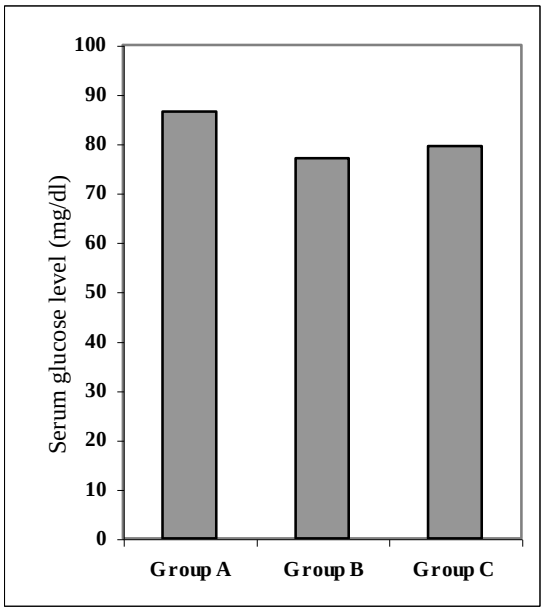


Fig.(1): Serum DHEA-S level (ug/ml) in normal women (group A) and SLE women (group B & group C)



Fig(2): Serum glucose level (mg/dl) in normal women and SLE women in both group B& group C

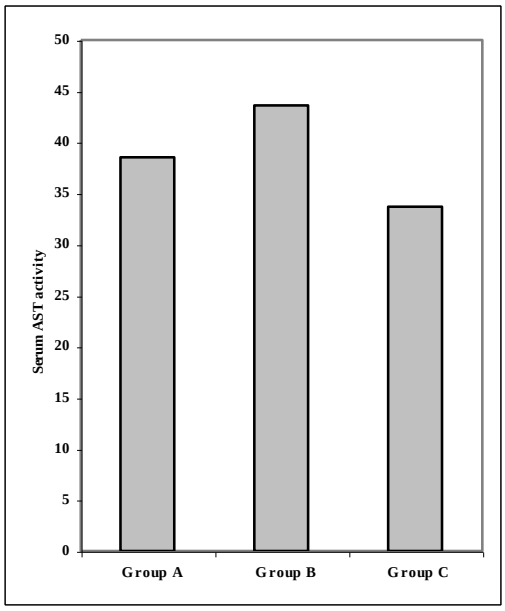


Fig.(3): Serum AST activity (u/l) in both women (group A) and SLE patient group C).

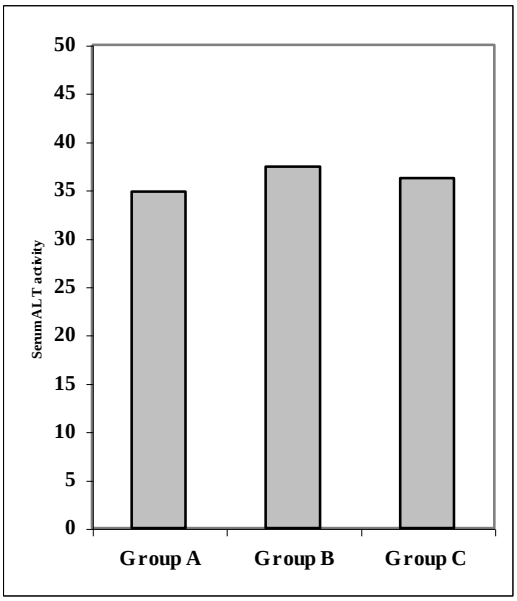


Fig.(4): Serum ALT activity in normal women (group A) and SLE patient (group B and group C).

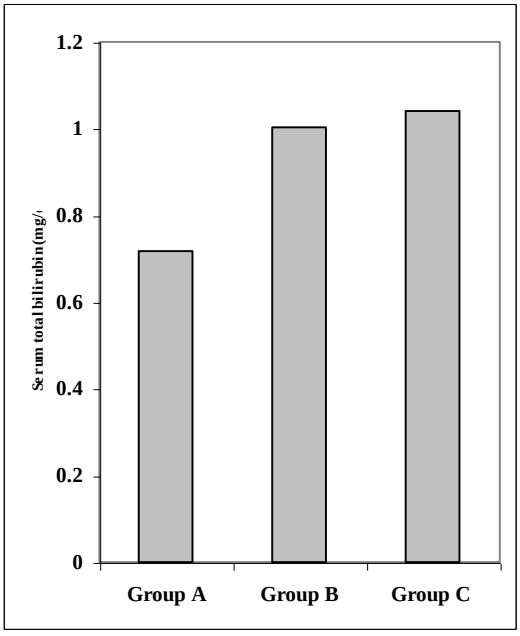


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Fig.(5): Serum total bilirubin level in normal and SLE women (group B and group C).

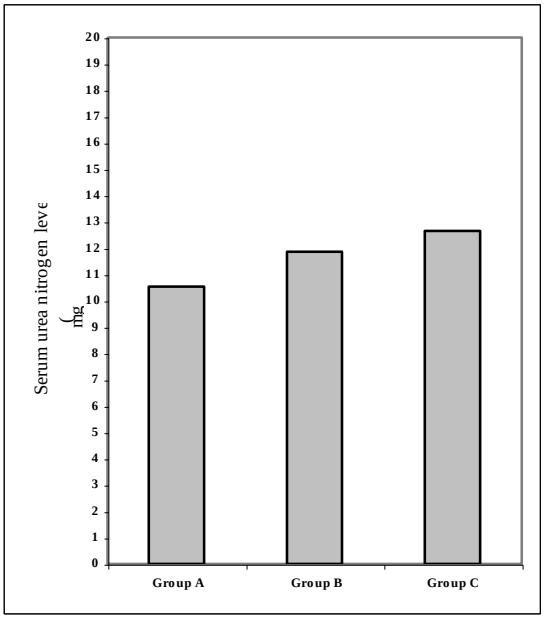

Fig.(6): Serum urea nitrogen level (mg%) in normal women (group A) and SLE women (group B and group C).

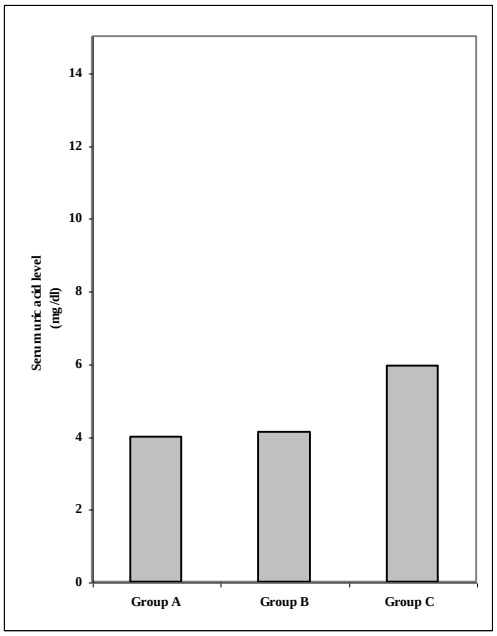

Fig.(7): Serum uric acid level (mg/dl) in normal women (group A) and SLE women (group B and group C).

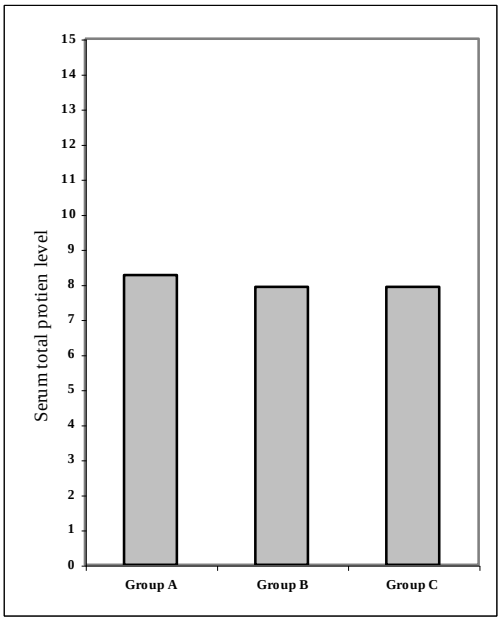

Fig.(8): Serum total protein level in normal women (group A) and SLE women (group B and group C).

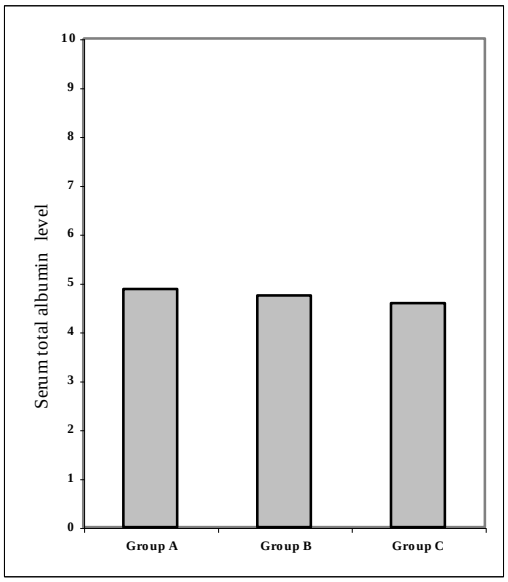

Fig.(9): Serum albumin level (mg/dl) in normal women (group A) and SLE patients (group B and group C).

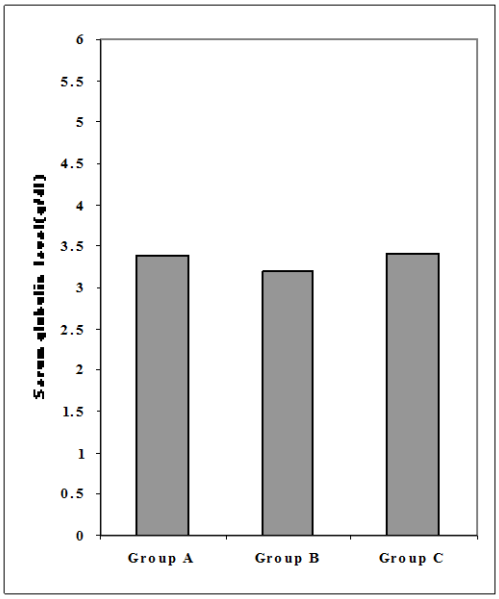

Fig.(10): Serum globulin level in normal women (group A) & SLE women (group B and group C).

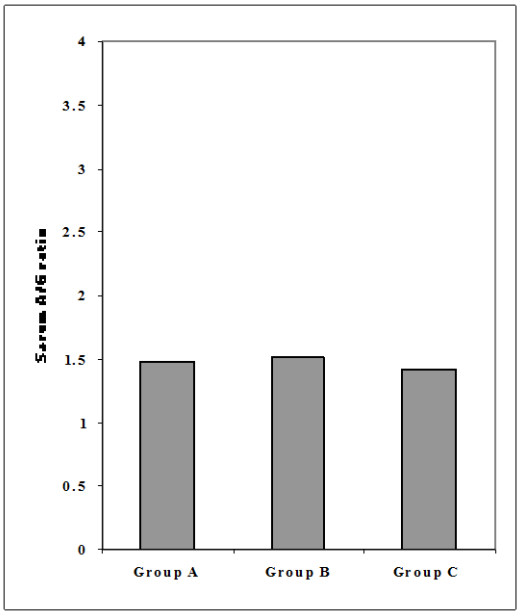

Fig.(11): Serum A/G ratio in normal women (group A) and SLE patients (group B and group C).

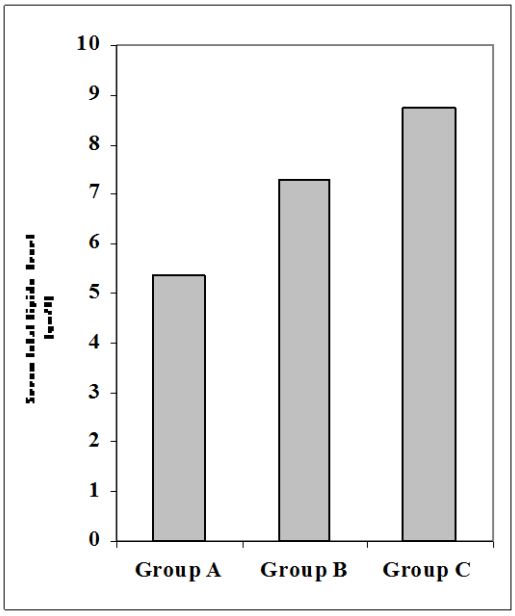

Fig.(12): Serum total lipids level (mg/l) in normal women (group A) and SLE women (group B and group C).

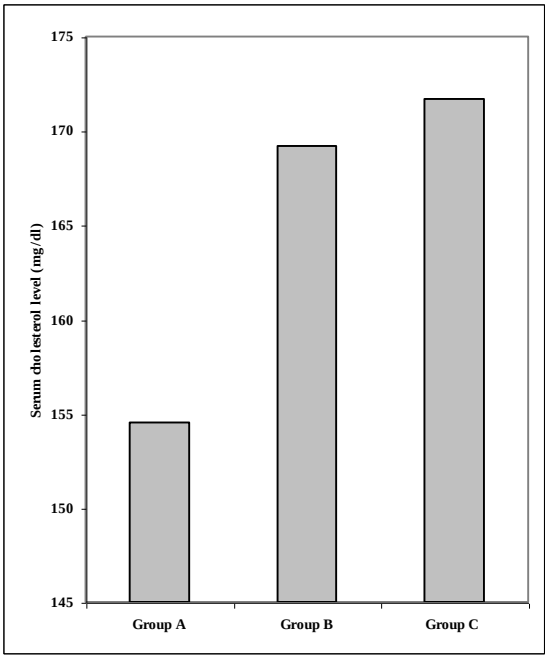

Fig.(13): Serum cholesterol level (mg/dl) in normal women (group A) and SLE women (group B and group C).

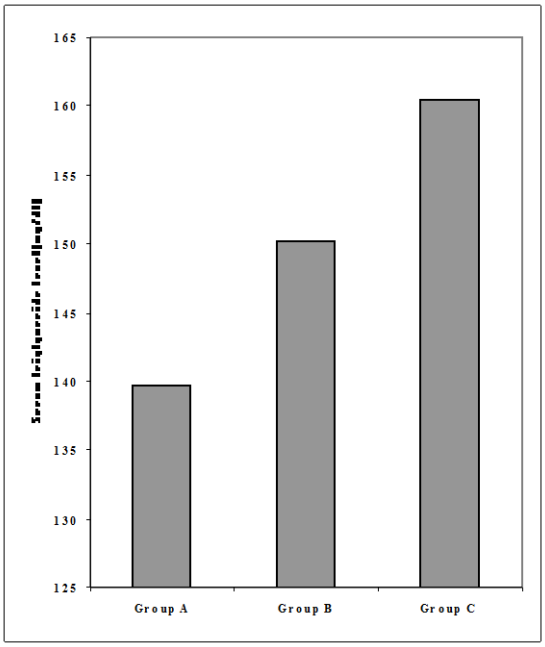

Fig.(14): Serum triglyceride level (mg/dl) in normal women (group A) and SLE patients (group B and group C).

Discussion:

The present study showed a significant decrease in the mean serum levels of DHEA-S in SLE patients. Dehydroepi-androsterone sulphate (DHEA-S) was the major adrenal hormone whose serum levels were significantly lower in SLE patients *(Vogl et al., 2003)*.

Merrill (2003) showed that deficiency of the weak androgen dehydroepian-drosterone (DHEA) and its sulfoconjugated metabolite DHEA-S has been assocaited with a number of serious illnesses , include-ing lupus.Observational clinical studies and *in vitro* experiments have suggested that DHEA treatment might have a significant impact on immunological function.

DHEA may be useful as a therapeutic agent for the treatment of mild to moderate SLE . Further studies of DHEA in the treatment of SLE are warranted *(Ronald et al., 1995)* .

The present study showed insigni-ficant change in fasting serum glucose level , normal transaminases activity and total bilirubin level in SLE patients in both group B and group C when compared with normal group . This attributed to normal liver function and normal glycogenesis rate *(Karmer , 1989)* . This indicate that liver activity was not affected by systemic lupus erythematosus disease .

The present data showed insignificant change in serum urea nitrogen and uric acid in SLE patients when compared with normal women. These results is in harmoney with non significant change of serum total protein, albumin , globulin levels and A/G ratio . This means that SLE disease has no affect on protein profiles and kidney functions because the present patients were under proper treatment.

Cholesterol is synthesized in the liver adrenal gland and in the intestine. Cholesterol is the precursor of steroid hormones and bile acids and is an essential constituent of cell membrane *(Teitz , 1983)*

Present results revealed that total serum lipids , cholesterol and triglyceride levels were significantly increased in SLE patients in both group B and group C when compared with normal group . The elevated serum triglyceride in the present study may be attributed to decrease clearance and increased production of the major transports of endogenously synthesized triglyceride (*Betteridge , 1986*) . The increased serum cholesterol may be explained by acceleration of intestinal cholesterol synthesis and increased rate of intestinal absorption . These results are similar to that observed by *Formiga et al.(2001*). While *Svenungsson et al. (2003)* was observed increase in serum total cholesterol (TC) and triglycerides and decrease in HDL level in SLE patients in comparison with controls .

Further investigations should be done to clarify the rule of environmental reasons and to search for other causes for SLE. Also genetic expression must be examined and follow up the effect of some drugs which may causes SLE like symptoms.

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تأثير مرض الذئبة الحمراء على بعض المعايير البيوكميائية لمرضى من النساء المصريات

إيمان جمال الدين عزت هلال*, مدحت صابر الشافعي, هاله حسن رحومه * ، مرفت أحمد جاد عبد الرحمن*****

*قسم علم الحيوان- كلية العلوم- جامعة الأزهر(بنات) **قسم المناعة الإكلينيكية و الحساسية- كلية الطب- جامعة عين شمس ***معمل الباثولوجيا الإكلينيكية- مستشفى الطلبة- جامعة القاهرة- الجيزة

يعتبر مرض الذئبة الحمراء مرض مناعي غير معروف السبب وهو يسبب طفحا جلديا مصحوبا بالتهاب الأنسجة الضامة وخاصة الأربطة وتكون الإناث في فترة الخصوبة أكثر عرضة للإصابة من الرجال بنسبة تغير 90%، وقد أثبتت معظم الدراسات أن نسبة هرمونDHEA تكون منخفضة في المصل في مرضى الذئبة الحمراءمقارنة بالأشخاص العاديين ولهذا يمكن تشخيص هذا المرض عن طريق قياس هذا الهرمون في المصل وقد ثبت بالنتائج العلمية أن العلاج بهذا الهرمون مسموح به وأنه يقلل من حدة ونشاط مرض الذئبة الحمراء كما أثبتت الأبحاث تحسناً ملحوظاً في المرضى المعالجين بهذا الهرمون، وقد تم قياس بعض المعايير البيوكميائية مثل وظائف الكبد والكلى وقد أظهرت التحاليل البيوكميائية زيادة ملحوظة في الدهون الكلية، الكوليسترول، الجلسريدات الثلاثية، ولكن لم يلاحظ أي تغير له دلالة إحصائية في مستوى الجلوكوز في المصل وأيضاً في وظائف الكبد والكلى والبروتينات، وقد بينت الدراسة أنه لابد من تخفيض الجرعة المستخدمة من الإسترويدات كلما أمكن وكذلك التوصية باستخدام هرمون الديهيدروإبياندروستيرون كعلاج مع الملاحظة المستمرة لمستواه في المصل.