ORIGINAL
PROF-1700

SYSTEMIC LUPUS ERYTHEMATOSUS, FEMALE OF FERTILE AGE

CHANGES IN REPRODUCTIVE HORMONES ESTROGEN AND PROLACTIN LEVELS

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ABSTRACT... Background: Systemic lupus erythematosus (SLE) is an important autoimmune disease and occurs when the body is mistakenly attacked by its own immune system. Prolactin acts as a cytokine and plays an important role in human immune response including autoimmune diseases. SLE is an immune complex mediated disease and is more common during pregnancy. **Objective:** Research is designed to analyze the level of serum prolactin in the pathogenesis of systemic lupus erythematosus and compared with estrogen in female of fertile age. **Study Design:** Observational **Period: Setting:** Study was carried out in the Department of Biochemistry, BMSI, in collaboration of ward-6 JPMC Karachi. **Material and methods:** Thirty five diagnosed cases of SLE and in addition 35 normal healthy controls from general population were included in the study. Serum levels of prolactin, estrogen, RA factor and ESR were estimated and correlated. **Statistical analysis:** The data was analyzed by using SPSS version 17. The student t-test & chi-square test was used the p-value ≤ 0.05 consider significant. **Results:** The results showed that patients suffering from SLE have highly significant ($p<0.001$) serum level of reproductive hormones prolactin and estrogen, in addition, significant changes in ESR indicate the infection when compared with control. Further, prolactin was negatively correlated with estrogen as well as with menarche while BMI have positively correlation with estrogen regardless of prolactin and menarche. **Conclusions:** Enhanced serum prolactin and estrogen changes in patients with systemic lupus erythematosus (SLE), may be used as a prognostic tool for autoimmune diseases.

Key words: Systemic lupus erythematosus, prolactin, estrogen, autoimmune diseases.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an immune complex mediated disease, which is more common in women. In this disease autoantibodies are formed against DNA. Antibodies against double stranded DNA are the hallmark of SLE. Female hormones play an important role in the expression of SLE[1]. Last decade evidence supported the hypothesis that both mild and moderate elevation of serum prolactin (PRL) participate in the clinical expression and pathogenesis of SLE[2].

Patient with SLE developed different combination of symptom and organ involvement, common complaints are fatigue, low grade fever, loss of appetite, muscle aches, ulcers of mouth and nose, facial rash (butterfly rash). White blood cells and blood clotting factors decreased in SLE increasing the risk of infection and bleeding[3].

Individuals with HLA DR2 or DR3 genes are predisposed to SLE; many different genes contribute to disease susceptibility. It is estimated that atleast four susceptible genes are needed for the development of the disease. Susceptibility to SLE involves human leukocyte antigen (HLA) class II genes. An association HLA DR2 and DR3 with SLE is a common finding in these patients[4].

MATERIAL AND METHODS

A total of 70 subjects were included in this study. A structured questionnaire regarding the demographic data was filled in by each patient. Consent was also obtained from the patient as well as control subjects. The subjects were divided into two groups: Group A, comprised of 35 diagnosed cases of systemic lupus erythematosus in fertile female patient age ranges between 16 to 45years.

Group B, comprised of 35 age matched healthy control group of fertile female from the general population having normal serum prolactin level.

According to American college of Rheumatology the selection criteria for SLE is based on eleven (11) criteria's

for diagnosing SLE, when at least 4 of the 11criterias are present[3].

1)Butterfly rash, 2) discoid skin rash, 3) photosensitivity, 4)ulcer of mouth and nose, 5) arthritis, 6) pleuritis/pericarditis, 7)kidney abnormalities, 8) convulsions, 9) blood count abnormalities,10) antinuclear antibodies and 11) anti dsDNA.

INCLUSION CRITERIA

Diagnosed cases of SLE in female of fertile age.

EXCLUSION CRITERIA

Patients with diabetes mellitus.
Infertility.
Age below 16 and above 45.
Patient taking steroids.
Patient taking oral contraceptive.
Lactating mothers.
Any thyroid disease.
Pregnancy.

SAMPLE COLLECTION AND STORAGE

Intravenous fasting blood 6 to 8 ml was collected from each patient and control subject. 2 ml blood was transferred to ESR tube containing ethylene diaminetetraacetic acid (EDTA) as anticoagulant. The remaining was transferred to a centrifuge tube and then centrifuged for 10 minutes. Serum of SLE patients and control group were analyzed for biochemical parameters. Serum prolactin and serum estrogen were estimated by ELISA method, rheumatoid factor was estimated by latex agglutination test, ESR was done by Western gren method.

RESULTS

Table I shows the comparison of biophysical parameters between systemic lupus erythematosus and age matched control groups. The mean value of age 23.49 ± 0.64 and parity 1.40 ± 0.19 of SLE and control subjects age 28.71± 1.13 and parity 2.46 ± 0.27 were observed it was found significantly lower in SLE group, where as menarche 12.74 ± 0.16 and BMI 20.51 ± 0.31 were observed statistically non-significant.

It was observed in table II the comparison of hormones, RA Factor and ESR between systemic lupus erythematosus and control group. The levels of serum prolactin 65.34 ± 24.22 and estrogen 80.13 ± 1.73, ESR 97.74 ± 3.13 and RA factor 122.91 ± 4.61 were significantly increased as compared with control subjects prolactin 9.92 ± 0.07, estrogen 30.31 ± 4.79, ESR 17.70 ± 0.86 and RA factor 16.47 ± 0.62 by using student t-test.

Table III shows highly significant but negative correlation of prolactin with menarche (-0.740) and estrogen (-0.967) similarly age (-0.638) show significant but negative correlation with menarche, BMI show significant but positive correlation with estrogen.

Table-I. Comparison of biophysical parameters between systemic LUPUS erythematosus (SLE) with control groups (Values are expressed as Mean ± SEM)

Parameters	Control (n=35)	SLE (n=35)
Age (years)	28.71±1.13	23.49*±0.64
Menarche (years)	12.63±0.17	12.74±0.16
Parity	2.46±0.27	1.40*±0.19
BMI (Kg/m^2)	21.78±0.66	20.51±0.31

**Significant difference with P<0.001. When compared with control*

Table-II. Comparison of hormones, ra factor and esr between systemic lupus erythematosus (SLE) with control groups (Values are expressed as Mean ± SEM)

Parameters	Control (n=35)	SLE (n = 35)
Serum prolactin (ng.ml)	9.92±0.70	65.34*±24.22
Serum estrogen (Pg/ml)	30.31±4.79	80.13*±1.73
RA factor (IU/ml)	16.47±0.62	122.91*±4.61
ESR (mm/hr)	17.70±0.86	97.74*±3.13

**Significant difference with P<0.001. When compared with control*

If r<0 then consider negative correlation, if the value of r>0 then consider positive correlation, if r = 0 then consider no correlation between two variables.

Table-III. Correlation of estrogen versus prolactin and BMI in SLE patients

Parameter	Menarche (r-value)	Estrogen (r-value)
Prolactin	-0.740*	-0.967*
BMI	NS	0.402*
Age	-0.638*	NS

NS non significant.

DISCUSSION

The incidence SLE was much higher in women as compared to men; this preponderance of SLE in women was thought to be mediated in part through the female sex hormone, estrogen and prolactin[5]. SLE occurs in young patients but late onset SLE patients had a more insidious onset and a longer time interval between disease onset and to diagnosis leading to higher mortality rate so these patients require greater attention[6]. Correlation of prolactin with SLE disease activity was found significant, as seen that immunosuppressive therapy decreased prolactin levels in direct correlation with decreased SLE activity. This finding emphasizes that prolactin may play a role in the pathogenesis and clinical expression of SLE[7].

Incidence of SLE was found to be highest in early age group (14-40years) 3 this was consistent with our study which also indicate that SLE occurs in younger age group. Similar study attributed the same finding indicating that early onset (below 40 years) is more fatal than the late onset disease[8].

In the present study BMI in the patient suffering from SLE, when it is compared with control subject was found insignificant[9]. This shows that increase BMI are independently associated with quality of life in patients with SLE, optimizing that weight can significantly improve the disease.

SLE frequently starts in women of child bearing age and show low parity (nulliparous) in women or one child mother. women who experience spontaneous abortions were at high risk[10]. Our study was also in agreement with low parity when compared with control.

A study suggested that patients suffering from SLE also showed hyperprolactinemia[11] our study was consistent with these findings. Hyperprolactinemia was frequently detected in SLE patients and a significant correlation existed between hyperprolactinemia and lupus activity[12]. The present study is in total agreement with these findings.

Sex hormones appear to play an important role as modulators of autoimmune diseases. Estrogen enhances humorol immunity[13]. One study indicated that estrogen exhibits anti inflammatory and anti- arthritic activity and women with SLE have reduced levels of estrogen[14]. Our results have high estrogen level in SLE and thus the present study disagree with the above said study.

RA factor is an antibody that is not usually present in normal individual. SLE patient also show RA factor positive,[15] our study showed significantly high value of RA factor in SLE was in total in agreement with the study previously done.

Our Data suggested that ESR was elevated in SLE patients and can be used to asses disease activity as ESR is an inexpensive diagnostic tool[16].

Correlation of prolactin with SLE disease activity was found significant, as seen that immunosuppressive therapy decreased prolactin levels in direct correlation with decreased SLE activity. This finding emphasizes that prolactin may play a role in the pathogenesis and clinical expression of SLE[7], our findings are in total agreement.

CONCLUSIONS

Enhanced serum prolactin and estrogen changes in patients with systemic lupus erythematosus (SLE), may be diagnostic and prognostic tool for autoimmune diseases.

SUGGESTIONS

We recommend that serum prolactin must be analyzed as diagnostic and prognostic tool for autoimmune diseases in SLE.

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Article received on: 00/00/0000 Accepted for Publication: 00/00/0000 Received after proof reading: 16/05/2011

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Article Citation:
Iqbal T, Shiekh S, Karira KA. Systemic lupus Erythematosus, Changes in reproductive hormones estrogen and prolactin in SLE in female of fertile age. Profesional Med J; Apr-Jun 18: (2) 255-258.

"Never quote in a rush."

(Shuja Tahir)