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Serum Prolactin in Rheumatoid Arthritis: A Possible Marker of Disease Activity

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Abstract: Rheumatoid arthritis is the most common rheumatic disease which may lead to crippling deformity if not treated properly. Traditional marker of inflammation (ESR, CRP) loss their value in advancing age to ascertain disease activity and many patients continue to have active disease despite aggressive treatment. This study was an endeavor to assess serum prolactin levels in RA patients and its correlation with disease activity. An observational analytic case control study was carried out at a tertiary care center in North-West India among 20 post-menopausal women having rheumatoid arthritis (the case) (diagnosed as per revised American college of Rheumatology 2010 criteria) and 20 age matched healthy post-menopausal women (controls), in accordance with the declaration of Helsinki and after informed consent from participants and permission from institutional ethics committee. The healthy female relatives for the RA patients were taken as control. Females having possible causes of hyperprolactinemia other than RA i.e. deranged renal function test, liver disease, thyroid disorder, seizure and drugs (steroids, antipsychotics, metoclopramide, H2 antagonist, imipramines at least 2 weeks prior to the study) were excluded. After detailed history and thorough rheumatologic assessment; after overnight fasting, venous blood samples of the study participants were drawn from left anticubital vein between 09:30 AM to 12:00 hours noon (at least 2 hours after awakening) and sent for complete blood count, fasting plasma glucose, urea, creatinine, uric acid, SGOT, SGPT, ESR (by Westerngren method), rheumatoid factor (by nephelometry) and CRP (by nephelometry). Serum prolactin was measured by chemiluminescence Immunoassays (CLIA). RA disease activity was measured by DAS28. ESR was significantly higher among RA cases (38.05±24.16 mm/Isthr) compared to control subjects (14.65±8.26 mm/Isthr, $p<0.05$). Serum prolactin was significantly higher among RA cases (41.08±35.52 ng/ml) compared to non-RA control subjects (10.33±6.19 ng/ml, $p<0.05$). Among RA cases, serum prolactin was significantly higher in CRP positive cases (n=18) (45.02±35.30 ng/ml) compared to CRP negative RA (n=2) (5.61±1.20 ng/ml) ($p<0.05$). Serum prolactin was found to have statistically significant correlation with ESR ($r= +0.912$, $p <0.05$), tender joint count ($r= + 0.833$, $p <0.05$), swollen joint count ($r= + 0.801$, $p <0.05$) and DAS28 ($r= + 0.930$, $p <0.05$). Serum prolactin did not show correlation with disease duration ($r= + 0.010$, $p > 0.05$). Prolactin levels are higher in RA patients compared to age/sex matched healthy controls serum prolactin correlated significantly with swollen joint count, tender joint count, ESR and DAS28 (markers of disease activity in RA).

Keywords: Rheumatoid arthritis, advance age, Serum Prolactin, disease activity.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common rheumatic disease which may lead to crippling deformity if not treated properly. Traditional marker of inflammation (ESR, CRP) lose their value in advancing age to ascertain disease activity in RA and many patients continue to have active disease despite aggressive treatment [1]. Recently prolactin a hormone secreted from anterior pituitary is found to be secreted by the immune system including synovial T-cells and

peripheral lymphocytes [2-4]. The excessive prolactin is reported to be associated with pathogenesis of RA and disease activity [5]. The macrophages have prolactin receptors (PRL receptors) and after binding to these PRL receptors, prolactin interfere with B cell tolerance induction and also affect proliferation and differentiation of T cells [6-9].

The immunomodulatory effects of prolactin is also confirmed with the finding of reversible suppression of immunity with hypo-prolactin treatment (hypophysectomy or drugs i.e. bromocriptin, cabergoline) [10-11]. During pregnancy, prolactin levels increases with duration of gestation and peak prolactin level are found at the end of the gestation and during lactation period. These pregnancy related prolactin changes are associated with the disease activity of RA during pregnancy and its exacerbation in the postpartum/lactation period [12-13]. Some studies reported association of serum prolactin in RA with disease duration, inflammatory burden (CRP, ESR) and radiological progression [14-18].

From the evidences described above it was hypothesized that prolactin might have some role in RA and may correlate with RA disease activity.

So, this study was an endeavor to assess serum prolactin levels in RA patients and its correlation with disease activity.

MATERIALS AND METHODS

An observational analytic case control study was carried out at a tertiary care center in North-West India among 20 post-menopausal women having rheumatoid arthritis (the case) (diagnosed as per revised American college of Rheumatology 2010 criteria) [19] and 20 age matched healthy post-menopausal women (controls), in accordance with the declaration of Helsinki and after informed consent from participants and permission from institutional ethics committee. The healthy female relatives for the RA patients were taken as control. Females having possible causes of hyperprolactinemia other than RA i.e. deranged renal function test, liver disease, thyroid disorder, seizure and drugs (steroids, antipsychotics, metoclopramide, H2 antagonist, and imipramine at least 2 weeks prior to the study) were excluded.

After detailed history and thorough rheumatologic assessment, data were collected in structured forms. After overnight fasting, venous blood samples of the study participants were drawn from left anticubital vein between 09:30 AM to 12:00 hours noon (at least 2 hours after awakening) and sent for complete blood count, fasting plasma glucose, urea, creatinine, uric acid, SGOT, SGPT, ESR (by Westerngren method), rheumatoid factor (by nephelometry) and CRP (by nephelometry). Serum prolactin was measured by chemiluminescence Immunoassays (CLIA). All tests were done at our institutional lab by a person who was blinded to the study and clinical state of the study participants. RA disease activity was measured by DAS28 [20].

STATISTICAL ANALYSIS

Microsoft Excel® and SPSS® 17.0 for Windows® were used for data storage and analysis. Continuous variables were expressed as mean ± standard deviation. Student's t test and Chi-Square test were used to determine statistical difference between variables. Pearson's coefficient was used to investigate the correlation between the two variables. Statistical significance was set at P value ≤ 0.05.

RESULTS

Total 20 RA cases (mean age 50.10±5.31 years) and 20 age matched controls (mean age 52.40±4.76 years) were taken in the study ($p > 0.05$). The age range of RA cases was 45-60 years and control subject was 45-62 years. ESR was significantly higher among RA cases (38.05±24.16 mm/Isthr) compared to control subjects (14.65±8.26 mm/Isthr, $p<0.05$). Serum prolactin was significantly higher among RA cases (41.08±35.52 ng/ml) compared to non-RA control subjects (10.33±6.19 ng/ml, $p<0.05$). (Table No.1)

Among RA cases, serum prolactin was significantly higher in CRP positive cases (n=18) (45.02±35.30 ng/ml) compared to CRP negative RA (n=2) (5.61±1.20 ng/ml) (p<0.05). (Figure No.1) Serum prolactin was found to have statistically significant correlation with ESR (r= +0.912, p <0.05), tender joint count (r= + 0.833, p <0.05), swollen joint count (r= + 0.801, p <0.05) and DAS28 (r= + 0.930, p <0.05). Serum prolactin did not show correlation with disease duration (r= + 0.010, p > 0.05) (Table No. 2).

Table-1: **Characteristic of study participants**

	Case RA (n 20)	Control (n 20)	P
Age (years)	50.10±5.31	52.40±4.76	>0.05
ESR (mm/Isthr)	38.05±24.16	14.65±8.26	<0.05
VAS	33.50±6.97		
TJC	6.25±2.89		
SJC	2.00±2.63		
DAS28	4.55±00.95		
Serum Prolactin (ng/ml)	41.08±35.52	10.33±6.19	<0.01

Table-2: Correlation of serum prolactin with various parameters in RA cases

	r	P
TJC and Prolactin	+0.833	<0.05
SJC and Prolactin	+0.801	<0.05
ESR and Prolactin	+0.912	<0.05
VAS and Prolactin	+0.292	<0.05
DAS28 and Prolactin	+0.930	<0.05
RA disease duration and Prolactin	+0.010	>0.05

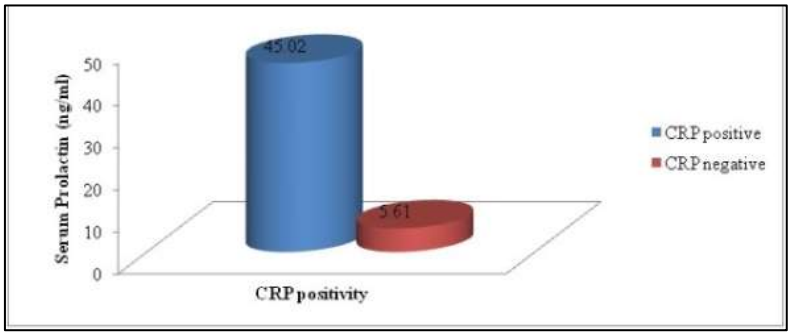

Fig-1: Serum Prolactin Level in RA cases according to CRP

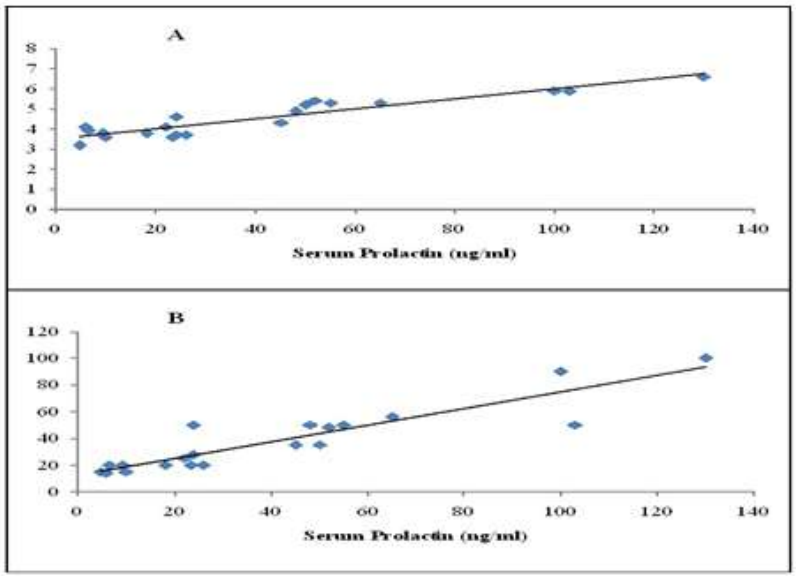

Fig-2: Correlation of serum prolactin with disease activity parameters with DAS28 (A) and ESR (B) in RA patients

DISCUSSION

In this study, the serum prolactin levels in RA patients compared to healthy control subjects and its correlation with disease activity were assessed. The serum prolactin was significantly higher in RA cases compared to healthy controls. This finding is similar to previous studies who also reported raised prolactin levels in RA patients [21-25]. Some authors deny this finding as they observed similar or lower prolactin in RA cases [26-27]. This difference in findings may be due to the fact that we have taken only post-menopausal women (≥ 45 years age) in the study while other authors had included women of all age group which might affected prolactin level in their studies. All RA cases were rheumatoid factor (RF) positive in our study while other authors included RF negative cases also which might affect prolactin level.

In our study, serum prolactin correlated significantly with swollen joint count, tender joint count, ESR and DAS28 (markers of disease activity in RA). The possible role of prolactin in disease severity and joint disease was also evaluated in previous study [18].

So serum prolactin may be used as tool to assess disease activity in RA patient when traditional markers are not useful i.e. in presence of infection, other diseases that increase ESR/CRP

CONCLUSION

Prolactin levels are higher in RA patients compared to age/sex matched healthy controls serum prolactin correlated significantly with swollen joint count, tender joint count, ESR and DAS28 (markers of disease activity in RA).

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