Severity of Rheumatoid Arthritis, and Levels of Vitamin D3 & C-Reactive Protein

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Abstract

Objective: Study was designed to assess the severity of rheumatoid arthritis, with level of vitamin D and C-reactive protein in a group of patients.

Method: This study was conducted at Govt Kot Khawaja Saeed Teaching Hospital. Duration of study was from June 2017 to June 2018. This cross sectional study was carried out on 50 consented patients with Rheumatoid arthritis fulfills the criteria of 2010 Rheumatoid arthritis classification. Both genders with age range 18-60 year were included in the study. Patients/controls were comprised as group 1(25 patients with mild type arthritis),group 2(25 patients with moderate form of arthritis) and group 3 (healthy controls).

Results: It is observed that most of the patients of group2 have small joint involvement with severe to moderate pain /swelling as compared to group 1. Mean difference /standard error of vitamin D and C-reactive protein among group 1 and group 2 were significantly higher as compared to controls.

Conclusion: Study found significant deficiency of vitamin D along with high values of C-reactive protein in patients with severity of arthritis.

Keywords: Rheumatoid Arthritis, vitamin D, C-reactive protein

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Introduction

Rheumatoid arthritis (RA) is an inflammatory agonizing disease of the synovial joints. The key characteristic of this complex autoimmune disorder is the inflammation of the small joints. It also involves different system of patients. Prevalence of RA was 26.9% in Pakistan, which shows >5% rise/ year. This showed that prevalence of RA in high in Pakistani population as compared to African, European and Japanese population.[1,2,3] RA is more prevalent in female in comparison to male gender. The chronic inflammation of synovium-part of the joint results in manifestation of several arcticular and extra-articular sits resulting in increased morbidity/ mortality. The aetiologyof RA may be based on genetic / non-genetic factors like hormonal, environmental and infectious issues.[4] Diagnosing of RA is not based to any specific test. However anti cyclic citrullinated peptide has some good specificity and may be related with severity of disease.[5] Levels of reactants of acute-phase like ESR and CRP are raised and may be relate with RA. Level of CRP greater than 3.0 mg/L is related with swollen to tender joints.[6,7]

Pathogenesis of rheumatoid arthritis shows that, it is an autoimmune, inflammatory ailment that included abnormal triggering of osteoblasts, B -cells and T- cells, fibroblasts, chondrocytes, proteolytic enzyme and dendritic cells results in injury of bone, cartilage and tendons as well as manifestation of systemic and extra-arcticular RA.[8] Due to the presence of vitamin D related receptors, vitamin D play an important role in controlling the immune / adaptive responses and boost the immune

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system, and low levels of vitamin D results autoimmunity.[9] Receptors of vitamin are also present in synoviocytes and chondrocytes. Changes in levels of circulating vitamin D may affect cellular signaling pathways resulting in many disorders particularly calcium homeostasis, metabolism of bon and dysfunction of immune system. Deficiency of vitamin D is related with various autoimmune problems including RA.[10,11] However a study found insignificant relations between the activity of rheumatoid arthritis ailment and the level of circulating vitamin D level[12]. Inadequate data are offered for finding the link of level of vitamin D3 with RA especially in country of Pakistan. Study is therefore designed to assess the severity of rheumatoid arthritis, with level of vitamin D and C-reactive protein in a group of women.

Material and Methods

A cross sectional study was carried out on 50 consented patients with Rheumatoid arthritis fulfils the criteria of classification of Rheumatoid arthritis[13]. Both male and female with age range 18-60 year were taken from Govt Kot Khawaja Saeed Teaching Hospital. Duration of study was from June 2017 to June 2018. RA was confirmed based on sign / symptoms and radiological findings on X-ray. Patients/controls were comprised as group 1(25 patients with mild arthritis), group 2(25 patients with moderate form of arthritis) and group 3 (20 age, sex matched healthy controls). The inclusion criterion was based on DAS scoring system. The patients freshly diagnosed by rheumatologist, using vitamin D supplement, or with any serious morbidity like SLE were not included in the study.

Patients were taken using consecutive convenient non-probability sampling. Letter of IRB was obtained from the Post Graduate Medical Institute. Demographic variables like age, socioeconomic status, profession and blood pressure were noted. Levels of vitamin D< 30.0 ng/ml were classified as hypo-vitaminosis D.[14]

Data was entered and analyzed by SPSS 20. Demographic variables including profession, socioeconomic status, health status and involvement of joints, swelling and severity of disease were expressed in frequency and percentages. Quantitative variables including age, blood pressure, pulse rate were expressed as mean±SD. One way Anova was used to find the significant different among patients groups and control subjects. P<0.05 showed significance.

Table 1: *Demographics of patients (group 1 and 2) and controls (group 3)*

Variables	Group 1	Group 2	Group 3
Age	36.4±10.1	37.4±10.2	32.7±11.0
Professional	12 (60%)	11(55%)	12(60%)
Non-Professional	8(40%)	9(45%)	8(40%)
Socioeconomic status			
Middle	18(90%)	18(90%)	18(90%)
Upper	2(10%)	2(10%)	2(15%)
B.P			
Systolic	129±9	132±7	132±10
diastolic	82±3	80±0	81±4

Table 2: *Clinical variables of group 1 and group 2*

Clinical variables	Group 1 Frequency and percentages	Group 11 Frequency and percentages
Small joint pain	11.0(55 %)	15(75%)
Swelling of joints	3.0 (15 %)	16(80%)
Tenderness of joints	16.0 (80 %)	0(0%)
Pain Grade		
Mild	0(0%)	19(95%)
Moderate	15(75%)	1(5%)
severe	5(25%)	0(0%)

Group 2: mild to moderate
Group 1: Moderate to severe

Results:

The Demographics of patients and control were tabulated as table 1.0. Mean age of the patient was 36 years. Majority of the patients belong to middle class and professional. All of the patients are normotensive.

Clinical variable s of patients and controls were tabulated

Table 3: *Group based comparison of vitamin D and C-reactive protein Values for patients among three study groups*

Groups (I)	Groups J	Mean Difference 1-J (vitamin D)	Standard Error	Mean Difference I-J (C-RP)	Standard Error	p- value
Group1	Group 2	32.75	3.37	-0.94	0.12	<0.001
Group1	Group 3	49.30	3.37	-2.71	0.12	<0.001
Group 2	Group 3	16.55	3.37	-1.77	0.12	<0.001

as table 2. It is observed that most of the patients of group 2 have small joint involvement with profound swelling. However, the tenderness and pain is mostly observed in group 1. In group 1 the status of aching is higher as compared to group 2. In group 1 aching status is moderate to severe as compared to group 2.

Group wise comparison of vitamin D3 and CR-P values among patients and controls was tabulated as table 3. By using One way ANOVAs, it is observed that mean difference /standard error of vitamin D and C-reactive protein among group 1 and group 2 was significantly higher ($P<0.001$) as compared to control group 3. Conversely, the mean difference / standard error of vitamin D and C-reactive protein among group 2 was higher significantly ($P < 0.001$) in comparison with controls.

Discussion

We observed that majority of the patients with age group 33 to 36 years belong to middle class, female and professional. All of the patients are normotensive. A study found that age group of RA patients was 44.0 years and belong to middle class with nominal income and the adverse outcome is the patients cannot afford expensive treatment of RA.[15] Studies reported RA is more common in female as compared to male. The reason may be that women face social penalties, including incapability to perform house hold services and decreased ability to do work as well as outdoor activities.[16,17] This may affect their exposure to sun which is best wad of getting vitamin D. Additional lack of vitamin D may worse RA.[18]

Patients with mild to moderate form of rheumatoid arthritis have small joint involvement, joint pain with profound swelling. However, the tenderness and pain is mostly observed in patients with moderate to severe form of arthritis. They also have high status of pain as compared to patients who have mild to moderate form of arthritis. A study was conducted to find out that concentrated management is appreciated to remission of disease in patients with moderately active form of rheumatoid arthritis. It is suggested that good management is based on monthly appointments, treatment based on counselling techniques, Medicines optimization, providing handbook to patient and shared planning of treatment.[19]

Group wise comparison of vitamin D and C-reactive protein levels among patients and controls showed that mean difference /standard error of vitamin D and C-reactive protein among patients with mild to moderate and in patients with moderate to severe form of rheumatoid arthritis was significantly higher as compared to control. Study also observed that among patients with moderate to severe form of arthritis the significantly low levels of vitamin D and high values of CRP as compared to patients with mild to moderate form of rheumatoid arthritis

A study was carried out in 100 Indian RA patients and found significant deficiency of vitamin D as compared to controls. Study also found level of CRP is positively and significantly correlated with severity of disease. However, deficiency of vitamin D is common in RA patients.[20]

A study was conducted in 102 RA patients living in Saudi Arabia. Their level of vitamin D3 was estimated. It is reported that circulating values of vitamin D< 20.0 ng/mL was defined as patient to vitamin D. Results of ROC curves showed that vitamin D<12.3 ng/mL forecast high RA disease activity, and vitamin D >17.90 ng/mL forecast mild form of RA. Study reported that vitamin D is a good predictor of ailment of RA Saudi Arabian patients.[21]

A total of 377 Chines patients with RA were divided into two groups i.e. group with normal level of Vitamin D and the group low values of vitamin D. Supplements of vitamin D was given for twenty-four months to the group of patients who have low level of vitamin D. The patients were followed and record the status of pain and swelling of joints of the patients. Additionally, the levels of C-reactive protein were estimated to judge the reappearance of RA based on disease activity. Study found that vitamin D as supplement may improve the sign and symptoms of disease. However, reduced values of vitamin D increase the risk of reappearance of RA.[22]

A study carried out in 42 Indian RA patients and estimates their DAS score, levels of CRP and vitamin D. Study found that deficiency of vitamin in RA patients was inversely correlate with DAS score/tenderness of joint and CRP. It is reported that each increase of dose of 10.0ng/ ml of vitamin D is related with reduction in the severity of disease and reduce 25 % CRP.[23] A study confirmed the immunomodulatory function of vitamin D3 besides its traditional role of controlling the metabolism of calcium and phosphorus in body.[24] Another study carried out in 790 patients living in UK and recorded their baseline demographic characteristics, duration of sign and symptoms, stiffness in morning,

fatigue, counts of swollen and tender joint counts and DAS score. Study found no apparent link between values of serum vitamin D and baseline characteristic, activity of disease of RA or progression from arthritis or arthralgia to RA.[25]

Limitations of study: Study was carried out in only one hospital. Sample size was small. Future studies are needed to take the patients form different hospitals that may confirm the results of this study. Additionally, there is a need to assess the doses of supplementation of vitamin D to find better treatment Moreover, studies assessing the dosage of vitamin D supplementation are also required to explore better treatment tactics.

Conclusions

Study found significant deficiency of vitamin D along with high values of C-reactive protein in patients with severity of arthritis. Supplementation of vitamin D3 may be needed for reducing the severity of the ailment. Screening of RA patients for finding the levels of vitamin D is needed. The treatment cost of RA is high and not correlated with the financial status of people. There is a need that Pharmacists should guide patients and aware patients about ailment and strictly use the medicine.

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Authors Contribution

MH: Conceptualization of Project
RK: Data Collection
HH: Literature Search
TK: Statistical Analysis
GR: Drafting, Revision
FA: Writing of Manuscript
S.S.U: Literature Review