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ASSESSMENT OF VITAMIN D ON METABOLIC DISORDERS IN ARTHRITIC PREDIABETIC PATIENTS- A PHARMACOLOGICAL APPROACH

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ABSTRACT: We planned to clarify the association between the Vitamin D supplementation and predisposition of metabolic syndrome including obesity, diabetes mellitus, hypertension and dyslipidemia in arthritic patient with pre diabetic condition and to assess prediabetes interfere in the disease progression. Retrospective observational study was conducted on 236 patients. Of these, Arthritis patients with no co-morbid condition and not supplemented with Vitamin D (47), Arthritis patients supplementing with Vitamin D (63), Arthritis patients with prediabetic condition (68), Arthritic prediabetic patients supplementing with Vitamin D (58) were recruited based on inclusion and exclusion criteria. All anthropometric parameters and clinical findings were recorded the predominance of women with RA was observed in this study and the body weight was increased substantially in entire study group irrespective of gender. A significant increase in metabolic parameters was observed in patients with arthritis who were off of Vitamin D supplementation ($p<0.05$). On the other hand no such significant increase was observed in vitamin D supplemented group ($p>0.05$. In the group of arthritic patients with prediabetes condition significant increase in metabolic parameters ($p<0.01$). There was no deterioration rather an improvement during the Vitamin D supplementation in prediabetic arthritic patients but lipid parameters were increased gradually in continuous visit. Predisposition of metabolic disorder was reduced with Vitamin D supplement. Prediabetes has shown positive correlation with the disease activity in RA patients. Moreover less association was observed between the lipid profile and Vitamin D status.

INTRODUCTION: Rheumatoid arthritis (RA) is an autoimmune disorder that causes chronic inflammation and pain in joints associated with increased disability, morbidity and mortality [1]. Etiology of the disease is attributable to genetic and non genetic factors as hormonal, environmental, and infectious factors [2].

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Vitamin D deficiency is most common health problem in more than 50% of the general population worldwide. Nearly 30% of the RA patients were strongly related to the vitamin D deficiency, at the same line RA has inverse correlation with the serum Vitamin D [3, 4]. Epidemiological studies suggest that vitamin D has a role in insulin resistance, type 2 diabetes, obesity, metabolic and cardiovascular syndrome, which is associated with systemic, chronic inflammation by reducing the circulating levels of proinflammatory cytokines and C-reactive protein [5, 6, 7].

Definition of metabolic syndrome is not yet clear since it has been tailored based on the race, age,

dietary habits and also by disease specific factors. The main components of Metabolic syndrome are elevation of mean arterial blood pressure (BP) dyslipidemia (elevated triglycerides, low density lipoproteins (LDL) and low high-density lipoproteins (HDL)), and glucose intolerance, while insulin resistance and obesity have gained increasing attention as the core manifestations of the syndrome [29]. In recent decades, other abnormalities were also included such as sleep apnea, nonalcoholic fatty liver disease and prothrombotic states [30].

Obesity is the most common risk factor for the prediabetes which is associated with hypovitaminosis due to inefficiency of adipose tissue to store 25-hydroxyvitamin-D [8]. Inadequate amount of serum 25 (OH) D can stimulate the lipogenesis, predisposing a patient to further weight gain and thus increasing the risk of diabetes [9]. Administration of Vitamin-D has been shown to decrease insulin resistance and increase the insulin sensitivity in diabetic patients. Henceforth it activates the pancreatic β cell function through the activation of Vitamin D receptor and by regulating peroxisome proliferator activated receptor (PPAR). Vitamin D may also affect insulin secretion and sensitivity indirectly by regulating extracellular calcium concentration in the beta cells and peripheral insulin-target tissues [10, 11]

Though arthritis is a major risk factor for the development of glucose intolerance and diabetes, prevalence and clinical associations are not well documented yet. Hence in the present study we planned to assess the role of vitamin D in the progression of prediabetes and other metabolic disorders in rheumatoid arthritis patients with prediabetic condition

MATERIALS AND METHODS:

Retrospective observational study was approved by Institutional Human ethical committee, PSGIMS&R (IHEC-13/381) and conducted on Rheumatoid Arthritis (RA) patients admitted in Rheumatology department at PSG Hospital. Data of the patients were collected from May 2011 to November 2013. In total, 236 subjects were identified as Rheumatoid Arthritis from the clinical reports and randomly recruited for the study based on inclusion and exclusion criteria. The subjects were included between age group of 30 to 65 years and diagnosed as RA with or without prediabetes (> 5.6 mmol/L) and Serum 25(OH) D (<25 ng/ml). The Subjects were excluded if the patients were suffering from chronic alcoholism, hepatic failure, cardiovascular diseases, renal disorder and chronic infection. Rheumatoid Patients were classified based on pre diabetic condition and Vitamin D supplementation.

In Group 1: Arthritis patients with no comorbid condition and not supplemented with Vitamin D (47), Group 2: Arthritis patients supplementing with vitamin D (63), Group 3: Arthritis patients with prediabetic condition (68), Group 4: Arthritic prediabetic patients supplementing with vitamin D (58) and all anthropometric parameters, physical examination findings, erythrocyte sedimentation rate (ESR) and hsCRP were observed. Medications used for RA, calcium and vitamin D supplements, anti-TNF agent and non steroidal anti-inflammatory drugs (NSAID), and disease-modifying anti Rheumatic drugs (DMARDs), including methotrexate, sulfasalazine, cyclosporine and prednisolone were documented. Patient data were collected in three continuous visits in the interval of three to four months.

Vitamin D deficiency was defined as a 25(OH) D serum level less than 15 ng/ml, vitamin D insufficiency as 25(OH)D levels of 15-20 ng/ ml, and severe vitamin D deficiency as 25(OH) D levels of less than 5 ng/ml. Vitamin D levels greater than 20 ng/ml were considered sufficient. HbA1c (<6%) as normal, HbA1c (6-6.4%) as prediabetes, HbA1c (>6.5%) as diabetes were Considered. Desired lipid profile TC<5.2 mmol/L, LDL < 2.6 mmol/L, HDL >1.3 mmol/L, and TG < 1.7 mmol/L. higher sensitive CRP<0.6mg/dl, Erythrocyte Sedimentation Rate (ESR) 0-22 mm/hr for men, and 0-29 mm/hr for women are obtained from respective associations.

Statistical analysis:

Documented data were analyzed by using Analysis of Variance (ANOVA) and Student‘t’ test by using prism software (user guide 6.1). Statistical significance was taken at the 95% level (P < 0.05).

Results were expressed as Mean ± Standard Deviation.

RESULTS:

Baseline Characteristics of the Study Population:

Demographic and clinical characteristics of patients included in this study are summarized in Table. There was a predominance of women in the entire group with RA, little varied in prediabetes group. The mean ages in all the groups were almost 40 - 50 years. Body weight increased in all the groups. During the study period patient underwent different treatment regimen such as NSAIDs and calcium (6.8%), DMARDs , NSAIDs and calcium (13.9%), DMARDs, NSAIDs, calcium and Prednisolone (14.3%), DMARDs and NSAIDs (4.6%), DMARDs, NSAIDs and Etanercept(2.5%), DMARDs, NSAIDs, calcium and Allopurinol (0.42%), Vitamin D3 with other drugs (50.8%) as mentioned in different tables based on the group.

Changes of metabolic parameters in patient with Arthritic Condition:

At the time of recruitment the mean BMI of the RA group was 25- 30 (kg/m2) indicating an obese sample. BMI and fasting glucose were gradually increased between the visit and they were showed statistically significant ($p<0.01$). We observed that the subjects in this group had Vitamin D insufficiency and it was significantly increased even at the last visit ($p<0.04$). During the first and second visit HbA1c level was within the normal range, whereas at the end of the third visit increased to 6.1% ($p<0.05$) which indicates prediabetic condition. No significant differences were found between the visit in diastolic pressure, whereas differences in systolic pressure was significant ($p<0.05$).

The mean value of ESR showed to be normal at the initial visit which was significantly increased in later visits ($p<0.05$). At the beginning, all the lipid parameters were optimal or near normal range, on later stage it changed remarkably, total CHO($p<0.05$), LDL ($p<0.05$) and TGL ($p<0.05$) greatly increased and HDL ($p<0.05$) was significantly decreased in later visits. The mean value of CRP level was significantly increased between the visits ($p<0.05$) as disease progression increased (**Table 1**).

The changes in metabolic parameters of arthritic patient supplemented with vitamin D has not shown any significant increase in BMI ($p>0.05$) although body weight has increased gradually. On the other hand systolic ($p=0.062$) and diastolic ($p=0.093$) BP was not showing any significant increase in this group. There was a marked decrease in the average fasting glucose level from 5.8 to 5.5 mmol/L ($p<0.05$).

In lipid profile analysis, we found that the mean score was slightly increased in total CHO and TG level, but not statistically significant ($p>0.05$).whereas HDL and LDL level were significantly improved between the visits ($p<0.05$).The mean value of vitamin D has improved to near normal range ($p=0.023$) on vitamin D supplementation. In the same way decrement of hsCRP level was observed in these patients ($p<0.05$) (**Table 2**).

Changes of metabolic parameters in Arthritic patient with prediabetes:

Table 3 demonstrates that condition worsened significantly among the visits in Arthritis patient with prediabetes with regard to weight, BMI ($p=0.01$), HbA1c ($p = 0.05$), fasting glucose ($p = 0.02$), ESR ($p = 0.05$), Blood pressure ($p=0.01$), lipid profile ($p=0.01$) and hsCRP ($p=0.05$).The mean value of Vitamin D decreased significantly ($p = 0.05$) as disease progression increased.

Arthritic prediabetic patient supplemented with vitamin D group failed to show any significant increase in weight, BMI ($p=0.13$),fasting glucose ($p = 0.07$), systolic BP ($p=0.07$), total CHO.($p=0.12$), LDL ($p=0.09$),TG($p = 0.13$), HDL($p = 0.09$) and ESR($p = 0.09$) at the same time steady state of the mean values were maintained. In other hand HbA1c ($p = 0.05$), diastolic BP ($p = 0.05$), hsCRP ($p = 0.04$) and 25(OH) D ($p = 0.05$) were significantly improved in continuous visit that indicates disease activity is greatly improved (**Table 4**).

TABLE 1: CHANGES OF METABOLIC PARAMETERS IN ARTHRITIS PATIENTS

Arthritis patients					
	visit 1	**visit 2**	**visit 3**	**P value**	**N (%)**
N			47		
Age			41±16		
Sex (M/F)%			37(63)		
weight (Kg)	62.4±8.2	62.9±9.1	63.1±10.1		
BMI (Kg/m2)	27.1 ±2.1	28.3±0.9	31±0.82	0.01	
Fasting Glucose (Mmol/L)	5.6± 1.1	5.8±0.6	6.3±0.21	0.01	
HbA1c (%)	5.4±0.14	5.7±0.41	6.1±0.72	0.05	
Blood Pressure					
Systolic (mmHg)	132.3 ±9.6	138.4±11.2	141±15.3	0.05	
Diastolic (mmHg)	79.1 ±7.6	81.7±6.3	82.3±9.1	0.0328	
Total CHO (Mmol/L)	4.86±0.31	5.2±0.24	5.6±0.71	0.05	
HDL (Mmol/L)	1.41±0.05	1.38±0.22	1.31±0.08	0.001	
LDL (Mmol/L)	2.92±0.31	2.91±0.62	3.4±0.34	0.01	
TG (Mmol/L)	1.53±0.06	1.82±0.04	2.13±0.11	0.001	
Hs-CRP (mg/dl)	0.63±0.02	0.71±0.01	0.73±0.02	0.01	
25(OH)D (ng/ml)	18.3±0.51	17.7±0.64	17.1±0.42	0.04	
ESR (mm/h),	18.9±1.48	20.4±2.17	22.1±2.31	0.05	
DMARDs	NSAID*	calcium			10(20.1)
NSAID*	calcium				7(14.5)
DMARDs	NSAID	Prednisolone	calcium		12(25.2)
DMARDs	NSAID*				11(23.1)
DMARDs	NSAID*	Etanercept			6(12.6)
DMARDs	NSAID	Allopurinol	calcium		1(2.1)

Data presented as mean ± standard error; NS – not significant; significance at $p < 0.05$. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

TABLE 2: CHANGES OF METABOLIC PARAMETERS IN ARTHRITIS PATIENTS SUPPLEMENTED WITH VITAMIN D

Arthritis and vitamin D					
	Visit 1	**Visit 2**	**Visit 3**	**P**	**N (%)**
N			63		
Age			38.6±11.4		
Sex (M/F)%			43(57)		
Weight (Kg)	58.3±12.6	59.8±11.2	60.2±13.2		
BMI (Kg/m2	25.3±0.9	25.8±1.1	26.1±1.2	0.189	
Blood pressure					
Systolic (mmHg)	126±12.4	122±13.4	125±10.4	0.062	
Diastolic (mmHg)	81.2±10.3	81.4±4.7	83.6±9.8	0.093	
Fasting Glucose (Mmol/L)	5.8±0.6	5.5±0.71	5.5±0.43	0.05	
HbA1c (%)	6.1±0.4	6.1±0.32	6.3±0.24	0.076	
Total CHO (Mmol/L)	5.14±0.91	5.23±0.72	5.28±0.21	0.142	
HDL (Mmol/L)	1.39±0.11	1.40±0.21	1.40±0.32	0.08	
LDL (Mmol/L)	2.64±0.23	2.68±0.61	2.7±0.52	0.05	
TG (Mmol/L)	1.87±0.35	1.91±0.21	1.94±0.34	0.072	
hsCRP (mg/dl)	0.69±0.12	0.67±0.22	0.67±0.34	0.05	
VIT D	18.2±2.1	19.4±1.5	21.3±1.6	0.023	
25(OH)D (ng/ml),					
ESR	20.3± 1.1	20.5±0.9	20.9±1.6	0.141	
DMARDs	NSAID	calcium	vitamin D3		15(23.8)
NSAID*	calcium	vitamin D3			13(20.5)
DMARDs	NSAID	Prednisolone	vitamin D3	calcium	11(17.3)
DMARDs	NSAID	Cyclosporin	vitamin D3		6(9.4)
DMARDs	NSAID*	Etanercept	vitamin D3		8(12.6)
DMARDs	NSAID*	calcium	vitamin D3		10(15.8)

Data presented as mean ± standard error; NS – not significant; significance at $p < 0.05$. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

TABLE 3: CHANGES OF METABOLIC PARAMETERS IN ARTHRITIS PATIENT WITH PREDIABETES

	Arthritis patient with Prediabetes				
	Visit 1	**Visit 2**	**Visit 3**	**P**	**N (%)**
N			68		
Age			55±16.4		
Sex (M/F)%			41(59)		
Weight (Kg)	61.4±9.8	61.6±10.1	62±14.2		
BMI (Kg/m2	26.5±2.2	28.4±1.3	32.6±1.4	0.01	
Blood pressure					
Systolic (mmHg)	126.1±15.2	130.4±12.5	136±11.2	0.01	
Diastolic (mmHg)	80.4±9.4	83.1±8.9	85.7±10.4	0.01	
Fasting Glucose (Mmol/L)	6.1±0.2	6.4±0.65	6.8±0.12	0.02	
HbA1c (%)	6.1±0.2	6.3±0.31	6.7±0.62	0.05	
Total CHO (Mmol/L)	5.1±0.7	5.3±0.4	5.7±0.9	0.05	
HDL (Mmol/L)	1.46±0.2	1.41±0.7	1.33±0.3	0.01	
LDL(Mmol/L)	2.31±0.5	2.8±0.2	3.2±0.2	0.001	
TG (Mmol/L)	1.44±0.6	1.81±0.1	2.3±0.6	0.01	
hsCRP (mg/dl)	0.73±0.02	0.77±0.04	0.81±0.01	0.05	
VIT D 25(OH)D (ng/ml),	19.6±2.4	18.1±3.2	15.61±3.1	0.05	
ESR	20.2±2.21	22.3±3.4	23.6±2.8	0.05	
DMARDs	NSAID*	calcium			23(33.8)
NSAID	calcium				9(13.2)
DMARDs	NSAID*	Prednisolone	calcium		22(32.3)
DMARDs	NSAID	calcium	Etanercept		14(20.6)

Data presented as mean ± standard error; NS – not significant; significance at $p < 0.05$. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

TABLE 4: CHANGES OF METABOLIC PARAMETERS IN ARTHRITIC PREDIABETIC PATIENT SUPPLEMENTED WITH VITAMIN D

	Arthritic Prediabetic patient supplemented with vitamin D				
	Visit 1	**Visit 2**	**Visit 3**	**P**	**N(%)**
N			58		
Age			39±13.6		
Sex (M/F)%			39(61)		
Weight (Kg)	57±11.2	58.3±10.3	58.1±12.6		
BMI (Kg/m2	26.8±2.5	27.3±0.5	27.6±1.2	0.13	
Blood pressure					
Systolic (mmHg)	135.9±151	137.2±11.7	137.3±15.2	0.09	
Diastolic (mmHg)	82.3±12.7	83.5±9.6	85.±10.4	0.05	
Fasting Glucose (Mmol/L)	6.4±0.3	6.5±0.21	6.5±0,41	0.07	
HbA1c (%)	5.6±0.2	5.7±0,43	5.7±0.61	0.05	
Total CHO (Mmol/L)	4.72±0.42	4.81±0.22	4.83±0.41	0.12	
HDL (Mmol/L)	1.47±0.51	1.47±0.16	1.48±0.72	0.09	
LDL (Mmol/L)	2.92±0.11	2.90±0.72	2.90±0.24	0.09	
TG (Mmol/L)	2.07±0.22	2.06±0.09	2.06±0.04	0.13	
hsCRP (mg/dl)	0.74±0.11	0.74±0.21	0.72±0.43	0.04	
VIT D 25(OH)D (ng/ml)	19.3±3.2	22.1±3.8	22.6±4.2	0.05	
ESR	20.4±1.1	20.2±3.1	19.8±2.2	0.09	
DMARDs	NSAID	calcium	vitamin D3		13(22.4)
NSAID	calcium	vitamin D3			5(8.6)
DMARDs	NSAID	Prednisolone	calcium	vitamin D3	16(27.5)
DMARDs	NSAID	Cyclosporin	calcium	vitamin D3	15(25.8)
DMARDs	NSAID	Etanercept	Calcium	vitamin D3	9(15.48)

Data presented as mean ± standard error; NS – not significant; significance at $p < 0.05$. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

TABLE 5: PATIENTS PREDISPOSED TO DIFFERENT METABOLIC DISORDER AT THE END OF THE STUDY

Metabolic disorders	Arthritis n (%)	Arthritis and Vitamin D n (%)	Arthritis and PD n (%)	Arthritis and PD and Vitamin D n (%)
Obesity	32 (68)	18(28.5)	44(66)	24(41)
Prediabetes	28(59.6)	21(33.3)	20(30)	29(49)
Type 2 Diabetes Mellitus	13(27.6)	9(14.4)	47(70)	11(18.7)
Hypertension				
Primary	21(44.7)	26(41.6)	16(24)	21(35.7)
Secondary	14(29.8)	11(17.6)	36(54)	24(40.8)
Dyslipidemia	40(85.2)	29(46.4)	59(88.5)	44(74.8)

Data presented as percentages (%).Conditions are obtained based on the diabetes, hypertension and dyslipidemia guidelines.

DISCUSSION: The study was designed to assess the association between vitamin D supplementation and predisposition of prediabetes in arthritic patients, Another objective of this study is to evaluate the relationship between vitamin D3 use, the rate of onset and prevalence of metabolic syndrome such as hypertension, diabetes and dyslipidemia condition. Vitamin D deficiency and lack of vitamin D supplementation is the major hallmark for the most of the metabolic disorders [12]. Awareness and importance about the vitamin D sufficiency has increased in recent decades even in optimal healthy volunteers. Surprisingly urban subjects with age >50 are well affected by vitamin D deficiency than rural subjects, which might be due to less exposure to sunlight and less physical activity relating to calcium dysregulation [13].

In this study, fairly female subjects were enrolled more than the male subjects, indicating that females are more prone to RA. Also they have early onset of RA and high prevalence rate. This might be due to unusual sex hormone shifting since estrogen is a good predictor for the up regulating immunoglobulin production [14]. Virtually 12-20% of the subjects in non vitamin D group are higher predisposition rate to obese condition than vitamin D supplemented group. Irrespectively mean value of body mass index ratio was increased in all the groups these results in consistent with our previous reports which indicates that BMI was reduced in patients supplemented with vitamin D or sunlight exposure [31] these changes probably is due to synergistic role of RA with prediabetes might dominate the therapeutic effect of vitamin D or by increasing the lipogenesis.

Gradual raise of mean fasting glucose level was observed in non vitamin D groups this might be due to glucose intolerance or inability to secrete insulin from pancreatic β cells due to lack of vitamin D since all the subjects in this group are state of vitamin D deficiency which is similar to our previous report [15]. On the contrary, subjects supplemented with vitamin D have not shown any improvement in the blood glucose reduction but the values are remained unvaried. Hence, the study clearly indicates that RA patient supplemented with vitamin D has less risk of prediabetes compared to non vitamin D patients and it seems that vitamin D might maintain or improve the insulin resistance and insulin sensitivity [10]. At the same time rate of predisposition of prediabetes has reduced nearly 20% in vitamin D supplemented group as compared to non vitamin D group. Notable increase of patients shifting from the prediabetic to the Type 2 DM condition(12% to 17%) in not vitamin D group was observed which is consistent with Wasko MC et al study this is probably due to inflammation induced insulin resistance activity since vitamin D has been predicted as a good anti inflammatory agent [16, 17].

The prevalence of hypertension is considerably higher about 42% in RA than in the average population due to systemic, low-grade inflammation and physical inactivity [18]. Study point out that remarkable increase of BP in non vitamin D subjects might be due to low grade systemic inflammation. This can lead to hypertension by reducing nitric oxide production in endothelial cells, leading to vasoconstriction, increased production of endothelin-1 [19]. However vitamin D play a major role in the subsiding systemic and low grade inflammation by reducing hsCRP which is the primary marker for the inflammation [18]. In our study approximately 5-10% of the non vitamin D groups are more susceptible to the cardiovascular risk than the vitamin D supplemented groups. In addition to that we observed 2-3% of the non

vitamin D groups were entered into the secondary hypertensive condition in short period.

It was also observed that, ESR was greatly reduced in vitamin D supplemented group which indicates that immunomodulatory effect of vitamin D could also produce anti inflammatory, anti diabetic, anti obesity and anti arthritic effect via endocrine and paracrine manner [20] by decreasing antigen presentation and inhibiting the proinflammatory helper T cells. In view of the fact that ESR is a good predictor for the inflammatory response [21, 22] moreover hsCRP is also significantly increased in non vitamin D group which can up regulate the expression of AT1 receptors and activate rennin angiotensin system (RAS) that could increase the arterial blood pressure this is probably due to vitamin D deficiency or inadequate sunlight exposure and utilization of vitamin D by the body cells because serum vitamin D is an important biological marker for regulating the hsCRP level in blood [17] and significant decrease of blood hsCRP was found in vitamin D supplemented group these changes might be due to anti obesity and anti inflammatory activity of vitamin D since obesity has a role in increase the CRP level in blood [15] these factors could also be a reason for the reduction of BMI in vitamin D group. At the same time disease activity is greatly reduced in this groups which might be due to anti inflammatory activity of vitamin D by controlling cytokines release and immune tolerance [23, 24].

Tendency towards the changes in TC, LDL, HDL and TG were not showing significant improvement in any group with the supplementation of vitamin D these results matches with the report of Kane et al [25]. In fact some studies reported positive correlation with vitamin D [28]. In respect to this concept few studies reported that source of vitamin D is important in regulating lipid profile. Saedisomeolia et al reported that sunlight exposure is very effective than the vitamin D supplementation [10, 32].

In our previous report vitamin D has not shown positive correlation with the LDL, TG and TC but not in HDL level [31]. Even in the present study we found subjects are predisposed to dyslipidemia condition is invariably. Such controversial report between the studies might be due to duration of study period or co-morbidity of the disease condition or mode of vitamin D exposure [26, 27]

In conclusion, study reveals that RA has a link with increased prevalence and predisposition of metabolic syndrome. Our study also revealed, among the parameters lipid profile have shown less association with the vitamin D supplementation possibly due to less exposure of sunlight or inadequate intake of vitamin D. While in vitamin D supplementation, disease activity is comparatively less in arthritis patient than in arthritic prediabetic patients. Moreover, study also reveals that pre diabetes might have positive correlation with the disease activity in RA patients. However, prospective comprehensive studies are needed to further investigate the relationship between RA, vitamin D and prediabetes.

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