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FREQUENCY OF DIABETES MELLITUS TYPE II IN RHEUMATOID ARTHRITIS PATIENTS PRESENTING AT A TERTIARY CARE HOSPITAL IN KARACHI: A CROSS-SECTIONAL STUDY

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Abstract

Background: *Rheumatoid arthritis (RA) is a chronic inflammatory condition associated with increased risk of comorbidities, including type 2 diabetes mellitus (T2DM), due to systemic inflammation, glucocorticoid use, and metabolic alterations. Data on T2DM prevalence in RA patients from Pakistan remain limited.*

Objective: *To determine the frequency of T2DM in patients with RA and explore its association with sociodemographic and clinical variables.*

Methods: *This cross-sectional study was conducted at the outpatient department of Jinnah Postgraduate Medical Center, Karachi, Pakistan, from March to September 2025. A total of 137 newly diagnosed RA patients (aged 30–70 years) fulfilling the 2010 ACR/EULAR classification criteria were included using non-probability consecutive sampling. Exclusion criteria encompassed pre-existing thyroid disorders, other connective tissue diseases, malignancy, pregnancy, and major comorbidities. HbA1c ≥6.5% was used to diagnose T2DM. Data on demographics, anthropometrics, and lifestyle factors were collected. Analysis was performed using SPSS v27.0, with chi-square tests for associations ($p \leq 0.05$ significant).*

Results: *The mean age was 57.61 ± 10.44 years; 55.5% were male, and mean BMI was 29.34 ± 5.11 kg/m². T2DM was present in 37 patients (27.0%). Significant associations were observed with obesity ($p=0.05$), unemployment ($p=0.02$), and lower educational status ($p=0.05$). No significant associations were found with age, gender, residence, smoking, or family income.*

Conclusion: *The prevalence of T2DM in this Pakistani RA cohort (27.0%) is notably higher than many global estimates and aligns with the role of chronic inflammation and traditional risk factors. Obesity, unemployment, and limited education emerged as key associated factors. These findings highlight the need for routine metabolic screening (e.g., HbA1c) in RA patients to enable early intervention and reduce cardiometabolic complications.*

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic inflammatory disorder that affects between 0.5% and 1.0% of the adult population worldwide. It is characterized by chronic symmetric and erosive synovitis that affects preferentially peripheral joints leading to varying degree of physical disability.[1] In South Pakistan, the prevalence of rheumatoid arthritis is said to be 0.9/1000 and 1.98/1000 in poor and affluent districts respectively, whereas in North Pakistan, the prevalence of major rheumatic disorders is quoted as 148/1000.[2,3] Patients with RA have a reduced life expectancy, which is associated with an increased risk for cardiovascular events.[4] This is because patients with RA are more prone to accelerated atherosclerosis which in turn is a risk factor for cardiovascular disease.[5] It is an autoimmune-inflammatory disease associated with infectious and inflammatory factors characterized by lipoprotein metabolism alteration that leads to immune system activation with the consequent proliferation of smooth muscle cells, narrowing arteries, and atheroma formation. [6]

Multifactorial risk factors and enhanced danger of atherosclerosis is reported in many RA patients.[7] The high disease activity in rheumatoid arthritis leads to raised levels of Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), Interleukin-1 (IL-1), IL-6 and Tumor Necrosing Factors (TNF α), which lead to accelerated atherosclerosis.[8] Moreover use of Non-Steroidal Anti-Inflammatory Drug (NSAID's) is also considered a risk factor for CVD. [9-10]

The reported prevalence of diabetes in RA patients has been controversial. In a study conducted in Karachi, the estimated prevalence was found to be 8.2%.[2] Inflammatory markers have been a contributing factor in the development of insulin resistance. The glucocorticoid use affects appetite, body metabolism, fat distribution and intensify insulin resistance.[11,12] The pathophysiology of deranged glycemic index, BMI and waist-to-hip ratio (WHR) all are influenced by steroids intake. Moreover, even the patients taking medium to low dose steroid for a longer period of time lead to increased deposition of fats around the abdominal viscera. [13,14] Guimarães et al. evaluated the prevalence of diabetes mellitus type II in Rheumatoid arthritis patients and found it to be 15%.[15]

The study aims to determine the frequency of diabetes mellitus type II in rheumatoid arthritis patients in order to establish the local perspective as there is paucity of local data frequency, given that the genetics, socioeconomic, lifestyle and dietary habits of the Pakistani population are different from the rest of the world. By virtue of this data, strategies will be developed for screening of rheumatoid arthritis patients with HbA1c levels so that appropriate measures would be taken to prevent disability, poor prognosis and mortality. Moreover, rheumatoid arthritis and injudicious use of corticosteroids and non-steroidal anti-inflammatory medicines results into risk of having complications like cardiovascular problems, which sometime leads to early and unexpected deaths. Therefore, early identification of diabetes through regular screening of suspected patients would help in better management of both diseases and help in the prevention of cardiovascular complications.

MATERIALS AND METHODS:

This cross-sectional study was conducted at the outpatient department of Jinnah Postgraduate Medical Center (JPMC), Karachi, Pakistan, for six months from March to September 2025. Newly diagnosed patients of rheumatoid arthritis with joint pain (VAS ≥ 6) and morning stiffness lasting ≥30 minutes for more than one week were included. Both genders, aged 30–70 years, were eligible. Patients who did not provide consent, those having thyroid disorders (hypo/hyperthyroidism), connective tissue diseases (e.g., Systemic Lupus Erythematosus, scleroderma), vasculitis (granulomatous or eosinophilic polyangitis), malignancy, and pregnancy (confirmed by history and dating scan) were excluded. Patients with comorbid conditions such as asthma, myocardial infarction, congestive heart failure, chronic liver disease, Chronic Obstructive Pulmonary Disease, and stroke were also excluded. Participants were recruited using non-probability consecutive sampling. The required sample size

came out to be 137 patients, using WHO sample size calculator. This sample size was calculated by taking the prevalence of diabetes mellitus type II in rheumatoid arthritis to be 15%,[15] margin of error=6% and confidence level = 95%. Margin of error was set to 6% due to feasibility constraints.

This study was conducted after approval from College of Physicians and Surgeons Pakistan. Permission from the institutional ethical review committee of JPMC was taken prior to conduction of study. Informed consent was obtained from all the patients for assigning them to the study and using their data in research. Brief history of duration of Rheumatoid Arthritis and demographic information (age, gender, residence status, family monthly income status, educational status and occupational status) were collected. Each participant's height in meters was measured using wall mounted scale and weight to the nearest kilogram was measured using weighing machine. Blood sample was drawn by the researcher by using 5 cc disposable syringe that draw 5 ml of blood from peripheral vein and collect in specific tube for the measurement of HbA1c levels. Patients having HbA1c ≥ 6.5% were labelled as having diabetes mellitus.

Patients were classified as having rheumatoid arthritis according to the 2010 ACR/EULAR classification criteria.[16] This required the presence of synovitis in at least one joint, no better alternative diagnosis, and a total score of ≥6/10 across four domains: joint involvement (0–5 points), serology (RF/ACPA; 0–3 points), acute-phase reactants (0–1 point), and symptom duration (≥6 weeks = 1 point).

Data was analyzed using SPSS Version 27.0. Means ± SD was reported for the normally distributed continuous variables, while medians and interquartile ranges were reported for the non-normally distributed quantitative variables. Frequencies and percentages were calculated for categorical variables like gender, residence status, obesity status, family monthly income status, educational status, occupational status and diabetes mellitus type II status. Effect modifiers were controlled through stratification of age, gender, residence status, obesity status, family monthly income status, educational status and occupational status to see the effect of these on outcome variable (i.e., diabetes mellitus type 2 status). Post stratification chi square test was applied taking p-value of ≤ 0.05 as statistically significant.

RESULTS

The study included 137 participants with a mean age of 57.61 ± 10.44 years, ranging from 39 to 70 years. The mean body mass index (BMI) was 29.34 ± 5.11 kg/m², indicating that the study population was, on average, in the overweight to obese category. The mean height was 149 ± 12.71 cm, and the mean weight was 74.9 ± 6.78 kg, with weights ranging from 62 to 113 kg (Table 1).

Table 1: Descriptive Statistics of Continuous Variables (N=137)

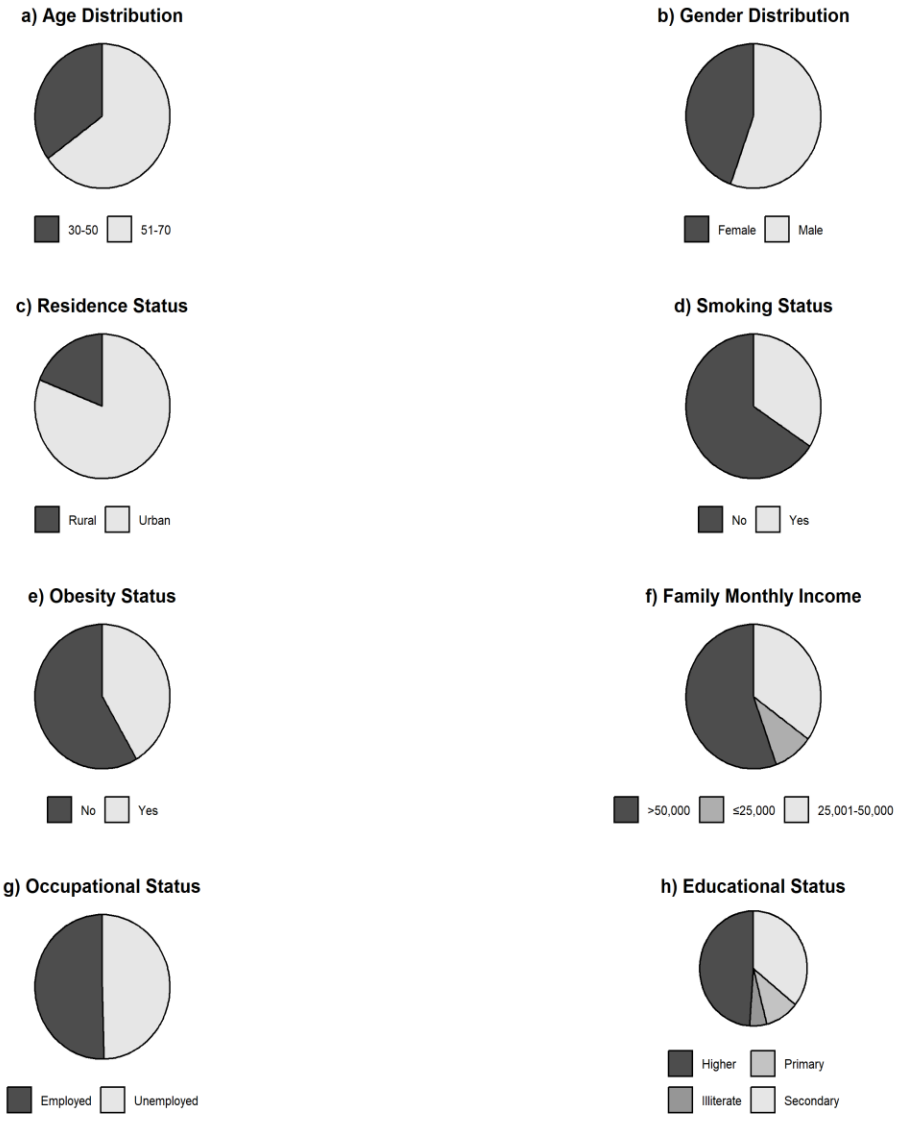
Variable	Mean ± SD	Range (Min-Max)
Age (years)	57.61 ± 10.44	39-70
BMI (kg/m²)	29.34 ± 5.11	23-33
Height (cm)	149 ± 12.71	129-156
Weight (kg)	74.9 ± 6.78	62-113

Distribution of Categorical Variables

The overall distribution of categorical variables is presented in Figure 1. The majority of participants were in the 51-70 years age group (65.0%), while 35.0% were in the 30-50 years age group. Males comprised 55.5% of the study population, and females represented 44.5%. Most participants resided in urban areas (81.0%) compared to rural areas (19.0%). Regarding lifestyle factors, 65.7% of participants were non-smokers, while 34.3% reported smoking. The prevalence of obesity in the study population was 41.6%.

In terms of socioeconomic characteristics, the majority of participants had higher family monthly incomes, with 55.5% earning more than 50,000, 35.0% earning between 25,000-50,000, and only 9.5% earning 25,000 or less. The study population was nearly evenly divided between employed (50.4%) and unemployed (49.6%) individuals. Educational attainment showed that 48.9% had higher education, 35.8% had secondary education, 10.2% had primary education, and 5.1% were illiterate.

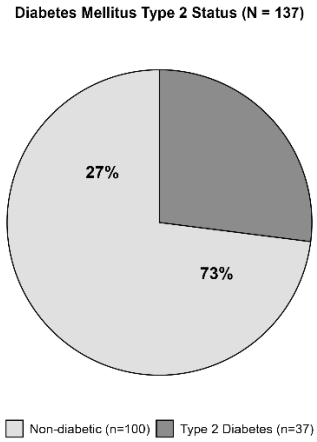
Figure 2. Pie Chart Distributions of Categorical Variables



Prevalence of Type II Diabetes Mellitus

Out of 137 participants, 37 (27.0%) were diagnosed with type II diabetes mellitus, while 100 (73.0%) did not have the condition. The stratified analysis of diabetes mellitus according to various sociodemographic and clinical variables is presented in Table 2 and Figure 2.

Figure 2.



Association Analysis

Non-Significant Associations

Several variables showed no significant association with type II diabetes mellitus. Age distribution was similar between diabetic and non-diabetic groups (p = 0.57), with 64.9% of diabetic patients in the 51-70 years age group compared to 65.0% in the non-diabetic group. Gender showed no significant association (p = 0.35), with 59.5% of diabetic patients being male compared to 54.0% in the non-diabetic group.

Residence status was not significantly associated with diabetes (p = 0.11), although a higher proportion of urban dwellers were observed in the non-diabetic group (84.0%) compared to the diabetic group (73.0%). Smoking status also showed no significant association (p = 0.12), despite a higher proportion of smokers in the diabetic group (43.2%) compared to the non-diabetic group (31.0%). Family monthly income showed no significant relationship with diabetes status (p = 0.83).

Significant Associations

Three variables demonstrated significant associations with type II diabetes mellitus. Obesity status showed a borderline significant association (p = 0.05), with 54.1% of diabetic patients being obese compared to 37.0% in the non-diabetic group, suggesting that obesity may be an important risk factor for developing type II diabetes mellitus.

Occupational status was significantly associated with diabetes (p = 0.02), with a notably higher proportion of unemployed individuals in the diabetic group (64.9%) compared to the non-diabetic group (44.0%). Conversely, employed individuals were more prevalent in the non-diabetic group (56.0%) compared to the diabetic group (35.1%).

Educational status also showed a significant association with diabetes (p = 0.05). Illiterate individuals comprised 13.5% of the diabetic group but only 2.0% of the non-diabetic group. Conversely, those with higher education represented 43.2% of the diabetic group compared to 51.0% of the non-diabetic group, suggesting an inverse relationship between educational level and diabetes prevalence, although the distribution across all educational categories was complex.

These findings indicate that obesity, occupational status, and educational level are significantly associated with type II diabetes mellitus in this study population, while demographic factors such as age, gender, and residence showed no significant associations.

Table 2: Association Between Sociodemographic and Clinical Variables with Type II Diabetes Mellitus (N=137)

			Diabetes Mellitus Type II		
Variable	**Category**	**Total** n (%)	**Yes** n (%)	**No** n (%)	**p value**
Age (years)	30-50	48 (35.0%)	13 (35.1%)	35 (35.0%)	0.57
	51-70	89 (65.0%)	24 (64.9%)	65 (65.0%)	
Gender	Male	76 (55.5%)	22 (59.5%)	54 (54.0%)	0.35
	Female	61 (44.5%)	15 (40.5%)	46 (46.0%)	
Residence Status	Urban	111 (81.0%)	27 (73.0%)	84 (84.0%)	0.11
	Rural	26 (19.0%)	10 (27.0%)	16 (16.0%)	
Smoking Status	Yes	47 (34.3%)	16 (43.2%)	31 (31.0%)	0.12
	No	90 (65.7%)	21 (56.8%)	69 (69.0%)	
Obesity Status	Yes	57 (41.6%)	20 (54.1%)	37 (37.0%)	0.05*
	No	80 (58.4%)	17 (45.9%)	63 (63.0%)	
Family Monthly Income	≤ 25,000	13 (9.5%)	4 (10.8%)	9 (9.0%)	0.83
	25,000-50,000	48 (35.0%)	14 (37.8%)	34 (34.0%)	
	> 50,000	76 (55.5%)	19 (51.4%)	57 (57.0%)	
Occupational Status	Employed	69 (50.4%)	13 (35.1%)	56 (56.0%)	0.02*
	Unemployed	68 (49.6%)	24 (64.9%)	44 (44.0%)	
Educational Status	Illiterate	7 (5.1%)	5 (13.5%)	2 (2.0%)	0.05*
	Primary	14 (10.2%)	4 (10.8%)	10 (10.0%)	
	Secondary	49 (35.8%)	12 (32.4%)	37 (37.0%)	
	Higher	67 (48.9%)	16 (43.2%)	51 (51.0%)	

*Statistically significant at $p < 0.05$ (chi-square test).

DISCUSSION

Rheumatoid arthritis (RA) is a chronic and disabling disease characterized by persistent synovitis, systemic inflammation, and the presence of autoantibodies. Inflammatory mediators such as C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor (TNF)-α are frequently elevated in patients with type 2 diabetes, as well as in the sera of patients many years before the clinical onset of RA, suggesting a critical role in the immunopathogenesis of this disease. This observation also suggests that low-grade inflammation should have already existed in patients with RA during the preclinical phase. In addition, smoking causes chronic lung inflammation and could subsequently lead to the production of autoantibodies, resulting in the development of RA among genetically susceptible individuals. Therefore, it is plausible that chronic low-grade inflammation observed in patients with type 2 diabetes could also contribute to the development of RA in these patients.

Our study included a total of 137 patients. Out of 137, 37 (27%) had diabetes mellitus type II while 100 (73%) did not have.

The literature on the association between rheumatoid arthritis (RA) and the risk of incident type 2 diabetes mellitus (T2DM) reveals conflicting findings, likely reflecting differences in study populations, adjustment for confounders (including antirheumatic therapies), follow-up duration, and the impact of chronic inflammation versus treatment effects.

Several large population-based cohort studies suggest a modestly increased risk of T2DM in RA patients, potentially attributable to shared inflammatory pathways. For example, one analysis of over 600,000 adults (excluding those with pre-existing T2DM) reported elevated RA-to-non-RA risk ratios for incident T2DM of 1.68 (95% CI 1.53–1.84) in men and 1.46 (95% CI 1.39–1.54) in women.[17] Another extensive cohort involving nearly 500,000 individuals found incidence rates of diabetes of 8.6 per 1000 person-years in RA

(95% CI 8.5–8.7) versus 5.8 in non-rheumatic controls, corresponding to an adjusted hazard ratio (HR) of 1.5 (95% CI 1.4–1.5). A similar elevation was observed in psoriatic arthritis (PsA) and psoriasis (PsO), with an incidence rate of 8.2 per 1000 person-years and adjusted HR of 1.4 (95% CI 1.3–1.5) versus controls,[18] supporting the concept that systemic inflammation in immune-mediated rheumatic diseases may promote insulin resistance and glucose dysregulation.

These observations are broadly consistent with multiple systematic reviews and meta-analyses (up to 2021), which have reported pooled relative risks for incident diabetes in RA ranging from approximately 1.23 to 1.43, although with notable heterogeneity across studies.

In contrast, other investigations have reported lower incident T2DM rates in RA compared to certain comparator groups. A large cohort study of 449,327 patients with RA, general non-RA individuals, hypertension, osteoarthritis (OA), or PsA found the lowest incidence rate in the RA group (7.0 per 1000 person-years) versus the highest in hypertension (12.3 per 1000 person-years). After extensive adjustment for >40 baseline covariates, RA was associated with a 24–35% lower risk of incident T2DM compared to these four reference cohorts.[19] This finding may reflect protective effects of certain disease-modifying antirheumatic drugs (DMARDs) commonly used in RA (e.g., methotrexate, hydroxychloroquine, or biologics), which have been linked in some analyses to improved insulin sensitivity or reduced diabetes risk, potentially offsetting the pro-diabetogenic effects of inflammation or glucocorticoids.

Cross-sectional data from smaller RA cohorts further highlight the high prevalence of traditional metabolic risk factors, including obesity (BMI-defined in ~27%), dyslipidemia (~34%), hypertension (~49%), and T2DM itself (~15%), often correlated with disease activity, waist circumference, and age.[15] Such comorbidities underscore the need for vigilant metabolic screening in RA patients.

Overall, while the preponderance of evidence (including meta-analyses) supports a modest increase in T2DM risk in RA, driven largely by chronic inflammation, important variability exists, and some studies suggest that optimal disease control with anti-inflammatory therapies may mitigate or even reverse this risk. The potential protective role of specific antirheumatic agents (e.g., TNF inhibitors, methotrexate, or abatacept) against incident diabetes remains an active area of research, with implications for integrated management of inflammation and cardiometabolic health in RA and related conditions. Future prospective studies, ideally incorporating detailed treatment exposure and inflammatory biomarkers, are needed to resolve these discrepancies and guide preventive strategies.

CONCLUSIONS:

The elevated prevalence of type 2 diabetes mellitus observed in this Pakistani cohort underscores the significant metabolic burden in rheumatoid arthritis patients, likely driven by chronic systemic inflammation, obesity, and potential effects of glucocorticoid/NSAID therapy. Socioeconomic factors, including unemployment and lower education, further amplify this risk in the local South Asian context.

These findings, set against limited regional data, strongly support routine HbA1c screening for early detection and integrated management of diabetes in RA patients. Such an approach can reduce cardiovascular complications, disability, and premature mortality.

DECLARATIONS:

Data Availability Statement:

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest Disclosure:

The authors declare that they have no conflicts of interest.

Ethics Approval Statement:
This study was approved by the Institutional Ethical Review Committee of Jinnah Postgraduate Medical Center, Karachi, Pakistan (reference number: [insert if available]).

Patient Consent Statement:
Written informed consent was obtained from all participants prior to enrollment in the study.

Permission to Reproduce Material from Other Sources:
No material requiring permission from third-party sources was reproduced in this manuscript.

Clinical Trial Registration
N/A

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