Disease-Related Outcomes Influence the Prevalence of Falls in People with Rheumatoid Arthritis

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ABSTRACT
Background Adults who had Rheumatoid arthritis (RA) are more prone to falls. Falling in RA increases the risk of hip fracture as decreased bone mineral density is a prominent feature in RA
Objective: The aim of the current work was to assess the prevalence of falls and its association with different clinical conditions and different physical performance status. **Patients and Methods:** This cross-sectional study included a total of 75 patients with RA, diagnosed according to 2010 American College of Rheumatology's Categorization Criteria, attending at Outpatient and Inpatient Clinics, Department of Rheumatology and Rehabilitation, Beni-Suef University Hospital. Participants were divided into non-fallers and fallers.
Results: The prevalence of falls among RA patients was 33.3%. Faller RA patients had significantly higher Health Assessment Questionnaire-Disability Index (HAQ-DI) and Clinical Disease Activity Index (CDAI) as compared with non-fallers (p-values< 0.001). Faller RA patients had significantly lower Berg Balance Scale (BBS) as compared with non-fallers (p-value <0.001), Faller RA patients had significantly longer 5-Time Sit Down-To-Stand Up Test (SST5) and longer Timed Up and Go Test (TUG) as compared with non-fallers (p-values< 0.001).
Conclusion: It could be concluded that the prevalence rate of falls in RA patients is high, most of them are associated with disease-related outcomes primarily (CDAI) and (HAQ-DI). This makes these tools useful to assess the risk of falls in RA.
Keywords: Rheumatoid Arthritis, Falling, Disease activity.

INTRODUCTION

Rheumatoid Arthritis (RA) is mainly a disease of the immune system. RA constituted 1% of the general population and the average age of onset occurs between 40-60 years [1]. Its persistent synovitis causes the destruction of the cartilage and bone as well as the bursa and tendon sheaths [2]. Both inflammation and damage interfere with a patient's normal mobility and balance and decrease the patient's musculoskeletal strength and joint flexibility which in turn leads to a high prevalence of falls. Patients with RA have higher morbidity and mortality rates, as well as a lower quality of life [3].

Disease activity is one of the main factors that affect the risk of falling [4], and correlates also with factors that are prevalent in older patients; (visual impairment, lack of physical activity, certain medications, and previous history of falling) [5].

Adults are the largest category prone to falls. It's estimated that around 68% of patients who fall experience injuries. Despite being a common issue with potentially serious consequences, falling into RA is still considered an under-researched subject which leads probably to an underestimation of the problem [6].

Falling in RA increases the risk of hip fracture as decreased bone mineral density is a prominent feature in RA. Besides the risk of bone fractures, falling increases the risk of serious injuries and hospitalization, and admission to care homes. Getting older and associated comorbidities are considered the most important risk for falls[7], while in RA patients falling incidence appears to be independent of age [8].

Also, disease duration doesn't seem to have a significant impact[9].

The aim of the current work was to assess the prevalence of falls and its association with different clinical conditions and different physical performance status.

PATIENT AND METHODS

This cross-sectional study included a total of 75 patients with RA, diagnosed according to 2010 American College of Rheumatology's Categorization Criteria [10], attending at Outpatient and Inpatient Clinics, Department of Rheumatology and Rehabilitation, Beni-Suef University Hospital.

Inclusion criteria: RA Patients, ≥ 18 years.
Exclusion criteria: Patients who had severe hearing or visual impairment, as well as neurological diseases like stroke, cognitive impairment, imbalance, and peripheral neuropathies. Patients suffering from gait abnormality due to lower limb disorder as joint disease or instability that is not related to RA were also excluded.

Participants were divided into non-fallers (50 patients) and fallers (25 patients). The Berg Balance Scale (BBS) and Timed-up-and-go Test (TUG) were used to test the physical function performance scales [11], yet their relation to falling RA was not sufficiently studied [12]. For example, the 5-Time Sit Down-To-StandUp Test (SST5) which was predominantly a test for lower limb strength was tested concerning falling in RA in one study [13].

1. Physical performance tests:

- **Berg Balance Scale:** The BBS is used to assess the balance. It tests if the subject can perform 14 movements

that are required in daily activities in a balanced manner. The scale ranged from 0-4, where zero means the person is unable to perform the task while 4 means the person can perform the task with no help This gives the test a total score range from 0 to 56 and it usually takes about 15 to 20 minutes to finish [14]. Currently, this test is used to point out older individuals with a risk of falling [11].

- **Timed up and Go Test:** it tests the person's ability to perform both dynamic and static balance. The amount of time taken by the subject to rise from an armchair and walk for 3 meters and then go back to his original seated position is recorded in seconds [15]. This test is used to evaluate balance, mobility, and falling risk in elderly and RA patients [11].

- **5 Time Set Down-To-Stand Up Test:** The SST5 measures lower limb strength and mobility. The subject begins the test by sitting upright on a chair with his legs separated by a space equal to the space between his shoulders and his arms crossed over his chest. The subject is instructed to stand and sit as fast as he can without using his arms, and then the instructor recorded time in seconds [14]. The test is considered a valid and reliable measure of lower limb function [16].

2. Clinical Disease Activity Index (CDAI):

The CDAI is used to measure disease activity in RA patients. It is scored by simply adding 4 parameters: tender and swollen joint count of 28 joints, patients, and physician global assessment of disease activity in a 0 to 10 cm visual analog scale [17].

RESULTS

The current investigation was a cross-sectional study of 75 RA patients distributed as (5) males and (70) females with ages ranging from (22 - 67) with an average of (40.81 ±10.85) years. Participants were classified as "fallers" and "non-fallers" based on the number of falls during the last 12 months. Faller patients were (25) participants (33.3%), while (50) participants were classified as non-fallers (66.7%) (Table 1).

Table (1): Distribution of the Studied Population according to Age, Gender and the Prevalence of falls; (N= 75):

		Frequency	%
Gender	Male	5	6.7 %
	Female	70	93.3 %
Age (year)	Mean ±SD	40.81 ±10.85	
	Minimum – Maximum	22 – 67	
RA patients	Fallers Patients	25	33.3 %
	Non-Fallers Patients	50	66.7 %

3. Health Assessment Questionnaire-Disability Index (HAQ-DI):

HAQ-DI is used to evaluate the musculoskeletal ability of RA patients. It has a validated Arabic version. It contains 20 items divided into 8 domains. Each item is scored from 0 to 3. The highest scores in each domain are added together and divided by 8. The score ranged from zero to three. A higher score indicates more disability [18].

Ethical approval:

The study was approved by the Ethics Board of Beni-Suef University and an informed written consent was taken from each participant or their parents in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

SPSS 25 (Statistical Package for the Social Sciences) for Windows 10 was used to catalogue and evaluate the gathered information.

Descriptive analysis statistics (min/max/mean/SD) for quantitative data and a percentage distribution for qualitative data. The chi-Square test ($\chi 2$) was used to compare categorical variables. Student t-test: To evaluate the similarity of means between two independent normal-distributed groups. A p-value of 0.05 or lower indicated statistical significance.

Studied faller participants had significantly older ages as compared with studied non-faller participants. The mean ages were (47.16 vs. 37.64) years old in faller and non-faller participants respectively with a statistically significant p-value (0.001). Among all studied RA patients; disease duration ranged from 1 year to 25 years. Patients with RA who fell and those who didn't didn't have significantly different disease duration; (p-value= 0.835). The number of tender joints was significantly higher among faller RA patients (ranging from 6 to 44 joints) as compared with non-faller RA patients (ranging from 0 to 25 joints).

The mean tender joints were (22.52 vs. 11.16) in faller and non-faller RA patients respectively with a statistically significant p-value= 0.001. No statistically significant difference between faller patients and non-faller patients regarding their gender; (p-value> 0.05) (Table 2).

Table (2): Relation between falls prevalence and patient's age, disease duration and number of affected joints; (N= 75):

	Falls Prevalence	N	Mean	SD	p-value
Age (year)	Fallers Patients	25	47.16	11.65	**0.001***
	Non-Fallers Patients	50	37.64	8.97	
Disease Duration (years)	Fallers Patients	25	7.68	5.79	0.835
	Non-Fallers Patients	50	7.56	6.03	
Number of tenders and swollen joints	Fallers Patients	25	22.52	9.53	**0.001***
	Non-Fallers Patients	50	11.16	7.16	

Skin manifestations were more prevalent among faller patients; twelve faller patients (48%) had skin manifestations vs. six non-faller (12%) with a statistically significant p-value= 0.001. Eye manifestations were more prevalent among faller patients; fourteen faller patients (56%) had eye manifestations vs. twelve non-faller (24%) with a statistically significant p-value= of 0.007. Renal manifestations were more prevalent among faller patients; twelve faller patients (48%) had renal manifestations vs. ten non-faller (20%) with a statistically significant p-value= 0.013. Loco-motor manifestations were more prevalent among faller patients; the majority of faller patients (76%) had loco-motor manifestations vs. only ten non-faller (20%) with a statistically significant p-value= 0.001. Constitutional, Reynaud's Phenomena, CVS, Pulmonary, GIT, and Extra-articular manifestations were nearly similar among both groups with no statistically significant differences (p-values >0.05).

Faller RA patients had more prevalent HTN as compared with non-faller RA patients (36% vs. 8%) in faller and non-faller respectively with a statistically significant p-value= 0.004. Faller RA patients had more prevalent DM as compared with non-faller RA patients (32% vs. 10%) in faller and non-faller respectively with a statistically significant p-value= 0.022 (Table 3).

Table (3): Relation between falls prevalence and Extra-articular Manifestation among studied RA Patients; (N= 75):

Extra articular Manifestation		Falls Prevalence N (%)		TOTAL	p-value
		Fallers Patients N= 25	Non-Fallers Patients (N= 50)		
Constitutional					
	No	20 (80.0)	44 (88.0)	64 (85.30)	0.276
	Yes	5 (20.0)	6 (12.0)	11 (14.70)	
Skin					
	No	13 (52.0)	44 (88.0)	57 (76.0)	**0.001***
	Yes	12 (48.0)	6 (12.0)	18 (24.0)	
Reynaud's Phenomena					
	No	21 (84.0)	46 (92.0)	67 (89.30)	0.249
	Yes	4 (16.0)	4 (8.00)	8 (10.70)	
Eye					
	No	11 (44.0)	38 (76.0)	49 (65.3)	**0.007***
	Yes	14 (56.0)	12 (24.0)	26 (34.7)	
CVS					
	No	23 (92.0)	28 (96.00)	71 (94.7)	0.407
	Yes	2 (8.00)	2 (4.00)	4 (5.30)	
Pulmonary					
	No	15 (60.0)	40 (80.0)	55 (73.30)	0.060
	Yes	10 (40.0)	10 (20.0)	20 (26.70)	
GIT					
	No	11 (44.0)	28 (56.0)	39 (52.0)	0.231
	Yes	14 (56.0)	22 (44.0)	36 (48.0)	
Renal					
	No	13 (52.0)	40 (80.0)	53 (70.7)	**0.013***
	Yes	12 (48.0)	10 (20.0)	22 (29.3)	
Loco-motor					
	No	6 (24.0)	40 (80.0)	46 (61.30)	**<0.001***
	Yes	19 (76.0)	10 (20.0)	29 (38.70)	
Comorbidities					
HTN					
	No	16 (64.0)	46 (92.0)	62 (82.70)	**0.004***
	Yes	9 (36.0)	4 (8.0)	13 (17.30)	
DM					
	No	17 (68.0)	45 (90.0)	62 (82.7)	**0.022***
	Yes	8 (32.0)	5 (10.0)	13 (17.3)	

Steroids were significantly more prescribed to faller RA patients as compared with non-fallers with a statistically significant p-value= 0.040. Muscle relaxants were significantly more prescribed to faller RA patients as compared with non-fallers with a statistically significant p-value= 0.035. Prescription of antidepressants was more prevalent with faller RA patients as compared with non-fallers with a statistically significant p-value= 0.001. Consumption of NSAIDs, Methotrexate, Antimalarial, and Leflunomide medications were nearly similar among both groups with no statistically significant differences (p-values >0.05) (Table 4).

Table (4): Relation between falls prevalence and Used Medications among studied RA Patients; (N= 75):

Used Medications		Falls Prevalence N (%)		TOTAL	p-value
		Fallers Patients N= 25	Non-Fallers Patients N= 50		
NSAIDs					
	No	11 (44.0)	30 (60.0)	41 (54.70)	0.143
	Yes	14 (56.0)	20 (40.0)	34 (45.30)	
Steroids					
	No	4 (16.00)	20 (40.00)	24 (32.00)	**0.040***
	Yes	21 (84.00)	30 (60.00)	51 (68.00)	
MTX					
	No	16 (64.00)	28 (56.00)	44 (58.70)	0.341
	Yes	9 (36.00)	22 (44.00)	31 (41.30)	
Antimalarial					
	No	5 (20.0)	14 (28.0)	19 (25.30)	0.324
	Yes	20 (80.0)	36 (72.0)	56 (74.40)	
Muscle Relaxant					
	No	18 (72.00)	46 (92.00)	64 (85.30)	**0.035***
	Yes	7 (28.00)	4 (8.00)	11 (14.70)	
Antidepressant					
	No	11 (44.00)	42 (84.00)	53 (70.70)	**0.001***
	Yes	14 (56.00)	8 (16.00)	22 (29.30)	
Leflunomide					
	No	7 (28.00)	20 (40.00)	27 (36.00)	0.223
	Yes	18 (72.00)	30 (60.00)	48 (64.00)	

Patients with RA who experienced falls had a substantially higher mean Erythrocyte Sedimentation Rate (ESR; 46.04 vs. 22.68) than those who did not have falls with a statistically significant p-value (0.001). Alanine Aminotransferase (ALT) was significantly higher among faller RA patients as compared with non-faller; the mean ALT was (25.00 vs. 15.76) in faller and non-faller patients respectively with a statistically significant p-value (0.001). White Blood Cells Count (WBC) was significantly higher among faller RA patients as compared with non-faller; the mean WBC count was (6.88 vs. 5.69) in faller and non-faller patients respectively with a statistically significant p-value (0.033). Serum Creatinine, Platelets count and Hemoglobin Concentration (Hb) showed a non-statistically significant difference between faller and non-faller RA patients; (p-values >0.05) (Table 5).

Table (5): Relation between fall prevalence and Laboratory Investigations among studied RA Patients; (N= 75):

Laboratory investigations	Falls Prevalence Mean ±SD		p-value
	Fallers Patients N= 25	**Non-Fallers Patients N= 50**	
ESR (mm/hr)	46.04 ±11.01	22.68 ±5.22	**0.001***
Serum Creatinine (mg/dl)	0.72 ±0.16	0.70 ±0.16	0.685
ALT (U/L)	25.00 ±6.40	15.76 ±3.81	**0.001***
WBCs $(x10^3/ul)$	6.88 ±1.60	5.69 ±1.31	**0.033***
Platelets $(x10^3/ul)$	295.76 ±71.22	285.40 ±70.51	0.599
Hb (g/dL)	11.20 ±1.36	11.22 ±1.69	0.956

*p-value ≤0.05 is considered statistically significant by Independent-Sample t-test analysis.
Erythrocyte Sedimentation Rate (ESR), Alanine Aminotransferase (ALT), White Blood Cells Count (WBC), Hemoglobin Concentration (Hb)

Faller RA patients had significantly higher Health Assessment Questionnaire-Disability Index (HAQ-DI) as compared with non-fallers; mean (HAQ-DI) scores were (1.43 vs. 0.60) in fallers and non-fallers respectively with a statistically significant p-value= 0.001. Faller RA patients had significantly higher Clinical Disease Activity Index (CDAI) as compared with non-fallers; mean (CDAI) scores were (38.36 vs. 15.60) in fallers and non-fallers respectively with a statistically significant p-value= 0.001. Faller RA patients had significantly longer Timed Up and Go Test (TUG) as compared with non-fallers; mean (TUG) time was (17.36 vs. 9.47 second) in fallers and non-fallers respectively with a statistically significant p-value= 0.001. Faller RA patients had significantly longer 5-Time Sit Down-To-Stand Up Test (SST5) as compared with non-fallers; mean (SST5) time was (16.13 vs. 9.39) in fallers and non-fallers respectively with a statistically significant p-value= 0.001) (Table 6).

Table (6): Relation between fall prevalence and Disease activity indices among studied RA Patients; (N= 75):

	Falls Prevalence	N	Mean	SD	p-value
HAQ-ID	Fallers Patients	25	1.43	0.27	0.001*
	Non-Fallers Patients	50	0.60	0.42	
CDAI	Fallers Patients	25	38.36	12.42	0.001*
	Non-Fallers Patients	50	15.60	6.53	
BBS	Fallers Patients	25	26.92	9.46	0.001*
	Non-Fallers Patients	50	48.92	5.03	
Time up and go test (sec)	Fallers Patients	25	17.36	5.67	0.001*
	Non-Fallers Patients	50	9.47	3.61	
SST-5	Fallers Patients	25	16.13	5.83	0.001*
	Non-Fallers Patients	50	9.39	2.34	

DISCUSSION

Falls have multifactorial causes in the old, for the most part, because of inborn factors, for example, diminished muscle quality, balance shortages, and step design changes. These age-related changes can likewise be seen in different infections [19].

Despite being relatively common and having potentially serious consequences, falls are considered still underestimated and under-investigated in RA [20]. Age and its related comorbidities associated with aging are the most important risk factors for falling [21]. Age and disease duration have surprisingly shown no significant relation to a falling incidence of RA. Few studies investigating the risk of falling in RA patients have identified several risk factors for falling [22].

Administration of NSAIDs, Antimalarial, Methotrexate, and Leflunomide were almost comparable among fallers and non-fallers RA patients with no statistically significant difference. In **Gaino et al.** [23] study; only the use of antidepressants and benzodiazepines was related to falls in RA patients, no other medications were linked to falling predominance.

Numerous instruments are available to screen individuals at risk of falls, for example, the Berg Balance Scale (BBS), Timed Up and Go Test (TUG), and 5-Time Sit Down-To-Stand Up Test (SST5). The TUG, BBS and SST5 values were worse for "intermittent fallers" than others and were thus viewed as significant fall predictors on univariate analysis.

In the current study; faller RA patients had significantly lower Berg Balance Scale (BBS) as compared to non-fallers; mean (BBS) time was (26.92 vs. 48.92) in fallers and non-fallers respectively with a statistically significant p-value= 0.001 which was like the **Gaino et al.** [23], study (52.5 in non-fallers and 48.70 in faller RA patients; p-value: 0.006).

Faller RA patients had significantly longer TUG time as compared to non-fallers, in **Gaino et al.** [23], study TUG scores were (11.5 in non-fallers and 13.8 in faller RA patients) with a significant difference (p-value: 0.030). Faller RA patients had significantly longer SST5 as compared to non-fallers, in **Gaino et al.** [23], study SST5 scores were (15.5 in non-fallers and 19.4 in faller RA patients) with a statistically significant p-value of 0.016.

In our study, faller patients were (25) participants (33.3%), while (50) participants were classified as non-fallers (66.7%). This percentage was nearly similar to the (35%) reported by **Jamison et al.** [24], that study the relationship between fear of falling and limiting RA. And the 33% foundin **Armstrong et al.** [25], hospital-based survey, where one in three patients stated falling in the last 12 months.

In contrast, this result was higher (14%) than that reported in another "retrospective" study that evaluates the frequency of falls and fall risk in patients with RA **Cakit et al.** [26] and (19%) were found in **Bugdayci et al.** [27].

However; some other studies reported higher fall prevalence among studied adult RA patients than our result; 52.1% [23], and 48.8% in **De Almeida Lourenço et al.** [28]. This discrepancy could be explained by different patient demographics and characteristics.

Like studies by **Gaino et al.** [23] and **Furuya et al.** [29], we could not get a significant association between RA disease duration and an increase in fall risk; on the opposite side; **Mahdi et al.** [30] study reported that duration of the disease was associated with the risk of falls in rheumatoid arthritis patients. Similarly, **Mikos et al.** [22] reported a statistically significant positive correlation between the number of falls and the duration of RA. Patients included in **Mahdi et al.** [30] study had much longer disease duration (15.1 years) than our patients (7.5 years) which can explain these different results.

CONCLUSION

It could be concluded that the prevalence rate of falls in RA patients is high, most of them are associated with disease-related outcomes primarily (CDAI) and (HAQ-DI). This makes these tools useful to assess the risk of falls in RA. Results from the Berg Balance Scale (BBS), Timed-Up-and-Go Test (TUG), and 5-Time Sit-Down-To-Stand-Up Test (SST5) were also connected to repeated falls, making these tests useful for gauging the potential for injury from falling.

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