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ORIGINAL ARTICLE

Causes of Pitfalls in Diagnosis of Rheumatoid Arthritis in Aswan University Hospital

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ABSTRACT

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Background - Rheumatoid arthritis (RA) is a symmetric, peripheral polyarthritis. It leads to deformity through the stretching of tendons and ligaments and destruction of joints through the erosion of cartilage and bone**. Aim -** to determine the causes of overdiagnosis of rheumatoid arthritis in Aswan university hospital rheumatology department. **Patients and Methods -** In this cross sectional study, 50 patients were included in the study selected from Rheumatology outpatient clinics, Aswan University Hospitals, Faculty of Medicine, Aswan University. **Results -** 6 Cases were male and 44 were female and their ages ranged between 22 to 70 years (mean 48.52±14.16 years), the median complaint duration (years) were 24±5.58 (12 – 48). 18 (36.0%) Cases Positive Morning stiffness and 32 (64.0%) were negative Morning stiffness and it ranged from 5 to 70 minutes (Median 26.67±21.49).40(36%) patients were misdiagnosed due to bilateral hand arthralgia , 18(36%) patients due to diagnosis by speciality other than rheumatology , 18(36%) patients due to RF positivity , 17(34%) patients due to presence of morning stiffness. **Conclusion -** RA misdiagnosis was associated with numerous factors, including the health care practitioner, community knowledge, overlapping symptoms between RA and other diseases, and laboratory error factors.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and destruction of the joints.[1] It affects 1% of the world's adult population, with a global incidence of approximately 5 in 1000 adults. Women are more commonly affected than men and can occur at any age. The highest incidence occurs in the sixth decade of life.[2]

A misdiagnosis can be defined as “a diagnosis that was unintentionally delayed (information was previously available), sufficiently misdiagnosed (misdiagnosed before a correct diagnosis was made), or overlooked (not diagnosed at all) compared to the final diagnosis estimation of the most specific information.[3]

Overdiagnosis poses a potential risk in rheumatoid arthritis screening, overdiagnosis leads to overtreatment, the problem of overdiagnosis and over treatment of rheumatic diseases has become a reality that has been addressed.[4]

This study aim to determine the causes of over-diagnosis of rheumatoid arthritis in Aswan

university hospital rheumatology outpatient clinic .

PATIENTS AND METHODS

In this cross sectional study, fifty patients were included in the study selected from Rheumatology and Rehabilitation outpatient clinics, Aswan University Hospitals, Faculty of Medicine, Aswan University.

Inclusion criteria: Patients presented to Aswan university hospital outpatient rheumatology clinic with preliminary diagnosis of (RA) and Age > 18 years old.

Exclusion criteria: Patients with confirmed diagnosis of (RA) and Age <18 years old (to exclude juvenile conditions).

Methods: After the protocol was approved by our ethics committee and the patients were informed in detail about the purpose and procedure of the study, the patients were referred to the outpatient department of the rheumatology department of the University Hospital of Aswan within 6 months. The preliminary diagnosis of RA was re-evaluated to confirm or rule out the diagnosis of RA as follows: complete medical history and medical history, careful general examination and joint examination, images were included; X-ray of the hands (posterior-anterior, soft and hard). Laboratory tests were included; Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF) and anticyclic citrullinated peptide (ACPA) antibody.

Statistical Methods: The data collected were processed using the Social Science Statistics Package (SPSS 25), coded, tabulated and entered into a computer. Data were presented and appropriate analyzes performed according to the type of data obtained for each parameter. Mean, standard deviation (±SD), and range for parametric numeric data. Frequency and percentage of non-numeric data.

Ethical Considerations: Ethical issues, both substantive and procedural, are included in this study. Participants agreed that they understand the nature of the study, the risks and benefits involved, and their right to discontinue participation in this study, without prejudice to their right to appropriate medical care at the study site, including contact address for questions about the study, and that you have given their consent to voluntarily participate in this study.

RESULTS

50 patients were found of wrong diagnosis of RA , these were the patients enrolled in the study.

Table 1: Demographic data and C/P for the study group.

		Mean / N	SD / %	Range
Age (Years)		48.52	14.16	(22- 70)
Sex	Male	6	12.0	
	Female	44	88.0	
Complaint duration (Years)		3.86	5.58	(0.17 -29)
Morning stiffness	No	32	64.0	
	Yes	18	36.0	
Duration(Min)		26.67	21.49	(5 - 70)

Previously known co-morbidity	Negative	42	84.0	
	DM	5	10.0	
	HCV	3	6.0	

Table 1: shows there were 6 Cases were male and 44 were female and their ages ranged between 22 to 70 years (mean 48.52±14.16 years), the Median Complaint duration (years) were 24±5.58 (12 – 48). 18 (36.0%) Cases were Positive Morning stiffness and 32 (64.0%) were negative Morning stiffness and their Morning stiffness (min) ranged from 5 to 70 (Median 26.67±21.49).

Table 2 : Lab investigations for the study group.

		Mean/ N	SD/ %	Range
ESR		50.90	21.67	(15 –110)
CRP	Negative	20	40.8%	
	Positive	30	60.0%	
RF	Negative	32	64.0%	
	Positive	18	36.0%	
Anti CCP	Negative	49	98.0%	
	Positive	1	2.0%	

Table 2 shows the Mean ESR were 50.90 ± 21.67, there were 30 (60.0%) Patients with positive CRP, 18 (36.0%) Patients with positive RF and One (2.0 %) Patient with positive Anticcp.

Table 3: Hand X-ray findings for the study group.

			N	%
X-ray finding	Normal		25	50.0%
	Abnormal		25	50.0%
X-ray findings	New bone formation		9	36.0%
	Erosions	Total	7	28.0%
		Punched out erosion	4	57.1%
	Cysts		6	24.0%
	Periosteal reaction		6	24.0%
	Small joint narrowing		4	16.0%
	Osteopenia		3	12.0%
	Juxtaarticular osteopenia		3	12.0%
	Gullwing sign		2	8.0%
	Small joints destruction		1	4.0%
	Subperiosteal bone resorption		1	4.0%
	Pencil in cup deformity		1	4.0%

Table 3 shows that 25(50%) patients have normal hand x-ray and 25 (50%) patients have abnormal hand x-ray. The abnormal hand x ray findings are divided into : 9(36%) patients have new bone formation , 7 (28%) patients have erosions, 6(24%) patients have cysts, 6 (24%) patients have periosteal reaction , 4(16%) patients have small joints narrowing , 3(12%) patients have osteopenia , 3(12%) patients have juxtaarticular osteopenia ,2(8%) patients have gullwing sign , 1(4%) patient has small

joints destruction , 1(4%) patient has subperiosteal bone resorption and 1(4%) patient has pencil in cup deformity.

Table 4: Who previously diagnose patients for the study group?

		N	%
Previously diagnosed by	Rheumatologist	23	46.0%
	Orthopedic	12	24.0%
	Neurologist	4	8.0%
	General practitioner	2	4.0%
	Oncologist	1	2.0%
	Patient him/herself	8	16.0%

Table 4 shows that 23(46%) patients were previously misdiagnosed by rheumatologists , 12 (24%) patients by orthopedics, 4 (8%) by neurologists , 2(4%) by general practitioner, 1(2%) by oncologist and 8(16%) by themselves (self reported with RA).

Table 5: Causes of previous diagnosis for the study group.

			N	%
Causes of misdiagnosis	Bilateral hand arthralgia		40	80.0%
	Diagnosed by different speciality		18	36.0%
	RF positivity		18	36.0%
	Morning stiffness		17	34.0%
	Elevated ESR		15	30.0%
	Bilateral hand arthritis		9	18.0%
	Positive CRP		8	16.0%
	Deformity	Total	6	8.0%
		Trigger finger deformity	3	50.0%
		jaccoud's arthropathy deformity	1	16.7%
		Nodules Presence	2	33.3%
	Delay in skin manifestation appearance		4	8.0%
	Community knowledge		4	8.0%
	Patient profession (Doctor)		3	6.0%
	Patient anxiety		3	6.0%
	Positive consanguinity		2	4.0%
	Anti CCP positivity		1	2.0%
	limited hand mobility		1	2.0%
	Marked delay in follow up		1	2.0%
	Previous lab error		1	2.0%

Table 5 shows causes of misdiagnosis 40(36%) patients were misdiagnosed due to bilateral hand arthralgia , 18(36%) patients due to diagnosis by speciality other than rheumatology ,

18(36%) patients due to RF positivity , 17(34%) patients due to presence of morning stiffness, 15 (30%) patients due to elevated ESR ,9(18%) patients due to bilateral hand arthritis, 8 (16%) patients due to positive CRP , 6(8%) patients due to presence of deformity , 4(8%) patients due to delay of skin manifestations , 4 (8%) patients due to community knowledge about RA , 3(6%) patients due to patient's profession , 3(6%) patients due to patient anxiety , 2(4%) patients due to positive consanguinity , 1(2%) patientsdue to anti ccp positivity , 1(2%) patients due to limited hand mobility

Table 6: Final diagnosis for the study group.

			N	%
Final diagnosis	Normal		3	6.0%
	Seronegative arthyropathy	Total	8	16.0%
		A.S.	2	25.0%
		PSA	4	50.0%
		S.P.A. with peripheral arthritis	1	12.5%
		Undifferentiated seronegative arthritis	1	12.5%
	O.A	Total	4	8.0%
		O.A.	1	25.0%
		Erosive O.A	2	50.0%
		Knee O.A.	1	25.0%
	S.L.E.		6	12.0%
	Diabetic arthropathy		5	10.0%
	Gout		4	8.0%
	Hyperparathyroidism		4	8.0%
	HCV related arthropathy		3	6.0%
	Hypothyroidism		3	6.0%
	Fibromyalgia		2	4.0%
	Post-COVID 19 reactive arthritis		2	4.0%
	Hyperthyroidism		1	2.0%
	Double crush syndrome		1	2.0%
	Myofascial pain syndrome		1	2.0%
	Overlap syndrome (SLE+ SSC)		1	2.0%
	Paraneoplastic syndrome		1	2.0%
	Cervical spondylosis		1	2.0%

Table 6 shows the final and correct diagnosis of our study group , 3(6%) patients were normal healthy population , 8(16%) were seronegative spondyloarthropathy , 4(8%) were osteoarthritis , 6(12%) were S.L.E. , 5(10%) were diabetic arthropathy , 4(8%) were gout , 4(8%) were hyperparathyroidism , 3(6%) were HCV related arthropathy, 3(6%) were hypothyroidism , 2(4%) were fibromyalgia, 2(4%)were post-covid19 reactive arthritis , 1(2%) was hyperthyroidism, 1(2%) was double crush syndrome , 1(2%) was overlap (SLE+ SCC) syndrome , 1(2%) was myofascial pain syndrome , 1(2%) was paraneoplastic syndrome , 1(2%) wascervical spondylosis.

DISCUSSION

Rheumatoid joint pain (RA) is a persistent, balanced, fiery immune system illness that at first influences little joints, advancing to bigger joints, and ultimately the skin, eyes, heart, kidneys,

and lungs. Frequently, the bone and ligament of joints are obliterated, and ligaments and tendons cracked.[5]

The ongoing cross sectional review was led to decide the reasons for overdiagnosis of rheumatoid joint pain in Aswan college medical clinic rheumatology short term facility. This study involved 50 patients with wrong determination of RA.

In the current review, periods of the included populace went from 22 to 70 years (mean 48.52±14.16 years). Our outcomes covered with **Leu Agelii et al.**[6] concentrate on which showed that time of misdiagnosed patients as RA at first side effect was 65 (46-72) years. while normal period of misdiagnosed patients in **Gomez et al.,**[7] study was 57.6 (±12 years). These outcomes might be upheld by the examinations which showed that RA regularly influences patients matured 30-50 years of age (Ke et al., 2021). Additionally, there were critical age-and sex-subordinate contrasts in the clinical treatment and in result of RA 8 years after determination. The distinctions were most articulated in men<40 and ladies ≥70 years, however whether they are because of sickness aggregate or therapy is muddled **Nilsson et al.**[8]

Concerning firmness grumbling in the current review, there were 18 (36.0%) positive cases with term went from 5 to 70 min (middle 26.67±21.49) while 32 (64.0%) were negative. On the other hand, around all patients misdiagnosed with RA experienced morning firmness in **Leu Agelii et al.**[6] study.

In the current review, 44 (84.0%) patients had no recently known co-bleakness, while 8 (16.0%) patients had recently known co-horribleness what partitioned into 5(10.0 %) patients with DM and 3(6.0%) with HCV}.

Tidblad et al., (2021) found a few distinctions in comorbidity commonness between patients with new-beginning seropositive and seronegative RA contrasted and matched controls from everyone. These discoveries are significant both for how we might interpret the evolvement of comorbidities in laid out RA and for early discovery of these circumstances. At determination of RA, respiratory, endocrine and certain neurological illnesses were more normal in RA versus controls, with a comparative example in seropositive and seronegative RA. Conversely, mental problems and malignancies were less generally analyzed in RA versus controls. The comorbidity trouble was marginally higher in RA patients contrasted and controls (P <0.0001).

Concerning examinations for the review bunch in the current review, there was positive CRP in 30 (60.0%) patients, positive RF in 18 (36.0%), positive Enemy of CCP in one (2.0 %) with mean ESR of 50.90 ± 21.67.

Our review contradicted **Leu Agelii et al.**[6] concentrate on which showed that RF of patients misdiagnosed with RA was positive in 9 (21%), and ESR was 20 (9-30) mm.

In the current review, a big part of the patients had typical hand x-beam while the other half had strange hand x-beam. The more recorded irregularity was new bone development followed by disintegrations then blisters, periosteal response, little joints limiting, osteopenia, juxtaarticular osteopenia, gullwing sign, little joints annihilation, subperiosteal bone resorption and pencil in cup disfigurement. Be that as it may, our outcome was lower than announced in **Leu Agelii et al.**[6] concentrate on which showed that 12% of misdiagnosed patients as RA had radiographic changes.

In the current review, the majority of the patients were already misdiagnosed by rheumatologists, while different patients by muscular health, nervous system specialists, general professional, oncologist and themselves (self-detailed with RA).

De Chock et al.[9] uncovered the intricacy of identification of RA and the patients' excursion from side effect beginning until reference to a rheumatologist. Overabundance torment gives off an impression of being the main trigger for looking for help in people defenseless to RA. GPs appear to assume a urgent part in RA identification, yet the intricacy of their job is underlined by the huge number of various beginning side effects credited to RA. Reference to a rheumatologist is thusly here and there deferred by clinical vulnerability, prompting a few GP visits and longer treatment delays. This, thusly, affects the patient's discernment and wellbeing conduct, which could later likewise antagonistically affect the sickness result.

Morning solidness was taken out from the characterization models update in 2010, to a limited extent because of reports noticing the absence of explicitness for RA, as well as clashing reports of its relationship with sickness movement. However morning solidness is not generally remembered for the arrangement rules, the side effect is essential to patients and is still regularly utilized by clinical rheumatologists to recognize fiery joint inflammation from degenerative joint pain **Orange et al.**[10]

ESR might increment during the intense stage reaction to RA, polymyalgia rheumatica (PMR), fundamental lupus erythematosus (SLE) and vasculitis. The responsiveness of this test is high; in any case, the particularity is exceptionally low. In 10% of RA patients and 20% of PMR patients ESR levels might be inside typical cutoff points **Birtane et al.**[11]

C-receptive protein shows raised articulation during provocative circumstances like rheumatoid joint inflammation, a few cardiovascular illnesses, and disease. As an intense stage protein, the plasma grouping of CRP strays by no less than 25% during provocative problems. The most elevated centralizations of CRP are tracked down in serum, for certain bacterial diseases expanding levels up to 1,000-overlap **Sproston et al.**[12]

The energy of hostile to CCP antibodies is a valuable marker as far as foreseeing the course and guess of the RA. A higher titer of hostile to CCP antibodies addresses a less fortunate visualization for the sickness. Assurance of the presence of hostile to CCP antibodies ought to be proceeded as a standard assessment in all patients with thought rheumatoid joint pain **Mekic et al.**[13] In rheumatoid joint pain and most non-rheumatoid joint pain rheumatologic sickness sera, anti-CCP energy is citrulline-dependent. Anyway in certain patients, especially patients with AIH-1, citrulline-independent reactivity in the anti- CCP2 test can happen. A positive CCP test in a non-rheumatic sickness (eg liver illness) ought to hence be deciphered with care, and ideally followed by a control ELISA with a non-citrullinated antigen **Vannini et al.**[14]

CONCLUSION

Rheumatoid arthritis misdiagnosis was associated with health care practitioner, community knowledge, overlapping symptoms and signs between RA and other diseases, and laboratory error factors. In order to conduct an accurate diagnosis and prevent the clinical and health cost implications of a mistake, it is important to take into account the awareness among Egyptian health care professionals to detect and manage diseases that mimic RA and RA-related comorbidities

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