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ASSOCIATION OF HISTORY OF DISEASES/LIFESTYLE WITH TREATMENT DELAY IN RHEUMATOID ARTHRITIS PATIENTS

Community Medicine

Dr Arup Mahapatra* MD, PG- Cum -Tutor (Community Medicine), Department of Community Medicine Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha - 751024 *Corresponding Author

Dr Basanta Kumar Behera MD, Professor (Community Medicine), Department of Community Medicine, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha - 751024

Dr Bhaskar Thakur Ph.D, Asst. Professor (Statistics), Department of Community Medicine, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha - 751024

ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that affects mainly the small joints of the hands and feet. RA is one of the most common inflammatory joint diseases and causes premature mortality, disability and compromised quality of life. RA is widely prevalent throughout the world. RA affects approximately 1% of the adult population in general, but this percentage increases with age. Women suffer three times more often than men in rheumatoid arthritis.

The authors discuss one class of barriers in help seeking of RA which are due history of diseases and lifestyles which are high risk factors of RA.

Aims & Objectives: The aims and objectives of the study are to identify the time interval between onset of symptom and presentation to a health care provider (rheumatologist) among RA patients and to analyze delay in help seeking due to history of diseases and lifestyle of RA patients before seeing the doctor.

Materials & Methods: The study tool consisted of a predesigned pretested questionnaire. Data collected were fed in Microsoft Excel and the analysis was carried out using standard statistical software Stata 15.1.

Results: Majority of participants tried to delay consulting rheumatologist who had a history of diseases or lifestyles having high risk of developing RA. There was a significant association between menopause with treatment delay ($p \leq 0.05$).

Conclusion: The RA patients may be educated to promptly consult a rheumatologist if they have a history of diseases or adapting to lifestyles which has high risk to RA, because comorbid conditions can delay treatment outcome.

KEYWORDS

ACR, EULAR, GP, help seeking, rheumatologist

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that affects mainly the small joints of the hands and feet. RA is one of the most common inflammatory joint diseases and causes premature mortality, disability and compromised quality of life. RA is widely prevalent throughout the world[1-2].RA affects approximately 1% of the adult population in general, but this percentage increases with age. Women suffer three times more often than men in rheumatoid arthritis. The incidence of this chronic disease ranges between 0.1 and 0.3/1000. RA usually manifests between the ages 20 and 50, and is more prevalent amongst females, with a sex ratio ranging from 2:1 to 4:1[3,4].

The joints most commonly involved in RA are the wrists, small joints of the hands and feet. As the disease progresses, larger joints such as the ankles, knees, elbows, and shoulders frequently become affected. RA is a polyarthritis. Joint involvement is classically bilateral and symmetrical.

Risk factors leading to the development of RA include obesity, smoking, high red meat consumption, a previous blood transfusion and an adverse pregnancy outcome. Protective factors include the oral contraceptive pill and adequate fruit intake. The signs and symptoms of RA are weight loss, fever, fatigue, malaise, depression and severe cases of cachexia. They generate high degree of inflammation and may precede onset joint symptoms .Excess mortality is predominantly due to cardiovascular disease.

According to the European League Against Rheumatism (EULAR) recommendations from 2016, each patient with persistent swelling in at least one joint should be referred to a rheumatologist and examined within 6 weeks of the onset of symptoms, and effective treatment should be started by the end of the 12th week[5]. Rheumatoid arthritis usually requires lifelong treatment, including various medications, physical therapy, education, and possibly surgery. Treatment is aimed at relieving symptoms and preserving joint function[6].Starting treatment within 12 weeks of symptom onset doubles the chance of achieving remission, and the necessity to use biological medicinal products in RA treatment decreases from 32.2% to 10%[7].

OBJECTIVES

1. To identify the time interval between onset of symptom and presentation to a health care provider (rheumatologist) among RA patients.
2. To analyze delay in help seeking due to history of diseases and lifestyle of RA patients before seeing the doctor.

MATERIALS & METHODS

This hospital based cross sectional study was undertaken in the Department of Rheumatology KIMS, Bhubaneswar from December 2016 to October 2018. The study population was patients diagnosed as rheumatoid arthritis by a rheumatologist.

Sample size:

Considering the prevalence of help seeking behaviour as 31%[8] in Rheumatoid arthritis with 95% confidence level and the desired level of precision as 6% and 10% non-respondents, the optimum sample size calculated was 250.

The Inclusion criteria were patients aged 18 to 65 years diagnosed with early rheumatoid arthritis using 2010 American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) criteria.

The study tool consisted of a predesigned pretested questionnaire including details about a) Demographic profile (Age, sex, marital status, BMI and socio-economic status) b) Time interval between onset of symptoms and reported to a doctor and c) Questionnaire on history of diseases and lifestyle of RA patients before first visit to doctor and their association with delay in help seeking.

All the analysis was carried out by using standard statistical software Stata 15.1.

RESULTS

The study of medical help seeking behaviour Rheumatoid arthritis patients attending Rheumatology OPD in a tertiary care hospital-Bhubaneswar included the patients who attended the Rheumatology OPD & diagnosed clinically as early Rheumatoid arthritis. A total number of 250 Rheumatoid Arthritis patients enrolled in this study. The results are analyzed and presented as per the objective in the following tables.

TABLE-1: SOCIO-DEMOGRAPHIC PARAMETERS OF PARTICIPANTS						
Age (Mean Age in yrs)	Male		Female		Total	
	42.96±18.49	48.20±12.51			47.59±13.40	
Sex	Male N=29	% 11.60	Female N=221	% 88.40	Total N=250	
BMI	Obese N=94	% 37.6	Not-obese N=156	% 62.4	Total N=250	
Marital Status	Married N	%	Unmarried N	%	Widowed N	%
	227	90.80	22	8.80	1	0.40
Social Economic Status	N=0 Upper %	N=175Upper Middle %	N=44 Lower Middle %	N=27 Upper Lower %	N=04 Lower %	Total N
	0.00	70.00	17.60	10.80	1.60	250

Table -1, depicts the socio- demographic characteristics (Age, sex, marital status, BMI & Socio-economic status of the study participants.

Table-2 Time Interval Between Onset Of Symptoms & Reported To A Doctor						
SEX	N	%	TIME INTERVAL			
			≦ 6 weeks		.> 6 Weeks	
			N	%	N	%
MALE	29	11.6	6	2.4	23	9.2
FEMALE	221	88.4	25	10.0	196	78.4
TOTAL	250	100	31	12.4	219	87.6

Table -2, depicts the time interval in between the onset of symptoms and reported to a doctor. Only 2.4% of the patients who were male reported to doctor within 6 weeks of onset of RA symptoms and 10% of the patients who were female reported to doctor within 6 weeks of onset of RA symptoms.

TABLE-3 ASSOCIATION OF HISTORY OF DISEASES/LIFESTYLE WITH TREATMENT DELAY							
History of diseases/habits	Response	Delayed		Not Delayed		Total	P value
		N	%	N	%	N	
Trauma or injury to joint	Yes	26	96.43	1	3.57	27	0.314**
	No	193	86.49	30	13.51	223	
Obesity	Yes	84	89.36	10	10.64	94	0.512*
	No	135	86.54	21	13.46	156	
Sedentary Lifestyle	Yes	64	82.75	5	7.25	69	0.127*
	No	155	85.64	26	14.36	181	
Metabolic disease	Yes	14	82.35	3	17.65	27	0.451**
	No	205	87.98	28	12.02	223	
Hereditary disease	Yes	60	89.55	7	10.45	67	0.571*
	No	159	86.39	24	13.11	183	
Associative Connective tissue disorder	Yes	2	100.00	0	0.00	2	1.000**
	No	217	87.50	31	12.50	248	
Hyper-mobility/ laxity of joint	Yes	159	89.33	19	10.67	178	0.193*
	No	60	83.33	12	16.67	72	
Smoking/ Tobacco chewing	Yes	43	93.48	3	6.52	46	0.222**
	No	176	86.27	28	13.73	204	
Hemophilia/ Sickle cell	Yes	5	83.33	1	16.67	6	0.552**
	No	214	87.70	30	12.30	244	
Muscle weakness	Yes	2	40.00	3	60.00	5	0.657**
	No	217	88.57	28	11.43	245	
Kneeling practices / squatting habits of >2hrs/day / prolonged standing	Yes	186	87.32	27	12.68	213	1.000**
	No	33	89.19	4	10.81	37	
Hypothyroidism	Yes	42	82.35	9	17.65	51	0.203*
	No	177	88.94	22	11.06	199	
	Total	219	87.60	31	12.40	250	
Menopause(Female)	Yes	109	82.35	12	9.92	121	0.049*S
	No	87	85.27	13	14.73	100	
	Total	196	87.60	25	12.40	221	
***Pearson λ^2 test **Fisher's exact test S- Significant**							

Table-3 depicts history of diseases and lifestyle of RA patients before first visit to doctor and its association with delay in help seeking. History of Menopause was found to be statistically significant($p \leq 0.05$).

DISCUSSION

All the study participants are ≥ 18 yr of age. The mean age of the total study participants is 47.59±13.40 years, of which mean age of male is 42.96±18.49yrs & female participants is 48.20±12.51 yrs(Table-1). Similar study also reveals in their study that the participants having mean age of the was 46.5±9.2 years as reported by Resorlu H et al[9].

The age profile is very nearer to other studies as Simons et al had subjects with mean age are 58 yrs[10]. The study by Hussain W et al, shows in their study from symptoms to diagnosis: An Observational Study of the Journey of Rheumatoid Arthritis Patients in Saudi Arabia that the mean age of the study participants was 43.3±12.0 years[11].Out of the total study participants, female participants 221(88.40%) are more as comparable to male counterpart 29 (11.60%). The study by Hussain et al[11]participants notably, the majority of these patients were female (84.8%) was found in their study, which is quite similar to this current study . Similar kind of study participants -female (96%) & male (29%) were found in the study by Iversion et al[12].

Among the study participants maximum were found to be non-obese 156 (62.4%), whereas obese were found to be 94 (37.6%)(Table-1). The risk of development of rheumatoid arthritis (RA) could be affected by immune activation in obesity. Other two studies reported no statistically significant associations between BMI or BMI categories and RA. [13,14].

The results from the Nurses' Health Study indicated a stronger association between obesity and RA development at a younger age.[15] Maximum study participants were married (90.80%), unmarried (8.80%) and widowed (0.40%)(Table-1). Similar study participants also found in Hazes JMW et al[16] as married (79%), unmarried (16%) and widowed (5%).

In a study on Marital Status in Rheumatoid Arthritis by Lars Hellgren[17] reported that no significant differences in marital status was found among the rheumatoid arthritis.

Socio economic status was assessed based on income, education and occupation and divided patients into five groups as per revised Kuppuswamy and B G Prasad socio-economic scales for 2016 [18]. Most of the study participants belong to upper middle socioeconomic status (70%), followed by lower middle (17.60%) & lower class (1.60%). None of the study participant has attained upper socioeconomic status (Table-1).

Patient delay was defined as the period from the onset of symptoms to the time that help was sought from a healthcare professional who could prescribe disease modifying treatment. As according to the European League Against Rheumatism (EULAR) recommendations from 2016, each patient with persistent swelling in at least one joint should be referred to a rheumatologist and examined within 6 weeks of the onset of symptoms, and effective treatment should be started by the end of the 12th week[5].

Among these females 196 (78.4%) of them took >6 weeks of time to report to a doctor after the onset of symptoms as compared to males 23 (9.2%). Both in males and females in total 219 (87.6%) have took >6 weeks time to report to a doctor, whereas only 31(12.4%) have reported within <6weeks of onset of symptoms(Table-2). In a study by Raciborski F et al [19] reported that after the onset of symptoms of rheumatic disease, 28% of patients delayed seeing any doctor for 4 months or longer; 36% of patients waited 4 months or longer for a referral to a rheumatologist; majority of the patients (85%) made an appointment with a rheumatologist within a month of receiving a referral and 25% of patients waited 4 months or longer to see a rheumatologist. In an another study by Mota et al reported that a significant reduction in diagnostic delay, probably reflecting a stronger awareness of the importance of early diagnosis in North America and Europe which is not a reality in Latin America (LA). [20]. The study by Hussain W et al shows in their study on from Symptoms to Diagnosis: An Observational Study of the Journey of Rheumatoid Arthritis Patients in Saudi Arabia observed that the mean time from onset of symptoms to first physician visit was 6.2±5.5 months[21].

The study by Smolen JS et al reported that rapid attainment of the targeted end point is critical, and to achieve the treatment goal of remission or at least low disease activity within the time frame of 6 months[5]. Like any other disease, the RA patient's journey involves 3 distinct stages: onset of symptoms to consultation (lag1), consultation to rheumatology referral or definite RA diagnosis (lag2), and diagnosis to proper treatment (lag3). These lag times have been of interest to rheumatologists and have been reported by numerous studies[22,23] with some studies focusing specifically on the factors that contribute to these delays and measures undertaken to overcome these.

Patients with RA often do not seek the advice of rheumatologists at the onset of their symptoms and non-rheumatologists fail to refer RA patients to rheumatologists soon enough. In Saudi Arabia, although patients consulted with physicians at a mean of 7 months after the onset of RA symptoms, very few subjects initially sought a consultation with rheumatologists, who were ultimately responsible for diagnosing most RA patients[21].

Table-3, describes Association of history of disease and lifestyle with treatment delay. In rheumatoid arthritis (RA), the immune system, which usually fights infections, attacks the joints by error, making them swollen, stiff and aching: over time it can cause severe disability. In this study it shows that study participants those who got trauma or injury to joint have delayed in treatment (96.43%) than those who do not have any injury (86.49%),. Another study by Molina et al, shows similar findings as joint damage and physical disability due to incurring an additional barrier to care[24].

In this study we have also found that study participants those who have found to be history of obese (89.36%), having a hereditary disease (89.55%), associative connective tissue disorder (100%), hyper-mobility/laxity of joints (89.33%) have found to be in treatment delay as compared to those who don't have the following histories and found to be statistically not significant ($p>0.05$). The majority of studies indicate a positive association between obesity and RA in women, and in an analysis from the Nurses' Health Survey, the presence of obesity in women aged <55 years was a risk factor for RA[25].

Other factors associated with RA patients like metabolic disease (82.35%), smoking/tobacco chewing(93.48%), hypothyroidism and menopause ladies (82.35%) have found to be in treatment delay as compared to those who don't have the following histories. Menopause was found to be statistically significant ($p<0.05$). Other studies also reported that smoking and periodontal disease have been linked to development of mainly seropositive RA[26,27]. As RA is an immune mediated disease, probably modified by sex hormones, cigarette smoking might be a risk factor[28]. Study by Chan K et al also reported that smoking is one of the most important extrinsic risk factor of RA for its development and severity[29].In a study by Hazes JMW et al reported that 33% smokers and 23% of alcoholics were found in their study of lifestyle and rheumatoid arthritis[30].

Irreversible joint damage occurs during the early stages of rheumatoid arthritis (RA). Delays can occur at several levels including delay on the part of the patient in seeking medical advice at symptom onset, delay in obtaining an appointment with a healthcare professional and delays in referral to a rheumatologist, diagnosis and commencement of disease modifying therapy. Despite increased recognition of the benefits of early treatment there remains considerable delay between symptom onset and the initiation of treatment[31-35].

It has also observed that participants who have the history of kneeling practices/squatting habits of >2hrs/day/prolonged standing has treatment delay (87.32%) ($p>0.05$), whereas participants who do not have muscle weakness and haemophilia/sickle cell disease shows treatment delay (88.57% & 87.70%) as compared to those have history of these two factors ($p>0.05$). To date there have been no systematic reviews of help seeking behaviour in RA, however, syntheses of the qualitative literature regarding help seeking in other conditions have been illuminating[36].

Among the female study participants history of menopause leads to treatment delay (82.35%), whereas though the menopause did not delay their treatment 9.92% towards rheumatoid arthritis. On the other hand 87 (85.27%) female study participants without history of menopause still delayed the treatment, whereas 14.73% of female did not delay their treatment without the history of menopause. Low testosterone levels have been described in both women and men with RA, and a high incidence of RA is found during the peri- and postmenopausal period in women[37] suggesting that hormones and hormonal changes may influence pathogenesis and disease progression. Other study also reveals that early menopause history influence the risk of RA and in particular, early menopause was a robust risk factor for RA[38].

Lastly the history of hypothyroidism also plays an important role in rheumatoid arthritis and history of hypothyroidism leads delay in their treatment(82.35%) whereas 17.65% did not delay their treatment. Other study reported that the presence of thyroid disorders among RA patients was significantly associated with female sex ($P<.001$). Furthermore, RA patients with thyroid disorders had significantly poorer initial response to the RA treatment compared with patients with isolated RA[39].

The limitations of the study are that sample consisted mainly of participants from a particular area of coverage and men were relatively underrepresented (1 male for every 7.6 females) instead of normally observed 1:3 ratio in RA.

CONCLUSION:

The RA patients may be educated to promptly consult a rheumatologist if they have a history of diseases or adapting to lifestyles which has high risk to RA, because comorbid conditions can delay treatment outcome.

REFERENCES

1. Chatruvedi V, Ravindran V, Thabah M. Rheumatoid arthritis Module I Clinical Features & Diagnosis.

2. Text Book of Harrisson's principles of Internal Medicine. 18thedition Vol-2 2738-2751.
3. Schumacher HR, Jr. (Ed.). Primer on the Rheumatic Diseases, 9th edition, Atlanta GA: Arthritis Foundation; 1988.
4. Kelley WN, Harris ED, Ruddy S, Sledge CB. Textbook of rheumatology. W.S. Saunders Company, Philadelphia, 1997.
5. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017; 76: 960-977.
6. Elliott RA, Ross-Degnan D, Adams AS, Safran DG, Soumerai SB. Strategies for coping in a complex world: adherence behaviour among older adults with chronic illness. J Gen Intern Med. 2007; 22(6): 805–10.
7. Gremese E, Salaffi F, Bosello SL, et al. Very early rheumatoid arthritis as a predictor of remission: a multicenter real life prospective study. Ann Rheum Dis 2013; 22: 858-862.
8. Van der Linden MP, le Cessie S, Raza K et al Long-term impact of delay in assessment of patients with early arthritis. Arthritis Rheum 2010; 62:3537–3546.
9. Resorlu H , Sahin B , Ertekin H , BilimS & Savas Y. An assessment of marital adjustment in patients with rheumatoid arthritis. Med Glas (Zenica) 2017; 14(1):67-72.
10. Simons G, Mallen C D, Kumar K, Stack R J, and Raza K. A Qualitative Investigation of the Barriers to Help-seeking Among Members of the Public Presented with Symptoms of New-onset Rheumatoid Arthritis. The Journal of Rheumatology. 2015; 42: 4, 585-592.
11. Hussain W, Noorwali A, Janoudi N, Baamer M, Kebbi L, Mansafi H et al.From Symptoms to Diagnosis: An Observational Study of the Journey of Rheumatoid Arthritis Patients in Saudi Arabia. Oman Medical Journal 2016, 31: 29–34.
12. Iversen M D, Scanlon L, Frits M, Shadick N A ,and Sharby N. Perceptions of physical activity engagement among adults with rheumatoid arthritis and rheumatologists. Int J Clin Rheumtol. 2015; 10(2): 67–77.
13. Cerhan JR, Saag KG, Criswell LA, Merlino LA, Mikuls TR. Blood transfusion, alcohol use, and anthropometric risk factors for rheumatoid arthritis in older women. J Rheumatol. 2002; 29: 246–54.
14. Rodriguez LA, Tolosa LB, Ruigomez A, Johansson S, Wallander MA. Rheumatoid arthritis in UK primary care: incidence and prior morbidity. Scand J Rheum. 2009; 38: 173–7.
15. Lu B, Hiraki LT, Sparks JA, Malspeis S, Chen CY, Awosogba JA, Arkema EV, Costenbader KH, Karlson EW. Being overweight or obese and risk of developing rheumatoid arthritis among women: a prospective cohort study. Ann Rheum Dis. 2014; 73: 1914–22.
16. Hazes J M W, Dijkmans B A C, Vandenbroucke J P, Vries R R P de and Cats A.Lifestyle and the risk of rheumatoid arthritis: cigarette smoking and alcohol consumption. Annals of the Rheumatic Diseases 1990; 49: 980-982.
17. Hellgren L. Marital Status in Rheumatoid Arthritis. Acta Rheumatologica Scandinavica 1969; 15: 1-4.
18. Shaikh Z et al. Revised Kuppuswamy and B G Prasad socio-economic scales for 2016 Int J Community Med Public Health. 2017 Apr; 4(4): 997-999
19. Raciborski F, Kłak A, Kwiatkowska B, Batk B, Sochocka-Bykowska M et al. Diagnostic delays in rheumatic diseases with associated arthritis.Reumatologia 2017; 55(4): 169–176.
20. Mota LM H D, Brenol C V, Palominos P, and Pinheiro G D R C. Rheumatoid arthritis in Latin America: the importance of an early diagnosis.Clin Rheumatol. 2015; 34(Suppl 1): 29–44.
21. Hussain W, Noorwali A, Janoudi N, Baamer M, Kebbi L, Mansafi H et al.From Symptoms to Diagnosis: An Observational Study of the Journey of Rheumatoid Arthritis Patients in Saudi Arabia. Oman Medical Journal 2016; 31(1): 29–34.
22. Hernández-García C, Vargas E, Abásolo L et al Lag time between onset of symptoms and access to rheumatology care and DMARD therapy in a cohort of patients with rheumatoid arthritis.J Rheumatol 2000; 27: 2323–2328.
23. Rodriguez-Polanco E, Al Snih S, Kuo Y-F, Millán A, Rodriguez MA. Lag time between onset of symptoms and diagnosis in Venezuelan patients with rheumatoid arthritis. Rheumatol Int. 2011; 31(5): 657–665.
24. Molina E, del Rincon I, Restrepo JF, et al Association of socioeconomic status with treatment delays, disease activity, joint damage and disability in rheumatoid arthritis. Arthritis Care Res (Hoboken). 2015 July ; 67: 940–946.
25. Lu B, Hiraki LT, Sparks JA, Malspeis S, Chen CY, Awosogba JA, Arkema EV, Costenbader KH, Karlson EW. Being overweight or obese and risk of developing rheumatoid arthritis among women: a prospective cohort study. Ann Rheum Dis. 2014;73:1914–22.
26. Sugiyama D, Nishimura K, Tamaki K, Tsuji G, Nakazawa T, Morinobu A, Kumagai S. Impact of smoking as a risk factor for developing rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis. 2010;69:70–81.
27. Bingham 3rd CO, Moni M. Periodontal disease and rheumatoid arthritis: the evidence accumulates for complex pathobiologic interactions. Curr Opin Rheumatol. 2013;25:345–53.
28. Persellin R H. The effect of pregnancy on rheumatoid arthritis.BuU Rheum Dis 1976; 27: 922-6.
29. Chang K, Yang SM , Kim SH, Han KH, Park SJ, and Shin J II. Smoking and Rheumatoid Arthritis.Int J Mol Sci. 2014 Dec; 15(12): 22279–22295.
30. Hazes J M W, Dijkmans B A C, Vandenbroucke J P, Vries R R P de and Cats A.Lifestyle and the risk of rheumatoid arthritis: cigarette smoking and alcohol consumption. Annals of the Rheumatic Diseases 1990; 49: 980-982.
31. Hellgren L. Marital Status in Rheumatoid Arthritis. Acta Rheumatologica Scandinavica. 1969; 15, 1-4.
32. Rodriguez-Polanco E, Al Snih S, Kuo Y-F, Millán A, Rodriguez MA. Lag time between onset of symptoms and diagnosis in Venezuelan patients with rheumatoid arthritis. Rheumatol Int. 2011;31(5):657–665.
33. Feldman DE, Bernatsky S, Haggerty J, et al. Delay in consultation with specialists for persons with suspected new-onset rheumatoid arthritis: a population-based study. Arthritis Rheum 2007;57:1419-25.
34. Robinson PC, Taylor WJ. Time to treatment in rheumatoid arthritis: factors associated with time to treatment initiation and urgent triage assessment of general practitioner referrals. J Clin Rheumatol 2010;16:267-73.
35. Kiely P, Williams R, Walsh D, et al. Contemporary patterns of care and disease activity outcome in early rheumatoid arthritis: the ERAN cohort. Rheumatology (Oxford) 2009;48:57-60.
36. Smith LK, Pope C, Botha JL. Patients' help-seeking experiences and delay in cancer presentation: a qualitative synthesis. Lancet 2005;366:825-31.
37. Doran MF, Pond GR, Crowson CS, O'Fallon WM, Gabriel SE: Trends in incidence and mortality in rheumatoid arthritis in Rochester, Minnesota, over a forty-year period. Arthritis Rheum 2002, 46:625-631.
38. Pikwer M, Bergstrom U, Nilsson JA, Jacobsson L, Turesson C: Early menopause is an independent predictor of rheumatoid arthritis. Ann Rheum Dis 2012, 71:378-81.
39. Emamifar A, Hangaard J , Hansen I M J. Thyroid disorders in patients with newly diagnosed rheumatoid arthritis is associated with poor initial treatment response evaluated by disease activity score in 28 joints-C-reactive protein (DAS28-CRP) An observational cohort study. Medicine: 2017; 96:43.