Original Article

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Erythrocyte sedimentation rate as an indicator of compliance of rheumatoid arthritis patients: a case study in West Java, Indonesia

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Abstract

Rheumatoid arthritis (RA) is a systemic autoimmune disease which characterized by chronic inflammation. The medicines used to control inflammation. The compliance of the RA patients in medicines consumption can be assessed from the incidence of inflammation. The inflammation observed through erythrocyte sedimentation rate (ESR). The purpose of this study was to determine whether the ESR can be used as an indicator of compliance of RA patients in West Java, Indonesia. The subjects who participated in this study are patients who visit the private hospital or the community health centers in West Java, Indonesia. ESR was determined by the modified Westergren's method. The compliance was evaluated based on how subjects reported to have taken their prescribed medications. Subjects consisted of 36.66% of men and 63.63% of women. All patients received a combination of disease modifying anti-rheumatic drugs with non-steroidal anti-inflammatory drugs, and/or low dose corticosteroids. The compliance patients was 18.18% (ESR was 35.00 ± 17.80 mm/h), the non-compliant patients was 50.00% (ESR was ranging from 25 mm/h to 50 mm/h), and patients with uncomplete medications because of drug unavailability was 31.82% (ESR was 40.00 ± 9.57 mm/h). This ESR value is higher than the normal. Statistical analysis showed that there is no correlation between compliance and ESR for all RA patients (rho = -0.235, n = 22) and for patients with progressive RA (rho = - 0.134, n = 8), but there is a correlation between compliance and ESR for patients with non progressive RA (rho = -0.792, n = 8). This study concluded that the ESR can be used as an indicator of the compliance of patients with non-progressive RA.

Keyword: Increased ESR; RA monitoring; Compliance; Chronic patients

1. INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease which characterized by chronic inflammatory process[1]. The RA prevalence is 0.1-0.3% (1 per 1000-5000) in Indonesia[2] and 0.5-1.0% in the general population[3]. The major problems in RA patients are dependency, pain, disability, and affective disturbance[4,5]. This disease causes limited mobility and activities, even unidentified systemic symptoms can cause damaged organ. This disease also leads to some problems, such as pain, tiredness, and sleep disorders[6].

The purpose of RA therapy is to improve the life quality of patients by reducing joint pain and swelling, stiffness relief and joint damage prevention[6]. RA therapy in Indonesia use combination of disease modifying anti-rheumatic drugs (DMARDs) with non-steroidal anti-inflammatory drugs (NSAIDs) and/or low dose corticosteroids. The long-term treatment of RA need monitoring of toxic and therapeutic benefit for the treatment duration[7]. The patient compliance, i.e taking a particular drug as prescribed, determine the success of the RA therapy[8-10]. The risk of unnecessary changes in treatment and causes preventable morbidity, mortality, and loss of health care resources and productivity increases in non-compliant patients[8].

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Erythrocyte sedimentation rate (ESR) can be used for inflammatory monitoring in the RA patients routinely, although ESR is not an etiologic diagnosis. It is caused by ESR procedure is simple, practical, convenient, economical, point-of-care inspection, and has important clinical significance[11-13]. Inflammatory process or tissue damage in the body cause increased ESR[12]. To our knowledge, this is the first study in Indonesia, which providing a correlation between disease duration and ESR, disease duration and patient compliance, patient compliance and ESR. This research was conducted on the RA patients who visit the private hospital or the community health centers in West Java, Indonesia.

2. SUBJECTS AND METHODS

2.1. Subjects

The subject were divided into two groups, i.e healthy control subjects and RA patients. This study was conducted after agreed by the Health Research Ethics Committee of Dr. Hasan Sadikin Hospital, Indonesia.

2.1.1. Inclusion Criteria

a. RA patients are the patients who visit the private hospital or the community health centers in West Java, Indonesia.
b. RA patients who meet at least four the clinical criteria from 2010 RA classification criteria[14] based on the rheumatologist examination.
c. Patients age was over 18 years old.
d. RA patients willing to participate in the present study by signed the informed consent and interviewed.

2.1.2. Exclusion Criteria

a. Patients who do not cooperate, i.e. patients who do not want to have blood taken.
b. History of drug abuse, including alcoholism
c. Patients with any other major medical disorder, i.e. diabetes mellitus, hypertension, chronic obstructive pulmonary disease, acute or chronic liver disease, acute or chronic kidney disease, tuberculosis, and systemic lupus erythematosus.

2.2. Methods

2.2.1. Determination of Erythrocyte Sedimentation Rate

The blood was collected from May to July 2015. The blood was taken from a peripheral vein and placed in a tube with anticoagulant. The modified Westergren's method used to determine ESR[15]. ESR was measured using 200 mm long disposable Westergren tubes at room temperature (25 ± 1 °C). Red blood cell sedimentation in the vertical tubes was recorded at 60 min and expressed as mm/h.

2.2.2. Analysis of Patient Compliance in Drug Consumption

Compliance was evaluated on the basis of how respondents reported to have taken their prescribed medications. Patients divided into four groups: noncompliant, i.e (1) mostly did not take the medication, (2) took less/more than prescribed, (3) did not always take their medications as prescribed, and compliant, i.e (4) always took their medications as prescribed. Noncompliant patient were asked why they failed to consumed their medications as prescribed[16].

2.2.3. Statistical Analysis

Data are presented as mean±standard error of the mean (SEM). Comparative data from RA patients and healthy control subjects was conducted with R version 3.2.0. Patient's data, i.e. disease duration, compliance, and ESR were analyzed using Spearman's correlation.

3. RESULTS

3.1. Subjects

Total subjects were 22 healthy control subjects and 22 RA patients. All patients were interviewed about age, height, weight, drug therapy, and medical treatment to reduce the pain such as surgery. Anthropometric parameter comparison between RA patients and healthy control subjects were shown in Table 1.

Table 1. Anthropometric parameter comparison between RA patients and control

Parameter	RA patients		Controls	
	Mean ± SD	Range	Mean ± SD	Range
Age (years)	36.95 ± 13.54	15 - 57	33.32 ± 10.91	20 - 54
Sex (M/F)	8/14	-	9/13	-
Height (cm)	160.82 ± 0.05	154 - 170	158.95 ± 0.06	145 - 170
Weight (kg)	55.18 ± 6.76	42 - 65	52.73 ± 7.24	45 - 65
BMI (kg/m2)	21.31 ± 2.18	17.26 - 24.97	20.87 ± 2.52	14.88 - 24.44

Data were expressed as mean ± SEM.

In this study, the most incidence RA is in the range of 40-49 years old patients. The youngest RA patients was a 15-year-old female patient.

Thirteen patients (59.09%) have education for 10-12 years. This study was conducted in the district, there is a small number of universities. Many patients do not continue their education to a higher level.

The range of disease duration was 1-24 months and the average were 9.09 $\pm$ 6.43 months. These results indicate that RA is a chronic disease that must be treated continuously to maintain the quality of life of patients.

3.2. Determination of Erythrocyte Sedimentation Rate

ESR of RA patients was 36.25 $\pm$ 13.02 mm/h for men and 33.93 $\pm$ 10.77 mm/h for women. These values are higher than the normal, i.e. 16.24 $\pm$ 2.45 mm/h for women and 15.83 $\pm$ 2.57 mm/h for men.

3.3. Analysis of Patient Compliance in Drug Consumption

DMARDs given to patients with positive rheumatoid factor (RF). The patients from the community health centers have not checked their RF, so they are only given NSAIDs to reduce inflammation.

Patients were divided to compliance patients (18.18%), non-compliant patients (50.00%), and patients with uncomplete medications because of drug unavailability (31.82%) (Table 2). The reason of non-compliance included side effect (9.09%), fear of side effects (18.18%), and - the withdrawal of symptoms (22.73%).

3.4. Statistical Analysis

The correlation between disease duration and ESR have a *P*-value = 0.063 and rho = 0.404 (n = 22). The correlation between patient compliance and ESR have a *P*-value = 0.293 and rho = -0.235 for all RA patients (n = 22), *P*-value = 0.267 and rho = -0.134 for patients with progressive RA (n = 8), and *P*-value = 2.76 x 10^{-7} and rho = -0.792 for patients with non progressive RA (n = 8).

4. DISCUSSION

The subjects consisted of 22 patients, i.e. 8 of men (36.36%) and 14 of women (63.63%) (Table 1). Higher RA incidence in women due to hormones, especially estrogen. Estrogen is a factor which affecting the autoimmune diseases, such as RA[17-20]. In this study, RA incidence ratio is only 1:1.75. This is because patients, especially female patients, not realizing that the pain is not caused by a heavy workload or fatigue. We suggested that patients are less aware of the importance of early treatment of RA which can cause the joint damage[21, 22]. All patients in this study had painful experiences in small joint of the hands, wrists, elbows, knees, and ankles. This fact is consistent with joints that are generally affected by RA[7].

Table 2. Distribution of ESR based on patient compliance

Compliance level	Percentage of patients (%)	ESR range (mm/h)	ESR average (mm/h)
4	18.18	15-50	35.00 ± 17.80
3	27.27	25-40	28.00 ± 7.58
2	22.73	25-50	31.25 ± 12.50
1	9.09	40	40.00 ± 0.00
Drug unavailability	31.82	25-50	40.00 ± 9.57

Data were expressed as mean ± SEM.

In this study, RA distributed among all age ranges (Figure 1). This is consistent with the literature, that RA can affect all ages[21-23]. In Indonesia, RA is considered as an elderly disease. If your age is under 50 years old, so there will be a lack of awareness to health monitoring which caused by joint pain in the morning for minimal three months. Education affects the patient awareness to medical check up when something goes wrong in their bodies. The patients with higher education showed higher awareness to health monitoring (Table 3). It is observed from the decreased ESR in patients with a better education. The shortest of disease duration was 1 month and the longest one was 24 months. The common disease duration was 1-6 months (Figure 2) and the average was 9.09 $\pm$ 6.43 months. Although the distribution of disease duration is 1-6 months, but the majority of the RA patients (77.27%) had pain experience for at least 3 months, before medical checkup. It can cause retardation of the early treatment. The patients were visited the doctor after they cannot move normally. These facts showed that the patients had a lack of knowledge or awareness of RA. From the interview, we were known that the patient was suggested that the pain due to severe activities. So, to relieve the pain, they were taking the painkillers, such as mefenamic acid.

The modification of Westergren method was made by using ethylenediamine tetraacetic acid (EDTA) as an anticoagulant. EDTA is a solid-based anticoagulant which will reduce the errors of dilution (<1%)[24-26]. Increased ESR is useful for evaluation of various pathological conditions, such as RA[11, 27]. ESR indicates the presence of tissue damage or disease, but not its severity. This value was used to follow the progress of the diseased state or monitor the effectiveness of treatment. In this study, ESR of male patients was higher than female patients. This value indicates that inflammation is more severe in male patients than female patients. We suggested that male patients had a higher pain threshold.

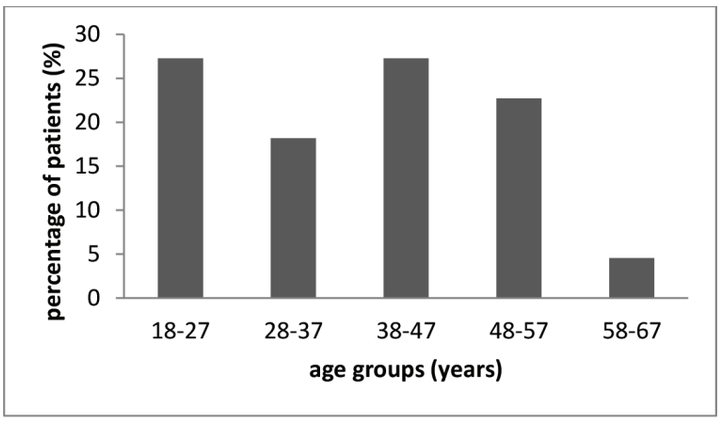

Figure 1. Distribution of patients among different age groups (n = 22)

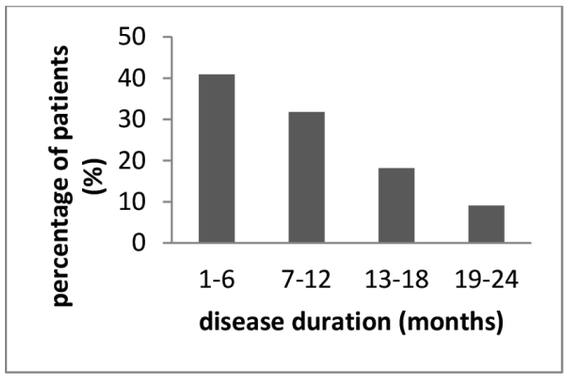

Figure 2. Distribution patients among different disease duration (n = 22)

Table 3. Distribution of ESR based on education duration

Education duration (years)	Percentage of patients (%)	ESR range (mm/h)	ESR average (mm/h)
1-6	9.09	25-50	37.50 ± 17.68
7-9	22.73	40-50	47.00 ± 4.47
10-12	59.09	15-50	31.54 ± 9.66
> 12	9.09	20-25	22.50 ± 3.54

Data were expressed as mean ± SEM.

Table 4 showed that only 36.36% of patients were given DMARDs therapy, i.e. patients RA with positive RF. DMARDs therapy aims to suppress the autoimmune reactivity[23]. The rest (63.63%) is not given DMARDs therapy, because they have not checked their RF yet. The RA patients without DMARDs therapy is a patient from the community health centers. The community health center is a health care facility that organizes public health efforts and the efforts of individual health first level, with more emphasis promotive and preventive efforts, to achieve the degree of public health the highest in its region[28]. If the patient's condition has not improved, then they referred to the hospital.

All RA patients (100%) treated with NSAIDs to reduce inflammation. Seventy-one point four three percent of RA patients from the community health centers treated with NSAIDs-corticosteroid combination. The side effects of corticosteroid is suppressing the immune system, so this side effects said gave benefit in RA therapy. Nine point nine percent of RA patients treated with NSAIDs combination, i.e. cyclooxigenase 2 (COX-2) selective NSAIDs (celecoxib and etoricoxib) and non-selective NSAIDs (meloxicam and piroxicam). COX-2 selective NSAIDs may reduce the NSAIDs side effects on the gastrointestinal tract and non-selective NSAIDs are used to reduce the treatment cost. Non-selective NSAIDs price is cheaper than the COX-2 selective NSAIDs. Paracetamol was used to reduce the pain.

The goal of appropriately and regularly therapy is to preserve the patient's life quality and maintain ESR around the normal value. All patients were felt the pain when they were late in medicine consumption. But, this incident does not make the patient compliance to have taken their prescribed medications. This is caused by the patients are customary with the pain, so their body was adapted and increase the pain threshold.

Table 4. Drug therapy in RA patients

Source of RA patients	RA therapy	Percentage of patients (%)
Private hospital	DMARDs-NSAIDs-corticosteroid	13.64
	DMARDs-NSAIDs	22.73
The community health center	NSAIDs combination	9.09
	NSAIDs-corticosteroid	45.45
	NSAIDs-paracetamol	9.09

Patient compliance was evaluated based on how the subjects reported to have taken their prescribed medications (Table 2). Patient compliance is very important to control chronic diseases[29] including RA. The non-compliant patients (68.18%) were likely older, retired, unemployed, less educated, and with lower income (Table 4). Mostly the non-compliance patients due to NSAIDs is not fully covered by insurance. So NSAIDs only consumed a portion of the prescribed. The patients have to buy the drugs beyond the insurance. It will be burdened to patients with lower income, so that the patient chooses not to consume the drug.

Spearman's correlation was chosen for statistical analysis, because of the non homogeneous distribution of the sample. There is no correlation between disease duration and ESR (rho = 0.404). The longest disease duration (24 months) has an ESR of 40 mm/h. This value (ESR = 40 mm/h) is also given by patients with short disease duration, i.e. 3 months. There is no correlation between disease duration and patient compliance (rho = 0.042). The longest disease duration (24 months) was the non-compliant patients. Long disease duration does not cause a patient to be compliant. From the interview, we found that the expense factor in the drug purchasing is the main reason for non-compliant patients in drug consumption. The patients not taking the drug if pain decreased, thus saving the expenses.

There is no correlation between patient compliance and ESR (rho = -0.235) for all RA patients (n = 22). The compliance does not guarantee a low ESR. The compliant patients with positive RF and progressive RA, make drugs can not decrease ESR, but only maintain the ESR. It is observed from patient medical records that the ESR range is in 45-50 mm/h and increased DMARDs doses can reduce the ESR. The compliance analysis was repeated for non-progressive RA patients. The result showed the correlation between patient compliance and ESR (rho = -0792) for patients with non-progressive RA (n = 8). Medical records of patient with nonprogressive RA showed that -compliance to drug consumption can maintain ESR values around the normal value. This study has some limitations, such as incomplete information from patient medical records and small sample size of respondents. The results of this study should be confirmed by a multicenter study.

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Conflict of interest disclosure

The authors declare no personal or professional conflicts of interest regarding any aspect of this study.

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