

Original Article

CORRELATION STUDY OF AGE, DISEASE DURATION, AND ERYTHROCYTE SEDIMENTATION RATE AMONG THE INDONESIAN RHEUMATOID ARTHRITIS PATIENTS

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ABSTRACT

Objective: The present study aims to determine the correlation between age, disease duration, and erythrocyte sedimentation rate (ESR) among the Indonesian rheumatoid arthritis (RA) patients.

Methods: The subject was the Indonesian RA patients and healthy control subjects. We were determined the correlation between age, disease duration, and ESR uses statistical analysis. The subjects who participated in the present study are patients who visit the Rheumatology clinic at one governmental hospital in Bandung City, Indonesia. ESR was determined by the modified Westergren's method. R software was conducted to data analysis.

Results: The number of subjects was 16.17% of men and 83.33% of women with the range from 20 to 77 y old. All patients received the combination of disease-modifying antirheumatic drugs, analgesic, and corticosteroid. The average of disease duration was 8.08±5.73 y. The experimental ESR of the RA patients was 22.50±12.23 mm/h for men and 31.75±15.03 mm/h for women. This value is only slightly higher than the normal value. We suggested that treatment with combination therapy can maintain the ESR.

Conclusion: Spearman's correlation showed that there is no correlation between age and disease duration ($\rho = 0.325$), between age and ESR ($\rho = -0.285$), and between disease duration and ESR ($\rho = 0.039$).

Keywords: Chronic patients, Increased ESR, RA monitoring, Westergren's methods.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease which characterized by the chronic inflammatory process. RA is associated with particular synovitis and periarticular osteopenia, which often associated with shortening of subchondral bone and joint margins [1]. Joint damage, malfunctions and defects have been reported in the progressive RA [2, 3]. It is important for early treatment and disease monitoring which effectively suppress the inflammatory process and prevents the bone and cartilage damage [4, 5]. The RA prevalence is range from 0.5% to 1.0% of the adult population worldwide [6]. The RA prevalence in Indonesia is range from 0.1% to 0.3% and the RA patients was 360,000 in 2009 [7].

The monitoring of an inflammatory process can be done with erythrocyte sedimentation rate (ESR) determination. ESR is not an etiologic diagnosis, but used in the clinic routinely. This is because of the ESR procedure is simple, convenient, economic, point-of-care inspection, and has important clinical significance [8-10]. Increased ESR indicates the inflammatory process or tissue damage in the body [9]. The RA patients have higher ESR than healthy people. To our knowledge, this is the first study providing a correlation between age and disease duration, between age and ESR, and between disease duration and ESR use a population of the RA patients in Rheumatology clinic at one governmental hospital in Bandung City, Indonesia.

MATERIALS AND METHODS

Subjects

The subject was divided into two groups, i.e. RA patients and healthy control subjects. The present study was conducted after approved by the Health Research Ethics Committee of Dr. Hasan Sadikin Hospital, Indonesia, No. LB.04.01/A05/EC/456/X/2014.

The inclusion criteria are

- RA patients are the patients of the Rheumatology clinic at one governmental hospital in Bandung City, Indonesia.

- RA patients who meet at least 4 the clinical criteria from 2010 RA classification criteria [11] based on the rheumatologist examination without serology examination.

- RA patients willing to participate in the present study by signed the informed consent and interviewed.

- Patient's age was over 18 y old.

The exclusion criteria are:

- Patients who do not cooperate.
- History of drug abuse, including alcoholism.
- 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.

Determination of erythrocyte sedimentation rate

The blood was collected from December 2014 to January 2015. The blood was taken from a peripheral vein and placed in a tube with ethylenediaminetetraacetic acid (EDTA) as an anticoagulant. All blood samples were mixed thoroughly immediately prior to testing. ESR was conducted with modified Westergren's method [12]. ESR was measured using 200 mm long disposable glass Westergren tubes at room temperature (25 ± 1 °C) and with blood at native hematocrit. Red blood cell sedimentation in the vertical tubes was recorded at 60 min and expressed as mm/h.

Statistical analysis

Data analysis was conducted with R software. The age, disease duration, and ESR of the RA patients were analyzed using Spearman's correlation.

RESULTS

Total subjects were 24 RA patients and 24 healthy control subjects. All patients were interviewed for age, how many joint with definite clinical synovitis (swelling), pain duration in the morning, disease

duration, drug therapy, ancestry, medical treatment to reduce the pain such as surgery, and quality of life. Anthropometric parameter

comparison between the RA patients and healthy control subjects was 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 (y)	43.13±13.23	20-77	32.33±10.95	20-54
Sex (M/F)	4/20	-	9/15	-
Height (cm)	157.96±0.05	150-170	158.67±0.06	145-170
Weight (kg)	56.17±8.45	36-75	52.50±7.06	45-65
BMI (kg/m ²)	22.51±3.26	16.00-28.44	20.85±2.49	14.88-24.44

Values are mean±SD (n=24)

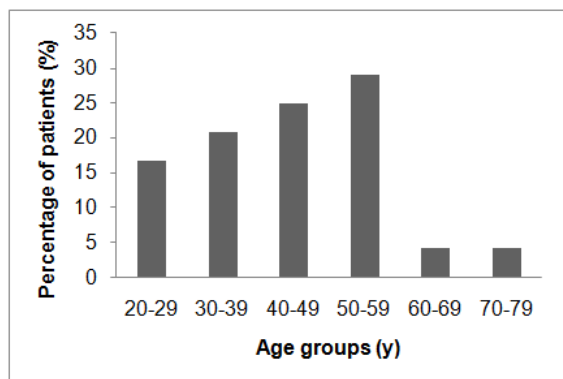


Fig. 1: Distribution of patients among different age groups (n = 24)

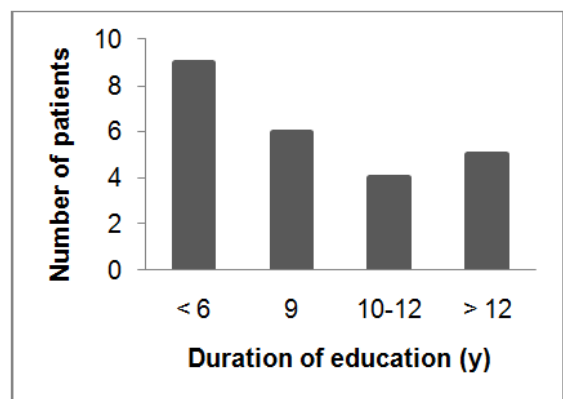


Fig. 2: Distribution of education duration among the patients (n = 24)

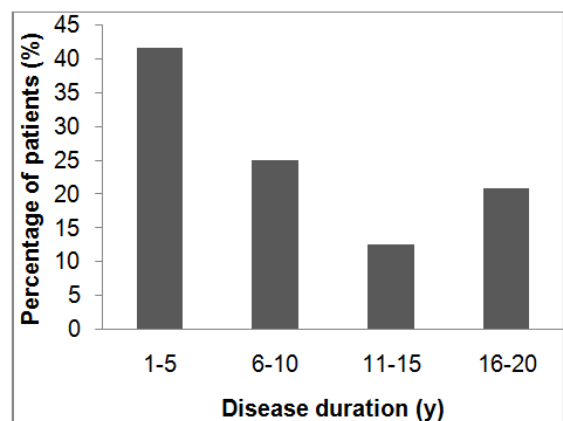


Fig. 3: Distribution patients among different disease duration (n = 24)

ESR of RA patients were 22.50±12.23 mm/h for men (n = 4) and 31.75±15.03 mm/h for women (n = 20). These values are higher than the normal, i.e. 15.24±2.15 mm/h for women (n = 15) and 12.08±2.35 mm/h for men (n = 9).

The correlation between age and disease duration has a *P-value* = 0.12 and $\rho = 0.325$. These values indicate that there is no correlation between age and disease duration. The correlation between age and ESR has a *P-value* = 0.18 and $\rho = -0.285$. These values indicate that there is no correlation between age and ESR. The correlation between disease duration and ESR have a *P-value* = 0.86 and $\rho = 0.039$. These values indicate that there is no correlation between disease duration and ESR.

DISCUSSION

The subjects consisted of 24 patients, i.e. 4 men (16.17%) and 20 women (83.33%). A study by Samanci *et al.* showed that the RA incidence in women (87.43%) is seven times higher than men [13]. In the present study, the RA incidence in women is five times higher than men. Higher RA incidence in women due to hormones, especially estrogen. Estrogen is a factor which affecting the autoimmune diseases, such as RA [14-17].

Higher RA incidence in women also caused by the sampling time, which done at 08:00 until 16:00. The sampling time corresponded to the Rheumatology clinic service time. We suggested that the men are still working at that time.

RA has a wide distribution and can affect all ages, but the most common is in the age of 40-50 y [18-20]. In the present study, the most incidence RA is in the range of 50-59 y old patients (Fig.1). Our result was different from the literature. We suggested that patients who visit the clinic for the treatment are less aware of the importance of early treatment of RA which can cause the joint damage [19, 20].

In Indonesia, RA is considered as an elderly disease, so when your age is under 50 y old, there will be lack of awareness to health monitoring which caused by joint pain in the morning for minimal three months. Thirty-seven point five percent of the subjects had an education up to 6 y, 25.00% had an education for 9 y, 16.67% had an education of 10 or 12 y, and 20.83% had more than 12 y of education (fig. 2). The patients with higher education showed higher awareness to health monitoring. Education affects the awareness of the patients to the medical checkup when something goes wrong in their bodies.

The shortest of disease duration was 1 y and the longest one was 20 y. The common disease duration was 1-5 y (fig. 3) and the average was 8.08±5.73 y. The majority of the subjects in this study (79.17%) had pain experience for at least 3 until 6 mo, 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 or diclofenac sodium.

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 [21]. All patients had joint stiffness that is worse in the morning. The stiffness duration directly associated with disease activity [21]. There were 8 patients who had a hand deformity. Hand deformity alters the mechanics of hand function, reducing grip strength and making it difficult to perform usual daily activity. All patients had pain experience in the knees. This incident was caused the subjects ability to walk is more slowly with shorter distance than healthy control subjects. There were 16.67% of patients who cannot climb the stairs. This is certainly interfering the patient activities. Twelve point five percent had had fluid suction of the knee joints to reduce pain due to swollen joints.

This study found that the youngest patients (20 y old) have been suffering for 10 y, i.e. from 10 y old. This patient had joint damage which can be observed from the damage of metacarpophalangeal and knee joint. This is due to lack of awareness of the patient's parents to recognize the RA symptoms in children and the difficulty to reach health facilities for patients who lived in outskirts where there is no rheumatologist.

Westergren method was chosen for ESR determination because of the procedure is simple, economical, and has a high accuracy [22]. The modification was made by using ethylenediaminetetraacetic acid (EDTA) as an anticoagulant. EDTA is a solid-based anticoagulant that does not cause significant dilution (<1%). It will reduce the errors of dilution [23-25]. Elevated ESR is useful for evaluation of various pathological conditions, such as RA [8, 26]. 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.

Increased ESR in RA patients showed nonspecific inflammation. In inflammatory process, the immune system releases the acute phase proteins, such as C-reactive protein, fibrinogen, immunoglobulin's, and acute phase cytokines, which causes the negative charge reduction in zeta potential on erythrocyte surfaces. So, erythrocytes are easier to form large aggregates known as rouleaux [8, 9, 27].

All patients who visit the Rheumatology clinic were treated with a combination of disease-modifying antirheumatic drugs (DMARDs), non steroidal anti inflammatory drugs (NSAIDs), and analgesic. Most patients (70.83%) were given DMARDs combination, i.e. methotrexate (MTX) and chloroquine (CQ). There are 20.81% of patients were given MTX, 4.17% of patients were given a combination of MTX and sulfasalazine, and 4.17% of patients were given a combination of MTX, CQ, and sulfasalazine. The DMARDs mechanism is to suppress the autoimmune reactivity [28]. All patients are treated with the analgesic (paracetamol) to reduce the pain and corticosteroids (methyl prednisolone) to reduce the MTX side effects [21]. 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 patient's are customary with the pain, so their body was adapted and increase the pain threshold.

Patient compliance was evaluated based on how the subjects reported to have taken their prescribed medications. Patients were divided into compliance patients (45.83%) and non-compliant patients (54.17%). The non-compliant patients was divided into the patients who mostly did not take the medication (8.33%), took less or more than prescribed (25.00%), and did not always take their medications as prescribed (20.83%). The reason of non-compliance included side effect (7.69%), fear of side effects (7.69%), the withdrawal of symptoms (15.38%), forgetting to take the medicines (23.08%), and drugs unavailability (46.15%). The non-compliant patients were likely older, retired, unemployed, less educated, and with lower income. Patient compliance is very important to control chronic diseases [29] including RA.

Most of the non-compliant patients due to MTX unavailability in hospital. In Indonesia, there is health insurance that covers the

medical expenses, including the medications. Because of poor drug management, the availability of certain medications sometimes does not convenient the requirement, so 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 drugs. Moreover, MTX is not available in all drugstores which visited by patients, so MTX is difficult to obtain. It is a challenge for the Indonesian government to improve drug management. So that patients are not aggrieved, because of drugs unavailability. Some limitations in this study were incomplete information from patient medical records and small sample size of respondents. The results of the current study should be confirmed by a multi center study.

Statistical analysis was performed using Spearman's correlation. This method was chosen because of the non homogeneous distribution of the sample. There is no correlation between age and disease duration ($\rho = 0.325$). The oldest patient was 77 y old female patients with 17 y of disease duration and the youngest patient is 20 y old male patients with 10 y of disease duration. This result is supported by the reference, which RA can occur in all ages [18]. There is no correlation between age and ESR ($\rho = -0.285$). The highest ESR (82 mm/h) was given by a 42 y old female patient. The oldest subjects in the present study, is a 77 y old female patients, had ESR = 18 mm/h. This value is close to normal ESR for women, i.e. $15.24 + 2.15$ mm/h. From the interview results, we found that the compliant patient who takes the prescribed medicines appropriately and regularly will have ESR around the normal value. These results are consistent with the goal of RA therapy with DMARDs, i.e. Inhibits the inflammatory process so there is no acute phase proteins can be released into the blood [28].

There is no correlation between disease duration and ESR ($\rho = 0.039$). The longest disease duration, i.e. 20 y, only gives ESR = 16 mm/h and the shortest one, i.e. 1 y, give ESR = 17 and 28 mm/h from two patients. These results are consistent with the results of correlation between age and the ESR. ESR can be used for monitoring the patient compliance of prescribed medications. Noncompliant patients had a higher ESR than the healthy control subjects. It is due to the acute phase proteins were released into the blood.

CONCLUSION

Spearman's correlation showed that there is no correlation between age and disease duration ($\rho = 0.325$), between age and ESR ($\rho = -0.285$), and between disease duration and ESR ($\rho = 0.039$).

CONFLICT OF INTERESTS

Declared None

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