Correlation of Uric Acid Levels and Rheumatoid Factor in the Elderly

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Abstract. Elderly people have dysfunctional changes in the immune system. Disease burden will increase due to uric acid particularly in elderly including arthritis. Rheumatoid factor (RF) is an examination that can identify the presence of rheumatoid arthritis. Reactive RF value in RA is 70%, while in people 65 years old is 20%. This research is to define the correlation between uric acid levels and rheumatoid factor in elderly. Methods use cross-sectional study; Participants: twenty-one elderly people. Measurements: whole blood and serum from elderly individuals, Accu Check, Antisera RF, Slide test. The research showed that normal uric acid levels with non-reactive RF were 15 people (93.8%) while with reactive RF was 1 person (6.3%). The results of uric acid levels increased with non-reactive RF were 2 people (40%) while with reactive RF was 3 people (60%). Uric acid levels and rheumatoid factor (RF) were analyzed using the Chi-square test. Both are interrelated ($p=0.028, P<0.05$). The conclusion of this research is that uric acid levels are correlated with rheumatoid factor in the elderly.

1. Introduction
The increasing age leads to the decreasing body immune. One cell playing important role in fortifying body immune system is lymphocyte cell. Aging will lead to a decrease of lymphoid tissue which in turn decreases body immune and finally cause vulnerability to cardiovascular disease, infection, inflammation, autoimmune, malignancies, and vaccination disorder.

Uric acid is end product purine metabolism. Each person has different uric acid level depending on age, gender, diet, physical characteristic, alcohol consumption, and renal function. Uric acid is also derived from dead cells [1]. Previous research concluded that cells experiencing apoptosis or necrosis could secrete DAMPs molecule like HMBG1, HSP, S100, uric acid, surfactant protein, beta-defensin, fibronectin, and others [2]. Blood uric acid level is the result of a balance between the amount to be produced and the amount to be secreted from the body. The decreasing renal function contributes significantly to hyperuricemia [3].

*Uric monosodium (MSU)* is crystal accumulated due to uric acid accumulations. MSU is a danger signal or Danger Associated Molecular patterns (DAMPs) which could create an immune response. MSU can be recognized by the immune system on myeloid ells like macrophage or dendrite hence...
inducing secretion of IL-1β cytokine and other pro-inflammation cytokines. Based on the previous research result, IL-1β is cytokine which can activate inflammasome.

The existing inflammasome activation process plays a role in autoinflammatory pathogenesis and another rheumatic inflammation disease like juvenile chronic arthritis, rheumatoid arthritis and gout [4].

Rheumatoid Factor (RF) is a prototype for rheumatoid arthritis and has a function for diagnostic and prognostic purposes. RF is also correlated with joint impairment [5]. Based on previous research, it was concluded that positive RF result or reactive RA result was more than 70% while in elderly aged 65 years old above was 20% 6 and for a healthy person was 1-5% [5]. RF is immunoglobulin reacting with Fc in IgG, typically in IgM form. RF IgM can be found in healthy elderly probably caused by immune system regulation. Positive RF prevalence in general increases along with aging [7].

Information about the correlation between uric acid level and RF in elderly remains partly understood hence research concerning with correlation between uric acid level and RF in elderly needs to be conducted.

2. Material And Methods
2.1. Research Methods
This research used a cross-sectional study design. Data collection was taken from laboratory test result on a uric acid level and RF in elderly. The sample in this research was 21 elderly, aged 60-70 years old who approved to contribute. Sample collection technique was performed by purposive sampling which inclusion criteria and agree to contribute. The exclusion criterion was elderly who had sick in the time of research. Data were analyzed by Chi-square test with α= 5%.

2.2. Research Instruments And Material
This research was used torniquete, needle, slide test, dropped pipette, digital uric acid examination device (Accu Check), macro-centrifugation, alcohol cotton, plaster, blood sample tube, reagent RF latex (PT. AIM), and uric acid stick (Accu Check).

2.3. Research Respondent Preparation
Elderly was provided with a consent form for participating in this research. After the consent provided blood was taken for sample and uric acid level and RF are examined.

2.4. Procedure
2.4.1. Uric Acid Test
Principle of Easy Touch instrument; when blood sample contacts sample target area of strip, blood will be automatically attracted into reaction zone of strip. Test result will be presented on screen few minutes later. Uric acid measurement stages are set the battery in and start the power on; previously set hour, date, and year in the instrument; check the expired date in the strip; check the instrument by inserting blue chip; if the “ERROR” appears on the screen it means error, if the “OK” appears on the screen it means the instrument was ready to use; within each uric acid strip bottle there was chip test; uric acid chip was used for uric acid test; on the screen number/code will appear identical with those in the strip bottle; after that blinking blood drop symbol will appear; the blood was contacted in the side margin of Easy Touch blood test instrument; contact the line part with arrow sign; blood directly infiltrates until the strip end and beep sound is heard; the result appears on screen after several seconds; strip was taken and removed; chip was stored again in the bottle after use and then be closed tightly (Acchu Check).

2.4.2. RF Test
RF is based on immunology reaction between IgG Latex binding and Rheumatoid Factor in patient’s serum. If the serum contained RF then the agglutination would result. RF measurement stage; let all reagent and serum reach room temperature before use; prepare slide, drop of RF-positive control
(50ul) on the first circle. A drop of negative control (50ul) on the second circle. Drop of the sample (50ul) on the third circle and so on; add a drop of RF latex reagent on each circle; stir thoroughly and shake the slide for 3 minutes and read the result in good light (PT Akurat Intan Madya, 2008).

## 3. Research Result

| Examination Name | RF Total | Uric Acid % | Significance Level |
|------------------|----------|-------------|--------------------|
| Normal           | 15       | 1           | 16                 |
| Hyperuricemia    | 93.8 %   | 6.3%        | 100%               |
|                  | 2        | 3           | 5                  |
|                  | 40%      | 60%         | 100%               |

Table 1. is data analysis result of SPSS 21 to identify the correlation between uric acid level and RF on elderly using Chi-square test with significance level of ($\alpha<0.05$). Based on the statistical test result, the correlation between uric acid level and RF in elderly obtained $p-value = 0.028$ ($p<0.05$) hence it can be concluded that correlation exists between uric acid level and RF in elderly.

The existing correlation between increasing uric acid level or hyperuricemia and RF due to uric acid is a danger signal which can generate an immune response. The increased uric acid is due to consumption of food or beverage with high purine. In addition, it can occur due to renal function disorder in secreting excessive uric acid in the blood. Other is obtained from tissue damage which generates uric acid accumulation in the blood. Tissue damage will increase along with the aging process. It occurs due to increased production and/or inadequate debris elimination process. The removed debris is due to damaged cell organelle or cell. The damaged organelle or cellular component, free radical from oxidative stress, metabolism remnants like extracellular ATP, lipid acid, uric crystal, ceramide, cardiolipin, amylin, succinate, per-oxidation lipid, and HMGB1 will be recognized as danger signal which triggers immune response necessary for physiological repair. However, as a result of accumulated damage, response to danger signal can be chronic [8].

Immune response occurred due to innate immune cells recognition in uric acid or MSU playing a role as danger signal or DAMPs [1]. As a consequence of the reaction, various pro-inflammation cytokine-like IL-1β, TNF-α, IL-6, IL-18 and IL-8 and others would result.

IL-1β is cytokine secreted by immune cell-like macrophage as result of reaction among MSUs which activate inflammasome NLRP3. The IL-β will cause neutrophil and mososit to penetrate the tissue leading to crystal accumulation which in turn causes inflammation. IL-β is cytokine which plays a role in RA disease pathophysiology. Based on previous research IL-1β was found in rat synovial that has been induced by arthritic collagen. IL1β can also induce auto-reactivity through several mechanisms. IL1β can play a role in renal tissue damage hence the renal cells produce monocyte chemotactic protein-1 (MCP-1). IL1β/IL1R signaling can influence response from the adaptive immune system and cause auto-reactivity from T cell [4].

IgM RF sometimes appears in healthy elderly. It is caused by the age factor which relates to immune system deregulation. RF can also appear as a result of immune response on inflammation and probably has a regulation effect on production immunoglobulin by controlling B cell activation. Positive rheumatoid factor prevalence is generally increased along with the aging [7].

Elderly experiences immune system change. The primary immune system change in aging is on T cell compartment where CD8+ memory T cell increases which previously was relatively not functioning. It was marked by the loss of surface markers like CD28 and CD27 and the rise of new surface marker like KLRG1. CD4+ T Cell population also experiences a similar change in CD8+ T cell but at a
different level. T reg population also increases along with the aging and Th17. B cell also experiences alteration with the aging process. The functional consequence of this change leads to decreased ability to fight new challenge. Clonally expansion, cytokine production, and specific antibody production are repressed. This situation causes increased infection, cancer and chronic diseases in the elderly. The increased characteristic inflammation mediator production from aging inflammation contributes to decreased adaptive immune response but it can reinforce innate immune response stimulation [9].

4. Conclusions
Based on statistic test result of the relationship between uric acid level and RF in elderly \( p = 0.028 \) (\( p<0.05 \)) is obtained hence it can be concluded that there is a relationship between uric acid level and RF on elderly.

5. References
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