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# CORRELATION BETWEEN DEGREE OF LEPROSY DISABILITY AND SERUM IL-6 LEVELS IN PATIENTS WITH LEPROSY REACTIONS: AN OBSERVATIONAL STUDY AT THE DONOROJO JEPARA LEPROSY HOSPITAL CENTER

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## ABSTRACT

**Background:** Leprosy is an infectious disease caused by *Mycobacterium leprae* bacteria which is still the focus of a global problem and causes disability in patients. The degree of disability in leprosy is assessed as mild and severe as a result of the inflammatory process. This study aims to determine the relationship between the degree of disability in leprosy and IL-6 serum levels as an inflammatory biomarker in leprosy patients. **Methods:** A Cross-sectional observational analytical study on leprosy patients aged 20-60 years, not pregnant, and undergoing treatment at Donorojo Jepara Hospital from March to April 2024. Serum IL-6 levels were analyzed using the ELISA method and tested for correlation with the degree of disability leprosy. **Results:** Statistical analysis of *Spearman's correlation rank test* shows a *p value = 0.279* and the results of the line pattern on the *Scatter dot graph* are not linear. **Conclusion:** There is no correlation between serum IL-6 levels and the degree of disability in leprosy patients at Donorojo Jepara Hospital.
***Keywords:*** *Degree of Disability in Leprosy, Leprosy, Serum IL-6*

## INTRODUCTION

Leprosy is a skin disease caused by infection of *Mycobacterium leprae* bacteria which often occurs in tropical areas such as Indonesia.[1] The number of leprosy cases in the world is still increasing by around 200,000 every year and Indonesia is one of the three countries with the highest leprosy cases.[2] Clinical symptoms that can appear range from skin lesions, impaired nerve function, ulcers, and disability, thus having a major impact on the patient's life.[3] This is the focus of *the World Health Organization* (WHO) to eliminate leprosy cases with one of its strategies being leprosy disability screening.[2,4]

Leprosy patients often come to health facilities with severe clinical symptoms, such as vision problems, ulcers, and even structural defects in the body.[2,5] WHO applies leprosy disability screening to patients who are first diagnosed with leprosy to then receive additional therapy according to their level of disability. There are three levels of leprosy disability, namely level "0" is categorized as mild and level "1-2" is severe. Those with leprosy in the severe category will receive additional *tapering-off steroid therapy* for 12-20 weeks.[1,4,6] Leprosy patients who experience this disability usually experience a leprosy reaction, which is an inflammatory episode with clinical symptoms that worsen the leprosy infection.[6,7]

Leprosy reactions are categorized as type 1 leprosy reactions/*Reversal reactions* (RR) and type 2 leprosy reaction/*Erytema Nodusum leprosum* (ENL).[7] Both immunopathological mechanisms are mediated by *T-helper-1* (Th-1) cells which produce various pro-inflammatory cytokines such as *Interleukin-2* (IL-2), IL-6, interferon, *Tumor necrotizing factor* (TNF) which then activate various inflammation pathways thus symptoms of a leprosy reaction appear.[6-8] One of the cytokines that plays an important role in showing the activation of this inflammatory mechanism is IL-6.[9] Previous studies have shown that the biomarker for detecting leprosy reactions is IL-6.[9-11] The cytokine IL-6 was chosen to be a biomarker of a leprosy reaction compared to other pro-inflammatory markers because of its important role in the immunopathology of leprosy and its complications in leprosy reactions.[10,12] IL-6 will then activate Th-17 differentiation which plays a role in tissue damage and the emergence of clinical leprosy reactions.[12,13] Signs of active inflammation and infection are also evidenced by increased levels of IL-6.[7,14] The three inflammatory pathways Nuclear factor kappa-B/NF-κB, Mitogen-activated protein kinase/MAPK, and Janus kinase-signal transducer and activator of

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transcription/JAK-STAT are also activated by IL-6 and these pathways also result in the production of cytokines, such as IL-6.[15] IL-6 levels have also been proven to be higher in leprosy reaction patients with severe leprosy disabilities compared to patients without leprosy reactions and mild disabilities.[11]

This study aims to determine the relationship between the degree of disability in leprosy and the serum IL-6 levels of leprosy reaction patients.

## METHODS

This study is a *cross-sectional observational analytical study* on leprosy reaction patients who underwent treatment at Donorojo Jepara Hospital from March to April 2024. The subjects of this study were 22 people with inclusion criteria: leprosy patients aged 20-60 years, not pregnant, and willing to take part in the research by signing *informed consent* (IC). The research data is the degree of disability in leprosy and the patient's *median cubital vein* blood serum which was taken when the patient agreed to IC. Serum IL-6 levels were analyzed using the ELISA method which was carried out in the GAKI laboratory, Faculty of Medicine, Diponegoro University, Semarang. Data on the degree of disability in leprosy were then analyzed for correlation with serum IL-6 levels using the *Spearman's correlation rank test* because the data distribution was not normal. Statistical analysis of data using computer application programs.

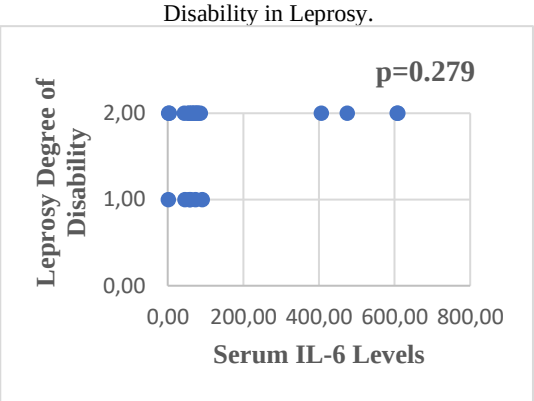
## RESULTS

**Table 1.** Characteristics of Research Subjects.

| Characteristics | Subject |
|---|---|
| **Gender, n(%)** | |
| - Male | 13(59.1) |
| - Female | 9(40.9) |
| **Age, n(%)** | |
| - 21-30 years old | 7(31.8) |
| - 31-40 years old | 2(9,1) |
| - 41-50 years old | 9(40.9) |
| - 51-60 years old | 4(18.2) |
| **Duration of illness in months, *mean* (min-max)** | 29(2 – 120) |

A total of 22 leprosy patients took part in this research with the dominant characteristics being an age range of 20-50 years and male gender. The duration of leprosy varies with an average of 29 months.

**Graph 1.** Correlation of Serum IL-6 Levels with Degree of Disability in Leprosy.




***Significant** $p<0.05$

The results of the statistical analysis of the correlation test of the degree of disability in leprosy with serum IL-6 levels showed a *p value of* $>0.05$ , so it can be concluded that there is no correlation between the two. The *scatter dot* graph does not show a straight line pattern, so it can be concluded that there is no linear relationship between IL-6 serum levels and the degree of disability in leprosy in this study.

## DISCUSSION

In accordance with the global epidemiology of leprosy where men are higher than women and adults are more likely to be diagnosed with leprosy than children.[16] The productive age group is more at risk of infection because of their high levels of work and social activity.[16,17] One study states that women are rarely diagnosed with leprosy because they have lower access to health facilities than men due to their greater activity, culture and social activities at home.[18] The average duration of leprosy is in accordance with several previous studies which stated that the average leprosy disease of research subjects was in the range of 12-48 months.[19]

Serum IL-6 levels can indicate an active inflammatory process. Previous studies in osteoarthritis patients showed high IL-6 serum levels compared to healthy patients.[20] Previous studies on leprosy stated that serum IL-6 levels in patients with leprosy reactions were higher than in patients without leprosy reactions.[11] A meta-analysis study stated that IL-6 is a potential marker for diagnosing leprosy reactions.[9] IL-6 is a pro-inflammatory cytokine produced by mononuclear phagocyte cells, vascular endothelium, or fibroblasts.[21] As a pro-inflammatory cytokine, IL-6 then activates three inflammatory

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pathways, namely Nuclear factor-kappa B/NF-κB, Mitogen-activated protein kinase/MAPK, and Janus kinase-signal transducer and activator of transcription/JAK-STAT.[15] In immunopathology of leprosy, IL-6 plays a role in triggering Th17 cell differentiation through the transcription factor ROR-γt in the JAK-STAT mechanism and plays an important role in the pathogenesis of leprosy reactions. Th17 also produces IL-17A, IL-17F, and IL-21 which play a role in tissue damage.[12]

The degree of disability in leprosy is assessed by the involvement of nerve damage, eye damage including visual impairment, and visible disability/deformity such as ulcers or claw deformity or foot deformities.[4,6] The immunopathology of leprosy disability begins with the immune response to leprosy infection and the complications that occur such as leprosy reactions. In the mechanism of these complications, there is a role of IL-6 as a pro-inflammatory.[7,9] An observational study showed significantly higher levels of IL-6 in the group of leprosy neuritis patients with nerve pain compared to leprosy neuritis patients without nerve pain, so this cytokine was concluded as a pain biomarker.[22] Another study also stated that IL-6 was increased in patients with nerve pain due to disc herniation and concluded that there was a link between IL-6 levels and chronic inflammation.[23.24] This nerve disorder or neuritis can lead to damage to the eyes and the appearance of ulcers on the skin lesions of leprosy patients.[6,7]

Serum IL-6 levels can also decrease or be suppressed due to anti-inflammatory therapy. Patients with leprosy reactions or with severe degrees of leprosy disability will be given steroid therapy in the form of prednisone along with antilepra MDT. [4] Steroids will work genomically or non-genomically in inhibiting the inflammatory process. Corticosteroids can work through their interaction with the Glucocorticoid receptor (GR) activating non-genomic mechanisms outside the cell nucleus and causing the activation of various anti-inflammatory proteins. The genomic mechanism mediated by GR is by inhibiting the transcription-translation process of the NF-kB element in the nucleus, thereby suppressing the production of various pro-inflammatory proteins that play a role in the NF-kB inflammatory pathway.[25]

## CONCLUSION

This study did not show a correlation between serum IL-6 levels and the degree of disability in leprosy reaction patients at Donorojo Jepara Hospital.

## ETHICAL APPROVAL

This research has received ethical approval by the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University with number 598/EC/KEPK/FK-UNDIP/XII/2023.

## CONFLICTS OF INTEREST

There is no *conflict of interest* in this research.

## FUNDING

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