

The differences in maternal and child health factors amongst leprosy patients in endemic and non-endemic areas



Flora Ramona Sigit Prakoeswa,^{1*} Faradiba Maharani,² Erlita Puspitasari,³
Muhammad Yulianto Listiawan,⁴ Anang Endaryanto,⁵
Cita Rosita Sigit Prakoeswa⁴

¹Dermatology and Venereology
Department, Faculty of Medicine,
Universitas Muhammadiyah Surakarta,
Indonesia.

²Faculty of Medicine, Universitas Sebelas
Maret, Surakarta, Indonesia.

³Department of Clinical Pathology, Dr.
Soetomo General Academic Hospital,
Surabaya, Indonesia.

⁴Department of Dermatology and
Venereology, Faculty of Medicine,
Universitas Airlangga/ Dr. Soetomo General
Academic Hospital, Surabaya, Indonesia.

⁵Department of Pediatric, Faculty of
Medicine, Universitas Airlangga / Dr.
Soetomo General Academic Hospital,
Surabaya, Indonesia.

*Corresponding to:
Flora Ramona Sigit Prakoeswa;
Dermatology and Venereology Department,
Faculty of Medicine, Universitas
Muhammadiyah Surakarta, Indonesia;
frsp291@ums.ac.id

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ABSTRACT

Introduction: Leprosy, a chronic infectious disease caused by *Mycobacterium leprae* infection arise new concern in pediatrics health problems. Total number of pediatric leprosy cases are hard to eliminate due to dominance of parenting and household position of mothers. In this study, we evaluated the roles of maternal and child health factors amongst leprosy patients in endemic and non-endemic areas.

Methods: Cross sectional study was conducted on Tuban Regency, East Java through interview guided by questioner on 106 pairs mother-child selected from local primary health center's registry data and selection through inclusion and exclusion criteria. Several parameters were analyzed: mother's age, children's age, gender of children, antenatal care, breastfeeding, and childbirth methods. Data were analyzed using ANOVA test.

Results: Statistically significant results were found in the age of mother ($p = 0.007$) and child ($p = 0.001$) with older ages observed in the population lived in the endemic area. Gender of children ($p = 0.997$), childbirth methods ($p = 0.172$), antenatal care ($p = 0.353$), and breastfeeding ($p = 0.507$) in this study showed insignificant results.

Conclusions: The differences in mothers and children ages are associated with leprosy among the population lived in leprosy endemic areas compared to the control group with delayed in diagnosis and long incubation period should be considered as factors contributed in this findings.

Keywords: children; endemic areas; leprosy; maternal.

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INTRODUCTION

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* which induce tissue and demyelinating lesions in the peripheral nerves.¹ *Mycobacterium leprae* infects macrophages, dendritic, and Schwann cells.¹ Although it slightly contributed to the death rate, leprosy cause various morbidity; varies from skin and peripheral nerves manifestation to tissue damage, deformity, disability, and stigma.² Due to its ability to cause complications, leprosy still considered a serious public health problem. Thus, the World Health Organization (WHO) has proposed the leprosy elimination program in 1991 to reduce the global prevalence of leprosy to less than one case per 10,000 population by the year 2000.³ Complex problem in leprosy transmission, play roles to the existed endemic areas left.

According to the latest WHO data in 2020, there were 177,175 registered cases of leprosy with a prevalence rate 22.7 per million population. India, Brazil, and Indonesia are three countries with the highest leprosy cases accounted for 80% global leprosy cases.⁴ In Indonesia, new leprosy cases reached 17,439 new cases with 1,121 among the new cases are with grade-2 disability (G2D), new cases of leprosy on female add up to 6,698 cases (38.41%) and 2,009 (11.52%) cases were pediatrics cases.⁴ East Java province holds the highest incidence of leprosy cases in the western part of Indonesia (Java and Sumatera Island) on 2019 with 2,940 cases and G2D rate 8.06 per million population, which female leprosy new cases reached up to 1,150 (39.12%) and pediatric cases 6.87% amongst total new cases registered. East Java has nine leprosy endemic cities/

districts where new cases constantly found, such as Tuban Regency.⁵

Data on distribution of leprosy patients showed men were more affected by leprosy than women. This difference in number possibly caused by underdiagnosis on female leprosy patients due to the sociocultural factors amongst women, such as limitation of mobility, low social status, and low education level.⁶ Previous study in Indonesia showed that female leprosy patients have been more affected due to stigma and discrimination towards leprosy disease.⁷ The position of women in the household also contributes to the increase risk of leprosy transmission to their child and the high incidence of leprosy amongst children. Child's populations tend to be the most vulnerable group to contract leprosy due to their immature immunity. Several factors contributes to the high leprosy rate

in pediatrics are delay in early diagnosis and difficulty in evaluating sensory loss in children.⁸

The improvement of the immune system performed gradually since the beginning of life start from perinatal health status which influenced by the environment. Antenatal care (ANC) was designed as a prenatal strategy to break transmission of any infection from mother to child by providing good health care such as preventing infection in pregnancy, providing good nutrition, minimalizing of drug using in pregnancy, choosing methods of childbirth delivery, and put an end to smoking habit or exposure to cigarette smoke.⁹ Exclusive breastfeeding in the early 6 months of live is beneficial for the development of child immune system and prevent malnutrition and infection, such as leprosy in children.¹⁰ Besides, the mother's bacterial load (acid-fast bacilli) is associated with the clinical form of the disease and portrayed the ability to spread and cause an infection.¹¹ Malnutrition, close contact, and the duration of contact with leprosy patients is a significant risk factors on leprosy.¹⁰

Population in endemic environment become more susceptible to leprosy due to proximity and close contact with person with the disease, especially patient with multibacillary (MB) type.¹² The risk to contract leprosy is nine times greater among household contacts with higher incidence observed among blood relatives in a nuclear family.¹³ Recent studies reported epidemiological data and factors related with pediatric leprosy cases and household contact, yet study about maternal with child leprosy cases not many reported.⁹ One of which, study by Duncan et al. reported thirty eight mothers with lepromatous leprosy (LL) and two babies within this group showed leprosy manifestation.¹⁴ Thus, this findings triggered the authors to conduct a study on maternal and child leprosy cases in endemic and non-endemic areas of leprosy in Indonesia and analyze the importance of maternal and child health factors to the susceptibility to contract leprosy.

MATERIALS AND METHOD

This observational analytic study with cross sectional design conducted in leprosy endemic and non-endemic villages, Tuban

Regency, East Java Province from March until June 2020. Tuban Regency with 173 leprosy cases in 2018, in which 43.35% cases were maternal leprosy and the leprosy cases amongst children accounted for 5.81% of the total cases, are considered one of the leprosy pockets.

Subjects of this study include pair of mothers and her child/children lives in endemic and non-endemic area. The inclusion criteria used for this study with leprosy group was individuals with confirmed diagnosis of leprosy, aged between 5-18 years old for children, and females in productive age around 20-49 years old. The exclusion criteria used were those with any leprosy reaction, diagnosed with inflammatory or autoimmune disorder, allergy, or infection other than leprosy, poor general condition, and pregnancy. All participants were given informed consent. Leprosy cases were selected from the local primary health center's registry data. Afterwards, to confirm the diagnosis, the subjects underwent clinical examination done by a dermatologist trained health and laboratory professional from Dr Soetomo General Hospital and Tropical Disease Centre of Airlangga University.

Subjects were divided into 5 groups as follows (Figure 1), group A were children with leprosy (L) and healthy mothers in endemic areas (H); group B are healthy children (H) and mothers with leprosy in endemic areas (L); group C are children with leprosy and mothers with leprosy in

endemic areas (L); group D are healthy children and healthy mothers in endemic areas (H); group E are healthy children and healthy mothers in non-endemic areas (H).

Research data were obtained by interview using questionnaire. Data were analyzed with SPSS® software (IBM Corp., Armonk, New York, USA). Descriptive statistics were done to present the data. ANOVA test was done to analyze the inter-group means comparison. A p-value of <0.05 was considered statistically significant.

RESULT

Data were obtained from 212 subjects, in which 38 were assigned to group A, 48 into group B, 6 into group C, 66 into group D, and 54 into group E. Subjects were pairs that composed of a mother and her child.

Table 1 and 2 shows the demographic characteristics of the child aged subjects and the mother. Gender of children distributed evenly throughout the groups with female as predominance gender observed in this study. Low antenatal care is observed in group C. Vaginal birth is the main childbirth methods in this study population. Breastfeeding coverage in the group C (mothers and their child with leprosy in endemic areas) also showed the least number of successes.

The statistical analysis (Table 3) showed statistically significant difference on almost all group on mothers and children

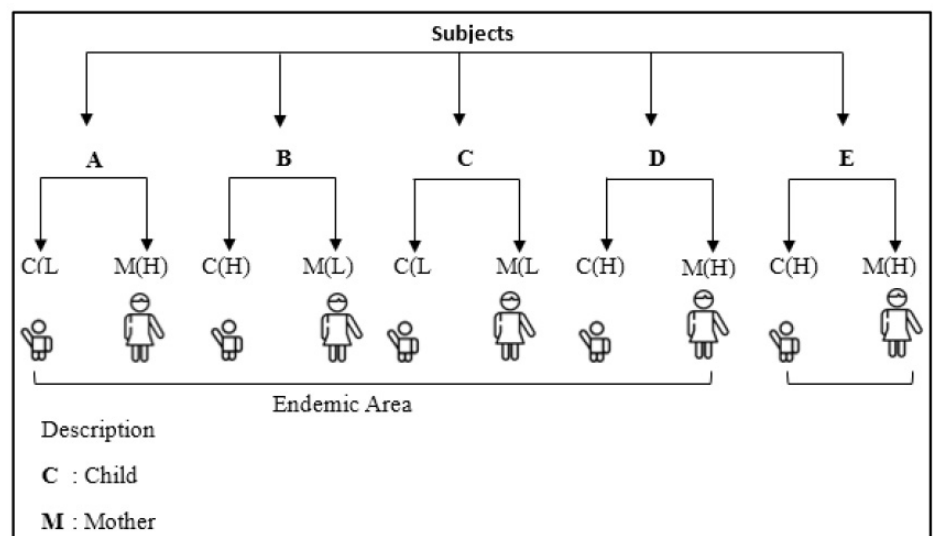


Figure 1. Schematic Figure of Group Allocation

age parameters, except for the comparison between group D (healthy populations of endemic areas) and group E (healthy population of non-endemic areas).

No significant difference found in other parameters in example gender of children, antenatal care, childbirth methods, and breastfeeding in all groups.

DISCUSSION

The significant difference observed in the age parameters, both on mothers ($p = 0.007$) and child populations ($p=0.001$).

Older ages observed in the average age of both populations in leprosy endemic areas. Our findings on children's age parameters are associated with previous studies that showed leprosy among children tends to occur in 5-14 years of age group. This higher frequency in older children could be caused by the long incubation period of leprosy (5-7 years), delay in diagnosis of early lesions, and adversities in assessing the sensory loss in younger children.¹⁵ Moreover, earlier study in Brazil supported our research finding and showed older ages of leprosy patients could be caused

by BCG immunization received in the first 2 month of life.¹³ BCG immunization administered in infancy are effective to induce protection against leprosy.¹⁶ The protective properties of BCG against *M. leprae* infection are mediated by antigen interaction contained in BCG vaccine, such as arabinogalactan and mycolic acid with specific *pattern recognition receptors* (PRR) such as *Toll-like Receptor 2* (TLR2) and *Toll-like Receptor 4* (TLR4) that has the ability to induce adaptive immune cells such as memory cells. BCG immunization was known to be able to induce 'trained immunity' or memory immune cells in innate immunity system.¹⁷ The mechanism used *Nucleotide-binding Oligomerization Domain-containing protein-2* (NOD2) on the macrophage with the increase of production rate of *Tumor Necrosis Factor- α* (TNF- α) and *Interleukin-6* (IL-6).¹⁸

Older ages observed in mothers population lived in leprosy endemic areas in this study may be associated with earlier study on China in 2015 that showed significant difference and higher number of cases observed in age 31-45 (34.3%) than age 15-30 (29.3%).¹⁹ Our findings also correlates with previous study that showed bimodal distribution of age with increased risk observed from age 5-15 years, peaked around 15 and 20 years, and the gradually increased of risk after age 30 years.²⁰ Other factors besides the long incubation period of *M. leprae* may contributes in this findings were the delay time to diagnose and get treatment in female populations are longer than male, the difference may take up around 4-6 months.²¹ Hormonal imbalance during pregnancy or puerperium might influenced to the disease.²¹ Unsignificant difference found between group D (healthy mothers and children) compared to control group showed endemicity of the area is not an associated factors in leprosy transmission.

Table 1. The average data of study population's age.

| Groups | Mothers Age (years) | Children Age (years) |
|--------|---------------------|----------------------|
| A | 44.74 \pm 7.37 | 16.00 \pm 3.38 |
| B | 42.12 \pm 7.78 | 12.38 \pm 5.17 |
| C | 44.67 \pm 3.51 | 18.33 \pm 0.57 |
| D | 38.42 \pm 7.88 | 11.67 \pm 4.11 |
| E | 36.74 \pm 5.66 | 9.69 \pm 3.70 |
| Total | 41.30 \pm 7.94 | 13.18 \pm 4.64 |

Table 2. Demographic characteristics of study populations.

| Variable | Total (%) | A (%) | B (%) | C (%) | D(%) | E (%) |
|--------------------|-----------|--------|-------|--------|-------|-------|
| Gender of Children | | | | | | |
| Male | 48.11 | 73.68 | 37.50 | 66.67 | 39.39 | 48.15 |
| Female | 51.89 | 26.32 | 62.50 | 33.33 | 60.61 | 51.85 |
| Antenatal Care | | | | | | |
| Yes | 70.75 | 63.16 | 70.83 | 33.33 | 72.73 | 77.78 |
| No | 29.25 | 36.84 | 29.17 | 66.67 | 37.50 | 22.22 |
| Childbirth Methods | | | | | | |
| Vaginal Birth | 91.51 | 100.00 | 87.50 | 100.00 | 93.94 | 85.19 |
| Caesarean Section | 8.49 | 0.00 | 12.50 | 0.00 | 6.06 | 14.81 |
| Breastfeeding | | | | | | |
| Yes | 88.68 | 84.21 | 95.83 | 66.67 | 90.91 | 85.19 |
| No | 11.32 | 15.79 | 4.17 | 33.33 | 9.09 | 14.81 |

Table 3. Statistically significant difference on almost all group.

| Parameters | A v. E | B v. E | C v. E | D v. E | (A+B+C+D) v. E |
|--------------------|-------------|-------------|-------------|-------------|----------------|
| Mothers Age | $P < 0.001$ | $P = 0.006$ | $P = 0.026$ | $P = 0.356$ | $P = 0.007$ |
| Children Age | $P < 0.001$ | $P = 0.036$ | $P < 0.001$ | $P = 0.057$ | $P = 0.001$ |
| Gender of Children | $P = 0.083$ | $P = 0.443$ | $P = 0.543$ | $P = 0.496$ | $P = 0.997$ |
| Antenatal Care | $P = 0.278$ | $P = 0.570$ | $P = 0.099$ | $P = 0.653$ | $P = 0.353$ |
| Childbirth Methods | $P = 0.079$ | $P = 0.811$ | $P = 0.474$ | $P = 0.261$ | $P = 0.172$ |
| Breastfeeding | $P = 0.928$ | $P = 0.202$ | $P = 0.414$ | $P = 0.492$ | $P = 0.507$ |

No significant difference found in antenatal care, childbirth methods, and breastfeeding parameters. Antenatal care was one of the prenatal strategies to prevent the dysregulation of child immune system by educating, providing, and evaluating nutritional status to the pregnant women since malnutrition on pregnancy affect the activation of (hypothalamic-pituitary) HPA axis, failure in maturation of immune competent cells, decreased transmission of IgG and other immune factors from mother to fetus, decrease T cell and B cell activity, failure differentiation of T cell, and decrease formation of lymphoid organs.⁹ The insignificant finding on antenatal care parameter may be due to the high coverage of antenatal care in Indonesia with complete four visitation reached up to 74.1% with best region observed in Java Island. Childbirth methods in this study found no significant results. Vaginal delivery was the dominant childbirth methods in this study populations. Previous study stated that vaginal delivery has several advantages including increase neutrophil chemotaxis, decreased neutrophil apoptosis, increased monocyte count, increased NK cell count, increased production of cytokine, and increased in microbiota diversity.⁹ This finding supports previous study that showed leprosy in young infants is transmitted due to exogenous infection from the mother through air during a short incubation period and do not prove the antenatal infection exists. Caesarean section could be suggested if there is another indication.²² Although breastfeeding is considered beneficial to fulfill the nutrition intake of the infants, possible transmission through direct contact with skin and the present of *M. leprae* in breast milk of mothers with leprosy infection need further investigation. The risk of acquiring leprosy infection in the breastfed infant through gastrointestinal tract remains uncertain and transmission by skin to skin contact between baby and the mother is more likely compared to the ingestion of breastmilk.²³

Gender of children with leprosy in this study were dominated with female. No statistically significant difference was found in this study. Previous studies showed various findings in the gender

distribution of leprosy pediatric patients. Study conducted in India by Rao (2009) showed male child are commonly affected than girls.²⁴ But this finding may not represent the true statistics due to neglectation of the female child conditions and higher mobility and opportunities for contact in male child. Meanwhile, Data from Brazilian Health Ministry in 2012, leprosy pediatric cases under 15 ages are evenly distributed.²⁵

CONCLUSION

The difference in mother's age and child's age are associated with leprosy among the population lived in leprosy endemic areas compared to the control group. Antenatal care, breastfeeding, childbirth methods, and gender of children showed no significant results compared to the control group. Therefore, further prospective studies about maternal and child health factors and other possible contributing factors such as long incubation period and delayed in diagnosis are needed to confirm our findings.

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ETHICAL CLEARANCE

This study was approved by the Health Research Committee of Dr Soetomo General Hospital, Surabaya (1664/KEPK/XI/2019).

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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AUTHORS CONTRIBUTION

The first, second, and third authors are responsible for writing and editing the

manuscript. The main idea is initiated by the first, fourth, fifth, and sixth authors. The manuscript supervised by fifth and sixth authors. The second and third authors analyzed the data. The first, third, and fourth authors involved in data findings.

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