JKKI: Jurnal Kedokteran dan Kesehatan Indonesia
Indonesian Journal of Medicine and Health
Journal homepage: https://journal.uii.ac.id/JKKI
P-ISSN 2085-4145 | E-ISSN 2527-2950

Intake of F-100 and honey as an effort to improve the nutritional status of children with pediatric tuberculosis

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Article Info:

Keywords: stunting, F-100, child nutrition, pediatric tuberculosis

Article History:

Received: August 13, 2022
Accepted: November 12, 2024
Online: December 27, 2024

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DOI: 10.20885/JKKI.Vol15.Iss3.art6

Original Article

ABSTRACT

Background: Stunting remains a significant nutritional challenge in Indonesia. If malnutrition in children is not addressed appropriately, it can lead to stunting. Children under five years old with pediatric tuberculosis (TB) are particularly susceptible to malnutrition. Specific interventions are needed to prevent stunting in this vulnerable group.
Objective: The study aimed to improve the nutritional status of children with pediatric TB to prevent stunting.
Methods: This study included 44 children under five years old with pediatric TB, who were patients at a private hospital and clinic. The subjects were divided into four groups of 10-12 children based on their arrival for treatment. Group A received standard medicine, F-100, and pure honey; Group B received standard medicine and F-100; Group C received standard medicine and pure honey; and Group D received only standard medicine. The F-100 and pure honey were administered once daily. Each group was followed up for six weeks. Weight and height were measured before and after the intervention. Statistical analysis was performed with a 95% confidence level.
Results: Administration of F-100 and/or honey significantly increased Z scores for height-for-age, weight-for-age, and weight-for-length/height between the pre-test and post-intervention ($p < 0.05$). Conversely, no significant improvement was observed in children receiving only standard medication ($p > 0.05$). The differences in Z score increases between groups, however, were not statisticallysignificant. Overall, the intervention reduced the prevalence of wasting (36.4% to 22.75%) and stunting (36.4% to 29.5%)
Conclusion: Supplementation with F-100 and honey improved nutritional outcomes but did not show statistically significant differences between groups. Further research is recommended to explore the effects of increased frequency and duration of supplementation.

INTRODUCTION

Childhood health plays a critical role in determining an individual's future well-being. Weight and height are key benchmarks for assessing child health. Certain diseases cause, such as pediatric tuberculosis (TB), can cause significant weight loss. Pediatric TB, a form of TB in children, is caused by infection from adults with active TB. TB remains a major health challenge in both Indonesia and the world. In 2021, there were 10.6 million new TB cases worldwide, resulting in 1.6 million deaths, and an estimated 1.7 billion people were latently infected. Indonesia ranks second after India in the global number of TB cases.1 Tuberculosis, caused by Mycobacterium tuberculosis, and the majority of infectious disease transmission sources is airborne.2 M. tuberculosis bacteria can be transmitted from one human to another through droplets when an active pulmonary TB sufferer coughs or sneezes.3 A person can become

infected by inhaling even a small number of these bacteria.[4]

Tuberculosis affects both adults and children aged 0-14 years. In 2021, there were 6 million cases in adult men, 3.4 million cases in adult women, and 1.2 million cases in children. The Indonesian Ministry of Health reported approximately 100,726 notified cases of pediatric TB in children under 15 years old in 2022, representing 14.5% of all TB cases in the country.[5] Diagnosing pediatric pulmonary TB is due to its non-specific symptoms, which resemble other condition such as pneumonia, viral or bacterial infections, malnutrition, and HIV.[6] About 50% of children with pulmonary TB are asymptomatic.[7] Diagnosis typically requires a combination of clinical symptoms, contact history with TB patients, radiological findings, nutritional assessments, and, when possible, bacteriological and tuberculin tests..[8]

Previous studies have shown that children under five with TB often experience malnutrition and underweight, which are correlated with the disease.[9] Tuberculosis can impairnutrient absorption in the digestive system, leading to weight loss. If this condition persists without adequate nutritional intervention, it can result in stunting[10]—a condition marked by impaired physical and mental growth.[10,11] Stunted or short stature or low length or height for age is utilized as a chronic malnutrition indicator describing the history of undernutrition in children below five years of age over a long time.[12,13] Short stature is defined if a child's height or length based on age and gender is below the 5th percentile of the standard anthropometric measure of nutrition for monitoring the growth and development of 6- to 24-month-old children using the length-for-age index from the reference standard of the World Health Organization (WHO) as a step to detect the status of stunting.[12] The short-term impact of such nutritional problem can include disruption of the brain development and intelligence, metabolic disorders, and physical growth disorders. Meanwhile, the long-term consequences may include a decrease in learning achievement and cognitive abilities as well as decreasing immunity.[14]

Stunting is a pressing nutritional issue both nationally and globally.[15] According to Riskesdas, the prevalence of stunting among children under five in Indonesia decreased from 37.2% in 2013 to 30.8% in 2018.[16] Despite this progress, further interventions are needed to achieve greater reductions and prevent recurrence. Children with stunting face a greater risk of contracting infectious diseases, stunted normal growth, and disrupted neurodevelopment, thus declining their cognitive functions, and as adults they will be more prone to chronic diseases.[17] Stunting affects stunted children's development both physically and cognitively as well as their growth.[18]

Stunting arises from multidimensional factors, including the nutritional and health status of the mother during pregnancy, conditions during infancy and toddlerhood, and the fetal period. Nutritional interventions are most effective when targeted at breastfeeding mothers, pregnant women, children aged 0-23 months, and children during their first 1,000 days of life.[19] Since 2022, the Indonesian Ministry of Health has focused on specific stunting interventions for children aged 6–23 months, emphasizing the importance of nutrition during early life.[20]

Providing high-nutrition Formula-100 (F-100) combined with honey has the potential to improve the nutritional status of children with pediatric TB. F-100, a food additive commonly used to treat malnutrition is rich in energy, fat, and protein, supplying essential nutrients.[21] Honey, is a natural liquid, a product of honey bees (*Apis sp.*) which has a sweet taste from *flora nectar* or other parts of plants.[22] Children who consume honey often exhibit increased energy, vitality, and resistance to infections.[23] Indonesian people use honey to increase the healing process of diseases and because it has bactericidal activity against pathogenic organisms.[16] This study aims to determine whether the administration of F-100 and pure honey can improve the nutritional status of of children under five with pediatric TB, thereby preventing stunting.

METHODS

Research design

This research was a true experimental study with a pre-test post-test control group design**.** The study was conducted between March and July 2021 in one private hospital and one private clinic in Yogyakarta.

Calculation of the sample size

The sample size referred to 5% α with Z α = 1,960), 80% β with Z β = 0.842, and standard deviation (SD) of 1. With the desired mean change of one, the number of samples obtained was 44 children. This number was summarized with a dropout estimation of 20% or 7 people. Therefore, the minimum number of samples was 41 people. The sample size was calculated using the sample size mean calculator formula from the sample-size.net website.

Research subjects

This study used a consecutive sampling method. Inclusion criteria included all patients registered as new or old cases from March to July 2021, who were willing to participate as evidenced by their parents signing informed consent. Participation were required to complete a minimum six-week participation period in selected private children's hospital and clinic, be aged one and five years, and have a tuberculosis diagnosis with a minimum score of 6 on the child tuberculosis assessment form.[8] Exclusion criteria included patients with other diseases or comorbidities, those with a history of allergies to honey or F-100 allergies, and participants unable to meet the minimum participation threshold. The number of subjects who were willing to take part in the research was 48 children, but four children were unable to participate in the study until the end. Therefore, the total number of subjects analyzed was 44 children (11 children in Group A, 12 children in Group B, 10 children in Group C, and 11 children in Group D).

Intervention

This study was conducted by grouping the research subjects randomly into four groups. They were grouped into four based on the order of patients' arrival. Group A was the group that received F-100 and pure honey, group B only received F-100, group C received honey, and Group D received no additional nutrition other than the medicine given. Every 100 ml of F-100 contains 4.2 g of lactose, 100 kcal (420 kJ) of energy, 5.9 mmol of potassium, 2.9 g of protein, 1.9 mmol of sodium, 0.73 mmol of magnesium, 0.25 mg of copper, and 2.3 mg of zinc. The protein energy percentage is 12% and the fat is 53% while the osmolarity of F-100 is 419 mOsm/L. A total of 19 g of F-100 was administered once a day. Honey was given once a day for one household tablespoon (approximately 5 mL). All the groups continued their regular daily diet and received standard medication from the same doctor. The intervention lasted six weeks for each participant. F-100 used in this study met WHO standards, ensuring its safety, while pure honey—a widely used and well-studied natural product—was also deemed safe. Body height was measured by using a stature meter (accuracy of up to 1 mm), and the body weight was measured by using a digital step scale GEA® (accuracy of up to 0.1 kg). The measurements of the body weight and body height were used for calculating the Z score for weight-for-age, weight-for-length or height, and length or height-for-age. The respective Z score values were calculated by using the application on https://sample-size.net/pediatric-growth.

Ethics

This study has gained ethical approval from the research ethics committee of the Faculty of Medicine of Universitas Islam Indonesia with the ethical clearance letter No. 22/Ka.Kom.Et/70/KE/II/2021.

Statistical analysis

The research results were then tested statistically with a 95% confidence level. The normality test used the Shapiro-Wilk test. The pre-test and post-test differences in the body weight, body weight-for-age, and body weight-for-length or height used the paired t-test, and the height-for-age differences were calculated by using the Wilcoxon test. The differences in the body weight, length or height-for-age, body weight-for-age, and body weight-for-length or height used the Kruskal-Wallis's test.

RESULTS

The average age of the respondents was 24.89 months, with an almost equal distribution of boys (21) and girls (23). The baseline nutritional indicators, including height-for-age, weight-for-age, and the weight-for-length/height Z scores, were below average across all groups. Before the interventions, the prevalence of wasting and stunting was 36.4% across all groups. After the six-week intervention, the incidence decreased to 22.7% for wasting and 29.5% for stunting, indicating a positive impact of F-100 and/or honey supplementation (Table 1).

Table 1. Characteristics of the subjects

Characteristics	Frequency (%)	Mean ± standard deviation	Min	Max
Sex				
Female	23 (52.3)			
Male	21 (47.7)			
Age (months)		24.89 ± 11.8	11	60
Z score				
Length/height-for-age		-1.51 ± 1.45	-4.23	3.86
Body weight-for-age		-2.37 ± 1.38	-5.31	1.87
Body weight-for-length/height		-1.69 ± 1.53	-5.23	-1.69
Children's nutritional status before treatment				
Wasting	36.4			
Stunting	36.4			
Children's nutritional status after treatment				
Wasting	22.7			
Stunting	29.5			

All groups exhibited significant increases in body weight from pre-treatment to post-treatment. The difference in the increase was the highest in the group given drug+F-100+honey and the drug+honey group. However, the difference in the body weight between the groups was not significant (Table 2).

Table 2. Measurement of body weight

Subject	N	Before treatment	After treatment	Difference	Paired t-test	Kruskal-Wallis's test
Drug+F-100+honey	11	9.51 ± 1.31	10.75 ± 1.57	1.23 ± 0.79	0.000	0.368
Drug+F-100	12	8.86 ± 1.42	9.63 ± 1.57	0.77 ± 0.45	0.000	
Drug+honey	10	11.01 ± 2.55	12.24 ± 2.13	1.23 ± 0.38	0.010	
Only Drug	11	9.95 ± 1.46	10.71 ± 1.4	076 ± 0.68	0.040	

The Z score of the height-for-age increased from the pretest to the posttest only in the group given drug+F-100+honey (p=0.010). However, the difference in the Z score of height-for-age between the groups was insignificant (0.000), and the p value of the drug+F-100 group was only 0.030 (Figure 1). The difference in the Z score of the weight-for-age between the groups was not significant (Figure 2). The Z score value for the body weight-for-length or weight-for-height increased from the pretest to the posttest only in the group given drug+F-100 (0.027). However, the difference in the height-for-age Z score between the groups was not significant (Figure 3).

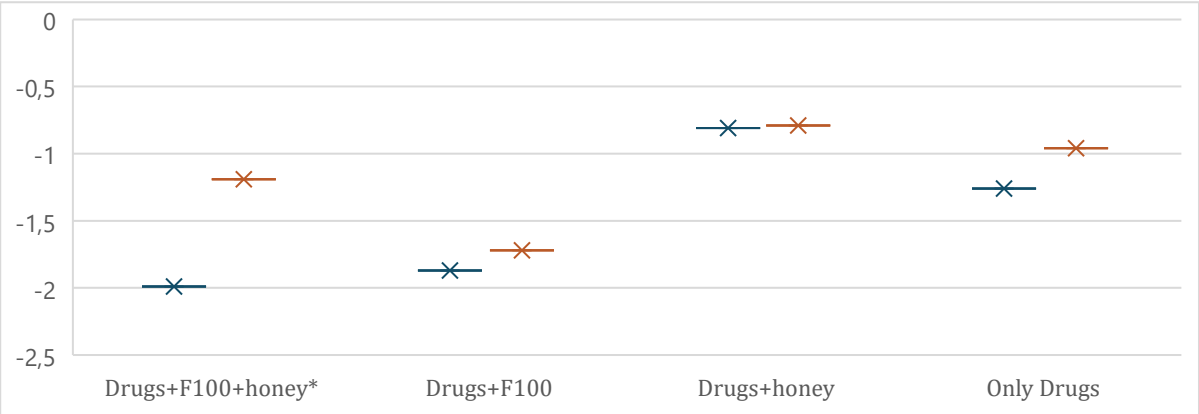

Figure 1. Z score of the length/height-for-age before (blue) and after (red) the treatment. Wilcoxon test; Drug+F-100+honey: p=0.013*; Drug+F-100: p=0.388; Drug+honey: p=0.508; Only drug: p=0.594; Kruskal-Wallis' test: 0.201

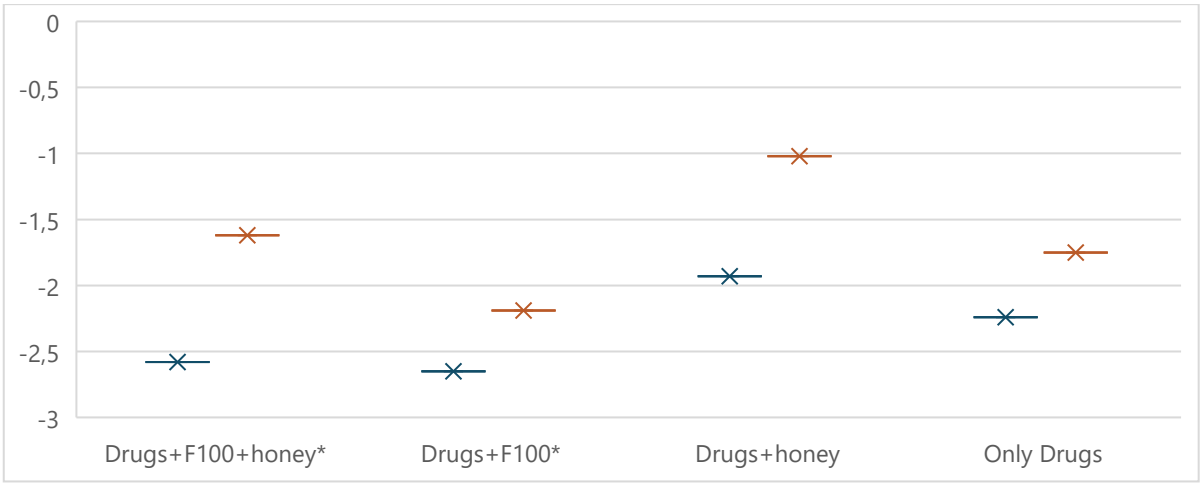

Figure 2. Z score of the body weight-for-age before (blue) and after (red) the treatment. Paired t-test; Drug+F-100+honey: p=0.003*; Drug+F-100: p=0.027*; Drug+honey: p=0.063; Only drug: p=0.086; Kruskal-Wallis' test: 0.389

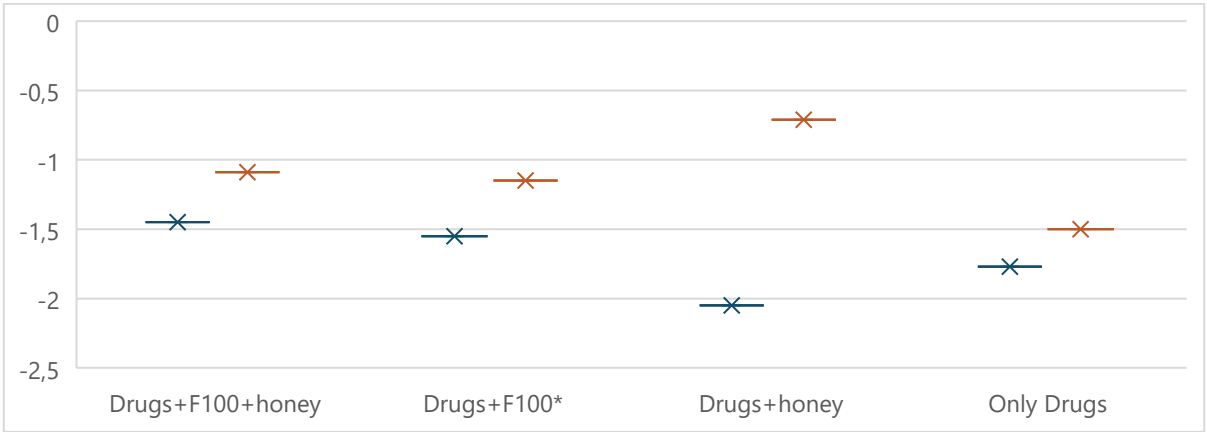

Figure 3. Z score of the body weight-for-length/height before (blue) and after (red) the treatment. Paired t-test; Drug+F-100+honey: p=0.432; Drug+F-100: p=0.027*; Drug+honey: p=0.062; Only drug: p=0.228; Kruskal-Wallis' test: 0.538

DISCUSSION

The results of the study indicate that administration of F-100 and honey has the potential

to enhance the nutritional status of children with TB. This aligns with previous research showing a significant influence of honey on improving the nutritional status of children with malnutrition, suggesting that healthcare providers can use honey to increase appetite and improve nutritional outcomes.[23] Similar findings have been reported by other researchers.[24] A study demonstrated that giving F-100 to children under five years old in South Tangerang Regency increased the Z score of the weight-for-age (W/A) and weight-for-height (W/H) indexes. This formula can serve as a complementary food to address acute malnutrition in children.[25] Additionally, consuming 5 ml of honey twice daily for eight weeks has been shown to improve the nutritional status of children under five.[26]

The findings of this study are consistent with those Mayangsari *et al.* who reported that that 63.08% of research subjects were categorized as having good adherence to F-100 consumption, which was significantly correlated with improvements in nutritional status.[27] This research aligns with Febriyanti *et al.* who highlighted challenges in program implementation, including differences in guideline adherence, parental roles, children's receptivity to food, and limited human resources.[28]

Similarly, Murwati reveals that there was an effect of F-100 on children's nutritional status in the work area of Sukoharjo Public Health Center (p=0.001).[29] This is further supported by Bintanah et al. in which F100 administration can improve the body weight of toddlers with malnutrition.[30] Although the research reports no effects of the presence of counseling on changes in the nutritional status of children aged less than five, there is an influence of F-100 consumption on changes in the malnutrition status of children under five. Consistent with this finding, a study by Froulina *et al*. shows the effects of mineral mix on the growth of severely malnourished children.[31]

Regarding the use of honey Harmiyati *et al.* found significant differences between intervention and control group in weight, height, z-score of weight-for-age, z-score of weight-for-height, and z-score of height-for-age with a p-value of <0.05. These findings suggestthat honey can significantly improve the nutritional status of malnourished children.[23] and is recommended for healthcare providers to enhance appetite and nutritional outcomes.

Similarly, Kholidah *et al.* concluded that F-100 can be an effective alternative in the diet therapy for for malnourished children during the rehabilitation stage.[32] Optimal nutritional status is crucia for child health, promoting growth and development while reducing mortality, morbidity, and disability.[33] Stunting in children under five years old can significantly influence their growth and development, including disturbing their stature and body weight, leading to shorter height and lower weight compared to their peers; such condition also causes walking delay and suboptimal development of their motor skills as well as impaired cognitive abilities, resulting in lower IQ levels compared to their cohort.[18]

Malnutrition, often initiated during pregnancy or infancy, becomes evident after the child turns two. The nutritional status of both the child and the mother plays an important role in child growth. The age between birth and 24 months becomes children's golden period that defines their quality of life. Any consequences of malnutrition during such sensitive period will be irreparable and permanent. During the golden period, it is imperative to fulfill nutritional requirements. Pediatric TB contributes to malnutrition by increasing metabolic demands and reducing appetite, which suppresses the immune system, prolongs illness, and delays recovery.[34] Based on the WHO guidelines, the nutrition management guidelines for TB patients include providing an adequate diet containing micronutrients and macronutrients which are very important for everyone, including TB patients. Children under 5 years old with pediatric TB generally experience malnutrition, and certain treatment is needed to prevent them from experiencing stunting. Indonesia's stunting rate exceeds that of several Southeast Asian nations, including Thailand (16%), Malaysia (17%), the Philippines (20%), and Vietnam (23%). According to WHO, Indonesia ranks fourth globally and second in Southeast Asia for the prevalence of stunted children under five years old.[21] Based on the age group of children under 5 years old, the highest stunting prevalence occurs to children aged 24-35 months old, at 42%. Meanwhile, based on gender, stunting occurs more often in boys (38.1%) compared to in girls (36.2%). The first

1000 days of a child's life is a crucial period where stunting may begin, leading to a long-term effect that can persist throughout the life cycle. Stunting in children is concerning as it is linked to a higher risk of morbidity and mortality, impaired development of the brain, delayed motor skills, and hindered mental growth. Non-optimal growth during the fetal period and/or during the first 1000 days of life has a long-term impact.[12]

Meanwhile, weight loss is caused by several factors including reduced food intake due to loss of appetite and decreased nutrients due to vomiting, diarrhea, nausea, abdominal pain, and metabolic changes.[35] In patients with pediatric TB, the presence of infection in the body causes continuous catabolism, making the energy formed from food intake difficult to support ideal growth. The severity of a disease and such other conditions as anemia can also worsen the problem. A change in TB patients' appetite is caused by an increase in the pro-inflammatory cytokines that directly affects the gastrointestinal tract including nausea and vomiting, reduces gastric motility, slows gastric emptying, modifies gastric acid secretion, and decreases intestinal motility. The indirect effects through the nervous system center occur in TB patients and interact with hormones and neurotransmitters that cause a decrease in intake.[36] Changes in the appetite in TB patients cause the daily nutritional needs of patients to be difficult to fulfill, thus worsening malnutrition in TB patients.

The intake of honey and F-100 is expected to meet patients' macronutrient and micronutrient needs by increasing the frequency and duration of administration to reach a significant amount. The main nutritional status of children is influenced by daily food consumption. In malnourished children, the nutrients consumed are insufficient or unable to fulfil the proper needs of the body. However, this study did not observe eating patterns, making it impossible to determine the adequacy of daily food intake. This limitation is supported by other studies demonstrating the positive effects of honey on toddlers' nutritional status.[37]

Further research should investigate the underlying causes of malnutrition in children with pediatric TB. Infections, extrapulmonary TB, or multidrug-resistant TB may contribute to malnutrition and require longer treatment or second-line therapy.[36] Expanding the sample size and scope of future studies will yield more meaningful results, since the limited number of the sample become one of our study's limitation. Additionally, the frequency and duration of F-100 and honey administration should be optimized for more significant impacts. Addressing these factors can improve the nutritional outcomes for children under five years old and help mitigate stunting in this vulnerable population.

CONCLUSION

The administration of F-100 and pure honey to pediatric TB patients, alongside standard drug treatment, resulted in significant improvements in Z-score values for body length/height-for-age between the pre-test and post-test assessments. Future research with a larger sample size and extended duration of administration is recommended to gain a more comprehensive understanding of the effects of F-100.

CONFLICT OF INTEREST

There are no conflicts of interest declared.

ACKNOWLEDGEMENTS

The authors would like to thank the Faculty of Medicine, Universitas Islam Indonesia for funding this research through the 2020 permanent lecturer grant scheme.

AUTHORS CONTRIBUTION

SM took part as the lead researcher, responsible for coordinating the overall research process. FJR took part as the research assistant, primary manuscript writer, data analyst, and correspondence coordinator, ABS took part as the research assistant and data collector.

LIST OF ABBREVIATIONS

TB: tuberculosis; *Riskesdas: Riset Kesehatan Dasar*; F-100: Formula-100; WHO: World Health Organization; TFC: Therapeutic feeding center; W/A: weight for age; W/H: weight for height; SSGI: *Survei Status Gizi Indonesia*

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