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Odds Ratio of Increase in Hemoglobin Level Associated with Consumption of Songgak Coffee in Patients with Pulmonary TB

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ABSTRACT

Pulmonary TB cases in Indonesia are the second highest in the world. The incidence of Anemia in pulmonary TB patients can be as high as 90%. Anemia can lead to poor outcomes in the recovery of pulmonary TB. Songgak coffee is a coffee with a mixture of spices that is commonly consumed by the people of Central Lombok to make the body healthy and increase vitality, including pulmonary TB patients. Songgak coffee is made from 7 types of spices mixed with coffee. The results of previous research show that Songgak coffee has quite good antioxidant content and is an immunostimulant. Antioxidants may increase Hemoglobin levels. This was a case-control study. A total of 26 new pulmonary TB patients were divided into 2 groups. Group A received songgak coffee as an additional anti-TB drug, while group B received anti-TB drug therapy alone. Hemoglobin levels in groups A and B were measured before drug administration and 14 days after treatment. The data collected were nominal data, reported as increasing and non-increasing. A total of 12 out of 13 patients in group A had an increase in Hemoglobin, while only 1 person in group B had an increase in Hemoglobin. The odds ratio value for increasing Hemoglobin levels in pulmonary TB patients who consume songgak is 12. The odds ratio value for increasing Hemoglobin in pulmonary TB patients taking songgak is 12. The odds ratio value for increasing Hemoglobin levels in pulmonary TB patients who take Songgak is 12 times higher than in pulmonary TB patients who do not take Songgak.

Keywords: Anemia; Hemoglobin; Odds ratio; Pulmonary TB; Songgak

INTRODUCTION

Tuberculosis (Tb) is a communicable disease that is a major cause of ill health and one of the leading causes of death worldwide. Tb is caused by the bacillus Mycobacterium tuberculosis, which is spread when people who are sick with Tb expel bacteria into the air. An estimated 10.6 million people (95% UI: 9.9–11 million) fell ill with TB worldwide in 2021, an increase of 4.5% from 10.1 million (95% UI 9.5–10.7 million) in 2020. The major contributors to the global increase between 2020 and 2021 were India, Indonesia and the Philippines.[1] In 2022, more than 724,000 new TB cases were discovered in Indonesia, and this will increase to 809,000 cases in 2023.[2] Based on data from "Satu Sehat NTB" in 2023, as many as 623 people with pulmonary TB were found and treated in Central Lombok Regency.[3]

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Anemia is very common in individuals with TB disease affecting more than 90% of patients in some studies. TB-related anemia is mostly caused by chronic inflammation characterized by increased levels of C-reactive protein and proinflammatory cytokines. Other causes include nutritional deficiencies, such as folate and vitamin B12 deficiencies, autoimmune hemolytic anemia, and fibrosis and bone marrow dysfunction.[4] Moderate or severe anemia in the early stages before anti-TB treatment is a significant risk factor for death.[5]

Research on medicinal plants and herbal medicine (Ristoja) conclusively identified over 4000 species of plant used by people in Indonesia until 2017. This herb has various benefits, including increasing vitality and eliminating aches and fatigue. The following plants are involved: *Helicteres isora* L., *Myristica fragrans* Houtt., *Piper retrofractum* Vahl., *Syzygium aromaticum* (L.) Merr. and *Piper nigrum* L.[6]

The Sasak people in Central Lombok have long been acquainted with and have utilised traditional herbal concoctions, commonly referred to as Songgak, which are typically consumed to enhance vitality. Within the Sasak cultural repertoire, there exists a wide array of Songgak, one notable example being Songgak coffee, which involves the infusion of seven distinct spices into coffee. The spices employed in the preparation of songgak coffee are herbs that are used to increase vitality and relieve aches and pains, including *Helicteres isora* L., *Myristica fragrans* Houtt., *Piper retrofractum* Vahl., *Syzygium aromaticum* (L.) Merr. and *Piper nigrum* L.[6] plus *Coriandrum sativum* L. and *Elaeocarpus grandiflora*. Songgak coffee is a beverage commonly consumed by the Sasak people for the purpose of enhancing vitality and alleviating aches and fatigue. The popularity of this beverage within the Sasak community suggests a potential for its consumption by individuals diagnosed with pulmonary tuberculosis in Central Lombok Regency.

Phenolic and flavonoid compounds represent the primary bioactive constituents in plants, which are frequently documented to exhibit antioxidant properties.[7] The assessment of antioxidant activity can be facilitated by the use of various methods, including 2,2′-diphenyl-2-picrylhydrazyl (DPPH).[8,9], Trolox equivalent antioxidant capacity (TEAC), and ferric reducing antioxidant power (FRAP) assay.[10] Previous studies have utilised the DPPH, TEAC and FRAP methods to measure total phenolic content (TPC), total flavonoid content (TFC) and antioxidant activity in water and ethanol extracts of Songgak coffee and its constituent ingredients. The correlation between TPC, TFC and antioxidant activity was determined using principal component analysis (PCA). The plot demonstrates that TPC and TFC are strongly diminished by the antioxidant activity (FRAP method) of songgak coffee and its constituent spices. The results obtained from this study suggest that the presence of flavonoids and phenolic compounds in seven herbal medicinal plants is responsible for the antioxidant properties of songgak coffee.[11]

It has been demonstrated that certain phytochemicals or herbs can exert a direct effect on the resolution of Anemia, while others exhibit a pleiotropic effect through their antioxidant activity. This may be achieved by increasing oxidative stress resistance or by initiating cellular mechanisms, such as autophagy. Other phytochemicals have been shown to target inflammation in the elderly population, thereby reducing the Anemia associated with chronic inflammation.[12]

Oxidation can occur in hemoglobin.[13] Various reports convey the benefits of antioxidants in improving red blood cells and hemoglobin levels. Some phytochemicals or herbs act directly to induce the resolution of anemia, and others act pleiotropically through their antioxidant activity, by increasing oxidative stress resistance or by triggering cellular mechanisms, such as autophagy, or, for example, by targeting inflammation in the elderly population and subsequently reducing the anemia associated with

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chronic inflammation.[14] The antioxidants in apple cider vinegar can have a positive impact on preventing hemolytic anemia in experimental animals that are induced by phenylhydrazine.[15] Research by Balushi et al, reported that various antioxidant mechanisms can improve erythrocyte cell morphology in sickle cell anemia.[16]

The odds ratio is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur in response to a particular exposure, in comparison to the odds of that outcome occurring in the absence of that exposure. Odds ratios are most commonly used in case-control studies; however, they can also be used in cross-sectional and cohort study designs.[17] This study aims to determine the benefits of songgak consumption on hemoglobin levels in pulmonary TB sufferers.

METHODS

Preparation of Songgak Coffee

The spices utilized in the production of songgak coffee are meticulously measured according to the prescribed composition. These ingredients are then subjected to a roasting process, employing an earthenware vessel on a wood-burning stove, until they reach the desired level of cooking. Subsequent to this, the roasted ingredients are ground and sieved using traditional techniques. The finely ground songgak spices are then mixed with coffee powder in the prescribed ratio.

The consumption of songgak coffee is achieved by brewing one teaspoon of the mixture with hot water, and sugar may be added according to taste.

Respondents

The respondents were new pulmonary TB patients who were about to receive treatment at Sengkol Health Centre and Kute Health Centre. The recommended number of samples for regression research is ≥ 25.[18] The total number of respondents was 26, who were divided into two groups: group A and group B. Group A was given songgak coffee in addition to anti-TB drugs, while group B was given anti-TB drug therapy only. Group A was selected based on habits or knowledge about songgak coffee, with members of this group required to have either known about songgak coffee or to have consumed it previously.

Treatment of respondents

This is a case-control study. To measure the odds ratio, data from 2 groups with a nominal data scale are needed.[19] In this study, we will examine the odds ratio of songgak coffee for increasing Hemoglobin levels in new pulmonary TB patients receiving first-line therapy. On the first day, when the patient with pulmonary tuberculosis arrived at the health center to receive anti-TB drugs, venous blood was drawn for the purpose of conducting a Hemoglobin and MCV test. Group A was administered anti-TB drugs and instructed to consume songgak coffee for a period of 14 days. Group B was administered anti-TB drugs according to the prescribed dose. After a period of 14 days, a second venous blood sample was collected from the respondents for further analysis, encompassing the measurement of hemoglobin and the MCV value.

The conduct of this research has been approved by the Research Ethics Committee of Poltekkes Kemenkes Mataram with the registration number DP.04.03/F.XLVIII.14/300/2024.

Measurement of Hemoglobin levels and MCV values

A complete blood test was conducted, comprising measurements of hemoglobin and mean corpuscular volume (MCV). The concentration of Hemoglobin was determined using a hematology analyzer (Mindray B20S). The examination procedure was conducted in accordance with the specifications of the instrumentation employed.

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Data analysis

Data analysis was odds ratio[20], with hemoglobin data collected twice from both groups, before treatment (day 1) and after 14 days of treatment (day 14). Both day 1 and day 14 hemoglobin data were compared and coded to obtain nominal data in increased and unincreased hemoglobin levels. Data were reported as "increased" if the hemoglobin level on day 14 was higher than on day 1. If hemoglobin on day 14 was equal to or lower than day 1, data were recorded as "unincreased". The nominal data were entered into a table, and the odds ratio was calculated according to the formula below:

$$Odds\ ratio\ value = \frac{(\frac{A\ increased}{A\ total})}{(\frac{B\ Increased}{B\ total})}$$

Note:

A increased	:	Total number of samples with increase in Hemoglobin level in group A
A total	:	Total sample in group A
B increased	:	Total number of samples with increase in Hemoglobin level in group B
B total	:	Total sample in group A

RESULTS AND DISCUSSION

Anemia is identified based on hemoglobin levels, in men below 13 mg/dl and in women less than 12 mg/dl.[21] A total of 13 out of 26 respondents experienced anemia (Table 1). Of the 13 people who experienced anemia, 6 of them were microcytic anemia characterized by MCV values below normal, while the other 7 people had normal MCV and MCH values (Table 2).

Table 1. Characteristic of respondent

	Normal	Anemia	Total
Group A	5	8	13
Group B	8	5	13
Total	13	13	26

Table 2. MCV levels in respondents with anemia

	MCV <80 (Micrositic)	MCV ≥80 (Normositic)
Group A	4	4
Group B	2	3

Anemia is very common in active TB cases.[22] The most frequent form is normochromic normocytic anemia[23] followed by microcytic anemia[24]. Microcytic features in anemia are often caused by iron deficiency and inflammation. Normocytic anemia can also be caused by inflammatory anemia.[25]

After 14 days, there was an increase in hemoglobin levels of 12 people in the group A (Figure 1) and 1 person in the group B (Figure 2).

The odds ratio was calculated by entering the data in table 4.

Table 3. Number of respondent with increased and unincreased hemoglobin levels in the group A and the group B

	Increased	Unincreased	Total
Group A	12	1	13
Group B	1	12	13

The odds ratio of increased Hemoglobin levels in group A was 12.nemia that occurs in patients with pulmonary TB is generally an inflammatory anemia.[26] Inflammatory disorders limit the absorption of iron from food due to increased levels of hepcidin in the circulation. Hepcidin is a liver peptide hormone in circulation. Inflammation leads to increased expression of hepcidin thus causing dysregulation of body iron levels.[27] Changes in body iron levels can result in chronic and acute iron deficiency, causing anemia. Inhibitors and antagonists of hepcidin play an important role in correcting inflammation-related anemia. Modulation of hepcidin with siRNA, antibodies, chemical compounds, and plant extracts provides new insights to develop advanced therapies for iron-related disorders.[28] A Songgak-making spice ingredient that has been reported as a

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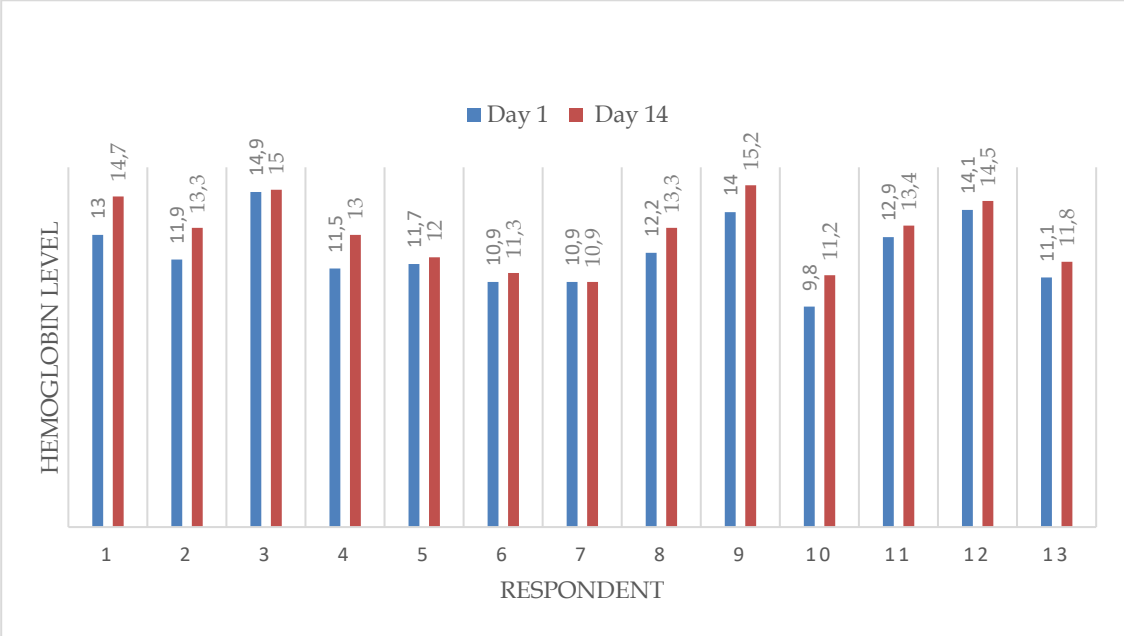

Figure 1. The hemoglobin level of group A

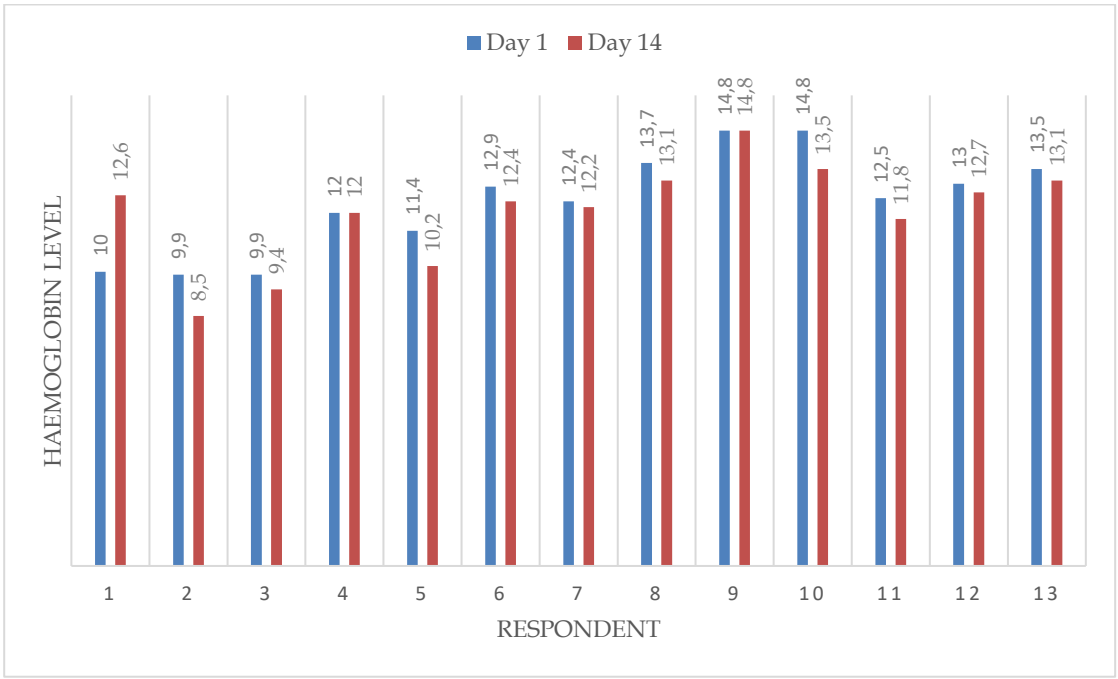

Figure 2. The hemoglobin level of group B

therapeutic candidate for the treatment of pre-inflammatory anemia is black pepper with inhibition of hepcidin-activating protein.[28]

One of the causes of iron deficiency anemia is inadequate fe intake.[28] Decreased appetite in patients with pulmonary TB can cause malnutrition due to lack of required food intake.[29] Nutrient intake also affects the hematopoietic system. Therefore, deficiencies in various micronutrients other than iron can affect the hematopoietic system in producing red blood cells. Micronutrients other than iron are essential for healthy blood system function, so adequacy of these nutrients also plays a role in the prevention of anemia.[4] Research on patients with pulmonary TB shows that the level of malnutrition is higher in patients with anemia than in patients without anemia.[30]

The results of a questionnaire to respondents about testimonials of Songgak consumption, most of them felt that their appetite had increased, their bodies felt fresher and their sleep became better. The increase in hemoglobin levels in TB patients (Table 2) can be explained because there is an increase in food intake along with an increase in the patient's appetite after songgak consumption, so that iron and other micronutrients needed for hemoglobin formation can be fulfilled.

A part from playing a role in erythropoiesis, iron is also needed in the immune system. Iron deficiency can cause a decrease in immunity or immune function.[15] The effect of songgak as an immunostimulant is evidenced by an increase in lymphocyte proliferation in inflammatory model animals given songgak.[31] Increasing the immune system by using songgak is in line with the increase in hemoglobin levels in patients with pulmonary TB who consume ATD + songgak.

Songgak also has good antioxidant activity.[15] Antioxidants have a role in the pathogenesis of iron deficiency anemia.[32] Kusumlata Yadav's research shows the relationship of iron deficiency anemia with oxidative stress and antioxidant activity. There was a significant increase in MDA levels in patients with iron deficiency anemia compared to controls or healthy people or not iron deficiency anemia. Oxidative stress occurs in patients with iron deficiency anemia. Antioxidant administration improves oxidation caused by oxidative stress.[33]

After 14 days, there was an increase in hemoglobin levels by 10 people in the treatment group and 1 person in the control group (Table 3). Odds ratio provides a measure of the strength of the relationship between two variables with a scale of 1 means there is no relationship, above 1 means there is a positive relationship, and below 1 means there is a negative relationship.[20] The interpretation of the odds ratio of songgak consumption on hemoglobin levels of pulmonary TB patients with ATD treatment is that the chance of an increase in hemoglobin levels versus no increase in hemoglobin levels is 12 times higher in pulmonary TB patients who drink songgak coffee compared to not drinking songgak coffee.

CONCLUSION

The findings of this study suggest that there is an increase in Hemoglobin levels in patients with pulmonary tuberculosis who consume songgak. The administration of songgak to patients with pulmonary tuberculosis may help to reduce the risk of Anemia, both due to the potential adverse effects of anti-TB drug therapy and inflammatory Anemia, and also due to the increased appetite that characterises the consumption of songgak coffee.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby affirm that the work presented in this article is original, and that they accept full responsibility for any claims pertaining to its content.

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