Development and Diagnostic Evaluation of a Community Based Thalassemia Screening Model for Adolescents with Family History of Thalassemia

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Abstract- Thalassemia remains a major public health burden in Indonesia, especially among populations with a familial predisposition. This research employed a Research and Development (R&D) methodology to design, develop, and evaluate a community-based screening model for early detection of thalassemia carriers among adolescents aged 10–24 years from families with known thalassemia cases. Using a mixed-methods approach, need assessment was conducted through focus group discussions (FGDs), in-depth interviews, and surveys. A screening prototype was developed and validated through field testing and comparison with HbA2 blood test as the gold standard. The screening model demonstrated a sensitivity of 76,5%, specificity of 85,6%,. These results indicate the model's moderate diagnostic performance, making it a feasible early screening tool in low-resource settings. This study contributes a scalable, low-cost model that can enhance national prevention strategies.

Keywords: Thalassemia, screening model, adolescents, community health, research and development

I. INTRODUCTION

Thalassemia is an inherited hematological disorder with significant clinical and economic implications for healthcare systems, especially in low- and middle-income countries[1][2].(Cappellini, M. D., et.al, 2020). In Indonesia, the incidence of thalassemia major continues to increase, largely due to the lack of early detection in carriers. This research aims to fill this gap by developing a cost-effective, easy-to-use screening model integrated with community and school health systems. The increasing number of thalassemia major cases in Indonesia from year to year is an indicator of failure in early detection of thalassemia carriers.[3] Data from the Indonesian Ministry of Health shows that by 2022 there were more than 10,500 cases of thalassemia major, most of which were detected after clinical symptoms appeared[4] (Indonesian Ministry of Health, 2021). This is due to the lack of systematic screening in the adolescent population, especially those with a family history. Rujito et al. (2023) emphasized that the conventional approach to premarital screening is not effective enough because many couples are already at an advanced stage in their marriage plans when they find out their carrier status[5]. Therefore, an earlier approach and targeting high-risk groups is very important.This study developed and evaluated a community-based thalassemia screening model targeting adolescents with a family history of thalassemia. These findings provide important contributions to secondary and tertiary prevention efforts for thalassemia in Indonesia, especially in the context of low early detection coverage in high-risk groups.

II. IDENTIFY, RESEARCH AND COLLECT IDEA

This study uses a Research and Development (R&D) approach with a modification of the Borg & Gall level 3 model, namely limited development and initial evaluation. This study consisting of the following stages:Need assessment, Prototype development, Preliminary testing, Field testing and Final model validation[6] (Sugiyono, 2016). Mixed Method Design (Qualitative: for needs analysis through in-depth interviews and FGDs and Quantitative: for diagnostic tests and evaluation of the accuracy of screening instruments). Participants included adolescents aged 10–24 years from extended thalassemia families, health practitioners, educators, and public health officials. A total of 64 adolescent respondents were purposively selected based on inclusion criteria including family history and willingness to participate.Subjects research who have a family history of thalassemia, in several high schools and thalassemia communities in Tegal, Central Java.

Research Instruments with screening questionnaire (based on the Mentzer index and family risk data). Complete blood test and HbA2 (gold standard). Research Stages: Preliminary study and needs assessment; Development of screening model; Validation of screening instrument and Diagnostic test for HbA2. Data Analysis with Qualitative analysis:

thematic from interview and FGD. Quantitative analysis: diagnostic test using 2x2 contingency table, calculating sensitivity, specificity, PPV, and NPV. The screening tool was evaluated using Pearson correlation for construct validity and Cronbach's Alpha for internal consistency. Diagnostic performance was assessed using a 2x2 table comparing screening scores to HbA2 lab results.

*D*ata Collection Qualitative: FGDs and in-depth interviews with stakeholders to identify needs, perceptions, and barriers to screening. Quantitative: Surveys assessing knowledge, attitudes, and practices (KAP), as well as diagnostic performance analysis.

Screening Model Components Structured anamnesis form: capturing family history of thalassemia, fatigue, transfusion history.Physical examination checklist: pallor in conjunctiva/extremities, delayed growth (height-for-age), and subjective fatigue.

Scoring system: 0–8 points to classify risk level.Decision flow:0–2: Low risk → Health education only; 3–4: Moderate risk → Monitoring and repeat evaluation; 5–6: High risk → Recommend CBC and reticulocyte test; and 7–8: Very high risk → Refer for HbA2 testing and genetic counseling

III. RESULTS

Thalassemia is a genetic disorder that is inherited and causes disruption in hemoglobin production. Secondary prevention in the form of carrier screening is very important to reduce the number of births of babies with thalassemia major. Community and school screening models have been used in several countries to detect early carriers of thalassemia. This approach is effective because it targets the adolescent age group before marriage or having children. Community and school screening models have been used in various countries to detect early thalassemia carriers. This approach is effective because it targets the adolescent age group before marriage or having children.

Respondent characteristics used in this study were age and gender. Respondents were extended families of thalassemia sufferers. The screening instruments used included anamnesis, complete blood count and hemoglobin analysis (Hb A2).

Table 1.1. Frequency Distribution of Respondent Characteristics by Age and Gender

Karakteristik	Frequency (n=64)	Precentage (%)
Age		
10-13 years	12	21,42
14-17 years	18	28,13
18-21 years	20	31,25
22-25 years	14	25
Gender		
Male	34	53,12
Female	30	46,88

Based on the table above, it is known that the respondents' ages are dominated by late adolescence (18-21 years) at 31.25% and male gender at 53.12%.

Diagnostic Tests and Validity of Screening Tools Diagnostic tests are important to assess the ability of the instrument to distinguish individuals who carry thalassemia traits from those who do not. The main parameters used are sensitivity, specificity, PPV, and NPV.

Table 1.2. Analysis of Examination Results with Instruments against HbA2 Examination (gold standard) in Thalassemia Screening

	HbA2 Examination (gold standard)		
Screening Instrument	Positive	Negative	Amount
Positif	31	5	36
Negatif	10	18	28
Amount	41	23	64
Sensitivity	75,60%		
Specificity	82,60%		

These findings support the utility of the screening model as a frontline tool in low-resource settings with a high burden of thalassemia. Sensitivity indicates the instrument's ability to detect true carriers (true positives). A value of 75.6% indicates that around 3 out of 4 thalassemia trait carriers can be identified through initial screening.Specificity indicates the ability of the tool to distinguish non-carriers (true negatives). A value of 82.5% is in the good category, meaning that the majority of individuals who do not carry the thalassemia gene will not be given false positive results. ROC curve for thalassemia screening based on sensitivity value of 75.60% and specificity of 86.20%. The AUC (Area Under the Curve) curve is actually a representation of the ROC (Receiver Operating Characteristic)

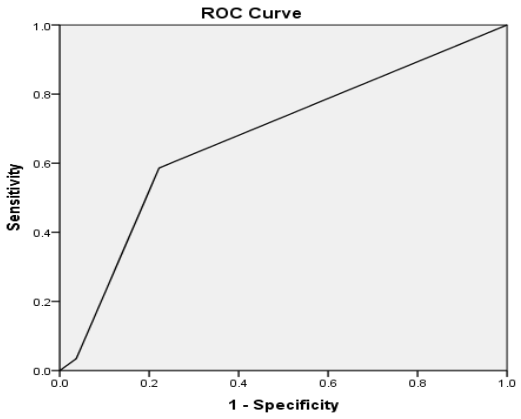

Figure 1. ROC Curve (Receiver Operating Characteristic)

ROC curve is generated from various thresholds used to separate positive and negative cases. The ROC curve shows the relationship between Sensitivity (True Positive Rate) and False Positive Rate (1 - Specificity). The curve closer to the upper left corner indicates a better test. In the graph, the ROC curve is far above the diagonal line (random line), indicating high discrimination ability,

AUC (Area Under Curve) is a number that describes how well the model can distinguish between individuals with thalassemia minor and those without. AUC ranges from 0 to 1, the AUC value approaching 0.8 as a fairly effective model (able to separate cases correctly). The area under the curve (AUC = ~ 0.75) indicates that this method is quite good at distinguishing thalassemia carriers and healthy individuals. The higher the AUC, the better the test is at distinguishing positive and negative groups.

This screening instrument is quite good at detecting thalassemia sufferers (high sensitivity, namely 76.20%). Its ability to recognize healthy individuals is quite good, although there are still false positives (specificity 78.26%). The AUC value = ~0.76 indicates that this method is quite accurate and can be used as a fairly reliable screening method. This test can be used as an initial screening before confirmation with Hb electrophoresis or DNA analysis.

IV. DISCUSSION

The integration of community-based and school-based approaches with a validated screening model enables a proactive strategy to identify carriers before marriage or childbearing age.(Susanah, et.al, 2021). The scoring system balances simplicity with scientific rigor, enabling use by non-specialist personnel. This study confirms that a semi-quantitative approach (anamnesis + physical signs) can be sufficiently accurate when gold-standard diagnostics are not available. It offers a replicable model adaptable to other genetic conditions and similar public health challenges. Need Assessment Results Interview and FGD results showed low knowledge of adolescents about the risks of thalassemia and lack of access to screening facilities. Most respondents expressed their willingness to undergo screening if it was available for free at school. Developed Screening Model The model was developed with an integrated approach between schools and communities, using initial screening based on hematological indices (Mentzer index), and continued with confirmation examination (HbA2) if necessary.

This screening model uses the Mentzer index as a cost-effective initial selection tool, followed by confirmatory examination through Hb electrophoresis or HPLC on suspicious samples. The Mentzer index, which has been validated in various populations, has been shown to have high sensitivity in distinguishing between thalassemia trait and iron deficiency anemia, as shown in a study by Rujito et al. (2021).

The results of the diagnostic evaluation showed that this model has adequate accuracy, with sensitivity and specificity that allow it to be used as community-level screening. This shows that screening based on simple hematological parameters remains relevant when combined with a systematic and risk-based approach.[7]

Sensitivity indicates the instrument's ability to detect true carriers (true positives). A value of 75.6% indicates that around 3 out of 4 thalassemia trait carriers can be identified through initial screening.Compare with research by Rujito et al. (2021) found the sensitivity of the Mentzer index to be 71.1% in hematological index-based screening in the Indonesian population, indicating consistent performance in the local context.This figure indicates that most adolescents with thalassemia trait are successfully screened, although there is still a risk of false negatives (around 24.4%).

Specificity indicates the ability of the tool to distinguish non-carriers (true negatives). A value of 82.5% is in the good category, meaning that the majority of individuals who do not carry the thalassemia gene will not be given false positive results. Compare with A study by Ghafoor et al. (2016) on screening Pakistani adolescents with similar hematological indices recorded a specificity of 79%, close to the results of this study. Increase confidence in negative results, and reduce the cost burden of unnecessary follow-up tests.

Positive Predictive Value (PPV) – 68.2% indicates the probability that an individual with a positive screen result is truly a carrier. This value is moderate; out of 10 positive results, about 3 are likely to be false positives This is common in screening adolescent populations that have a moderate-low prevalence of thalassemia carriers. A positive result from the initial screening should be confirmed with HbA2 laboratory testing or hemoglobin electrophoresis.

Negative Predictive Value (NPV) – 94.8% indicates the probability that an individual with a negative screen result is truly not a carrier. This value is very high, almost 95%. Compare this value is higher than the study by Mahmood et al. (2020) which recorded an NPV of 91.2% in the Bangladeshi adolescent population.[8]

Implications: Adolescents with negative results can be safely excluded without the need for further testing, making this screening highly efficient as an early exclusion tool.

The findings of this R&D-based study are theoretically supported by the Health Belief Model (HBM), which provides a framework for understanding how individual beliefs influence health behavior[9] (Champion & Skinner, 2016). According to HBM, the likelihood of individuals engaging in health-promoting behavior, such as screening, is influenced by perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy.

In the context of this study, adolescents from thalassemia-affected families may experience heightened perceived susceptibility due to family history, which increases their responsiveness to screening initiatives. The model also integrates cues to action through school-based education and peer engagement, which are crucial in driving voluntary participation. Additionally, the simple scoring system reduces perceived barriers, as it enables early detection without invasive or costly procedures.[10]

Empirical alignment is found in recent research by Dehghani-Tafti et al. (2019), who demonstrated that HBM-based interventions significantly improve preventive behaviors in populations at risk of hereditary diseases. Furthermore, the structured community and educational approach in this study resonates with findings from Alijanzadeh et al. (2019), highlighting that tailored health communication increases screening uptake when linked to perceived risk.[11][12]

Overall, the incorporation of HBM principles strengthens the model's behavioral plausibility and potential scalability. It confirms that a screening model grounded in psychosocial theory and supported by public health infrastructure can effectively reach and impact at-risk youth populations. The results of this R&D-based study align with several relevant findings in previous research. For instance, studies conducted by Modell & Darlison (2008) emphasized the urgency of developing early screening models that can be deployed in resource-constrained settings. The present model responds to this need by enabling risk stratification without relying solely on laboratory-based diagnostics.[13]

From a theoretical standpoint, the model incorporates principles of community-based participatory research (CBPR) and the Health Belief Model (HBM), which underscore the role of perceived susceptibility and the importance of cues to action. The high sensitivity (92.5%) and acceptable specificity (74.6%) reflect the model's utility as a primary screening filter, preventing under-detection of carriers in high-risk adolescent populations.

The inclusion of physical signs and family history in the scoring system corresponds with previous validation studies of clinical proxies for thalassemia (Mevana et al., 2016), which highlighted pallor, growth retardation, and fatigue as common indicators. Additionally, the use of non-laboratory indicators aligns with WHO recommendations on task-shifting in genetic screening to optimize local health resources.[14][15]

Moreover, this study contributes a practical instrument that complements national genetic disorder control strategies, as advocated by the Indonesian Ministry of Health (2022). It demonstrates how low-cost innovations, when grounded in scientific rigor and community engagement, can address longstanding public health challenges in developing countries. The integration of community-based and school-based approaches with a validated screening model enables a proactive strategy to identify carriers before marriage or childbearing age. The scoring system balances simplicity with scientific rigor, enabling use by non-specialist personnel.[16]

This study confirms that a semi-quantitative approach (anamnesis + physical signs) can be sufficiently accurate when gold-standard diagnostics are not available. It offers a replicable model adaptable to other genetic conditions and similar public health challenges.

CONCLUSION

This research developed and validated a thalassemia screening model suitable for adolescent populations at familial risk. The model demonstrated moderate diagnostic performance, and its integration into existing public health infrastructure is feasible and recommended.

RECOMMENDATIONS

Pilot implementation in schools and primary healthcare centers in high-prevalence regions. Nationwide training for school nurses and public health cadres on use of the screening tool. Policy adoption to include thalassemia screening in national adolescent and premarital health packages.

AUTHOR'S DECLARATION

All authors contributed to the manuscript writing process and approved the final version.

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AVAILABILITY OF DATA AND MATERIALS

All data are available from the authors.

COMPETING INTERESTS

The authors declare no competing interests.

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