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ORIGINAL RESEARCH

Alpha+ Thalassemia in Northwestern Tanzania: Molecular and Hematological Insights From Newborn Screening

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Purpose: This study aimed to determine the prevalence of alpha+ thalassemia and its hematological indices in a newborn population in Mwanza city, North-western Tanzania.

Patients and Methods: A cross-sectional study screened 803 newborns for alpha+ thalassemia that extracted DNA from dried blood spots using the Qiagen Mini Kit then analysed by multiplex PCR. Demographic data, anemia-related clinical information, and CBC parameters were collected at birth. Prevalence was determined by the proportion of newborns with the alpha+ thalassemia deletion. Fisher's Exact test assessed differences in demographic and clinical variables, while Student's t-tests and ANOVA evaluated hematological parameters. A P-value < 0.05 was considered statistically significant.

Results: Alpha thalassemia was detected in 49.6% (398/803) of neonates, with 38.6% heterozygous and 11.0% homozygous deletions. Significant differences in erythrocyte indices were observed across groups. Hemoglobin (Hb) levels were lower in heterozygous (_α/αα) and homozygous (_α/_α) newborns (16.42±3.62 g/dl and 16.04±3.37 g/dl, respectively) compared to the αα/αα group (17.03±3.35 g/dl, $p < 0.05$). Mean Corpuscular Volume (MCV) was reduced in heterozygous (_α/αα) and homozygous (_α/_α) groups (99.23 ±9.12 μm³ and 94.75±9.88 μm³, respectively) compared to αα/αα (102.41±9.56 μm³, $p < 0.0001$). Mean Corpuscular Hemoglobin (MCH) followed a similar pattern, being lowest in the homozygous group ($p \leq 0.0001$). Red Cell Distribution Width (RDW) was higher in homozygous (_α/_α) newborns (10.03±1.22) compared to heterozygous (_α/αα) (9.57±0.79, $p < 0.001$). Leucocyte counts were significantly higher in heterozygous (_α/αα) newborns (13.91±12.14) compared to homozygous (_α/_α) (12.60±7.91) and αα/αα groups (11.26±9.76, $p = 0.001$).

Conclusion: Alpha+ thalassemia is highly prevalent in North-western Tanzania and significantly affects blood indices. Neonatal screening is an effective tool for identifying affected children, especially in settings with high prevalence of a trait and low awareness of genetic inheritance.

Keywords: alpha thalassemia, newborn, Northwestern Tanzania

Introduction

Alpha + thalassemia is an abnormality of hemoglobin (Hb) synthesis, caused by variants in the alpha+-globin genes on chromosome 16, leading to reduced or absent α-globin chain production,[1,2] that affects 5% to 20% of the global population.[3–5] Normal individuals have two α-globin genes on each allele (HBA1, HBA2) resulting in a total of four functional α-globin genes (αα/αα). Variant can lead to four clinical characteristics depending on the number of genes affected by underlying mutations and the amount of functional protein that is produced: 1. Heterozygous (alpha+ thalassemia): Deletion/dysfunction of one α-globin gene, clinically normal.[6–8] 2. α^0 Thalassemia Trait: Deletion/dysfunction of two α-globin genes, mild anemia.[6] 3. Hemoglobin H (HbH) Disease: One functional α-globin gene, moderate to

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severe anemia, hepatosplenomegaly.[6] 4. Hb Bart's Hydrops Fetalis: No functional α-globin genes, severe anemia, often fatal in utero.[6–8] Mutations mainly affect the HBA2 gene, causing severe reductions in α-globin synthesis.[9,10] Excess γ-globin produced in the fetus and newborn will form γ-globin tetramers called Hb Bart's, and excess β-globin produced in adults will form β-globin tetramers called HbH, both leading to ineffective oxygen transport and hemolytic anemia.[11–14]

Alpha thalassemia is prevalent globally, particularly in Southeast Asia, the Mediterranean, the Indian subcontinent, the Middle East, and Africa.[3,15–17] Due to population migration, its presence has also increased in Northern Europe and the Americas.[18–20] In Tanzania, the prevalence of α-thalassemia is strongly associated with malaria transmission intensity—higher rates are observed in low-altitude, high-malaria regions.[21–23] Studies in the Eastern Arc Mountains reported frequencies ranging from 10% in high-altitude areas to over 50% in low-altitude zones.[22] Additionally, alpha+ thalassemia is linked to protection from uncomplicated malaria in older children.[24] Although beta-thalassemia is less common in sub-Saharan Africa, it is present; a newborn screening study in Northwestern Tanzania identified 0.2% with β^{+}-thalassemia and 1.4% with Hb S/β^{0}-thalassemia.[25] The co-inheritance of alpha- and beta-thalassemia with other hemoglobinopathies, such as sickle cell disease, can complicate clinical presentation and diagnosis, highlighting the need for targeted newborn screening and genetic counseling strategies.

At the molecular level, alpha+ thalassemia is most commonly caused by deletions or point mutations affecting one of the two α-globin genes (HBA1 or HBA2), located on chromosome 16p13.3. These genes encode α-globin chains, essential components of hemoglobin tetramers. Deletional variants such as $-\alpha^{3.7}$ and $-\alpha^{4.2}$, which arise from unequal crossover during homologous recombination, are the most prevalent globally. Non-deletional mutations—such as those affecting splice sites, polyadenylation signals, or coding regions—more frequently impact the HBA2 gene and result in reduced synthesis or instability of α-globin chains.[6,7,26] The consequent imbalance between α- and non-α-globin chains underlies the ineffective erythropoiesis and hemolysis characteristic of alpha thalassemia syndromes.

This globin chain imbalance is especially disruptive during fetal and adult stages. In the fetus, surplus γ-globin chains form tetramers known as Hb Bart's (γ_4), while in adults, excess β-globin chains form HbH (β_4). Both have abnormally high oxygen affinity and fail to deliver oxygen effectively to tissues, contributing to hypoxia and the clinical phenotype of anemia.[7,11] Additionally, unpaired globin chains precipitate in erythroid precursors, causing oxidative damage, apoptosis, and reduced red blood cell survival. Understanding these molecular mechanisms is critical for precise diagnosis through molecular genotyping, and for designing targeted screening strategies in populations where alpha thalassemia overlaps with other hemoglobinopathies, such as sickle cell disease.[6,26,27]

Main success in Tanzania for early diagnosis has been done to HIV, newborn get to know their HIV exposure status even before birth. Screening and prevention strategies aim to reduce affected births and deaths.[28] Carrier detection and counseling have proven effective in reducing disease incidence.[3] Therefore, this study aims to establish the prevalence of alpha+ thalassemia in newborns in Northwestern Tanzania, considering the high prevalence of sickle cell disease in the Northwest region of Tanzania where sickle cell disease is also common.[25,29,30]

Materials and Methods

Ethical Considerations

This was a cross-sectional study conducted between August and November 2014 after obtaining ethical clearance from the Catholic University of Health and Allied Sciences (CUHAS) and Bugando Medical Centre (BMC) Joint Research Ethics Committee (Research Certificate Number: BREC/001/36/2014). Written informed consent was obtained from the parent or guardian of each neonate. All neonates diagnosed with alpha thalassemia were invited to return to the clinic for discussion of abnormal test results, and appropriate counselling was provided. All procedures adhered to the principles of the Declaration of Helsinki.

Study Setting

The study was conducted at the Department of Paediatrics and Child Health of Bugando Medical Centre (BMC) and Sekou-Toure Hospital (STH) in North-western Tanzania. BMC is a zonal referral, consultant, and tertiary teaching hospital that serves the Lake Victoria and Western Zones of the United Republic of Tanzania. Sekou-Toure Hospital is

the regional referral hospital for Mwanza Region. Combined, the two hospitals serve a catchment population of approximately 16.2 million people and handle about 2300 deliveries per month.

Study Participants

Newborns aged <7 days with no history of blood transfusion at enrolment were recruited from the neonatal wards of the respective hospitals. Demographic information and findings from physical examinations were recorded.

Blood Samples Collection and Laboratory Analysis

At enrollment, a heel prick was performed to collect blood on a dried blood spot card for PCR analysis. Additionally, 0.5 mL of blood was collected into an ethylene diamine tetra-acetic acid (EDTA) tube from each eligible neonate for complete blood count (CBC) analysis. The CBC was performed using a Cell-Dyn 3700 hematology analyzer (Abbott Diagnostics, USA). Dried blood spot samples for alpha thalassemia variants were processed at the National Institute for Medical Research (NIMR) in Mwanza.

DNA was extracted from dried blood spots using the Qiagen DNA Blood Mini Kit (Qiagen, UK), following the manufacturer's standard protocol. This method ensures high-quality DNA suitable for downstream applications such as PCR. Specific primer panels targeting the common African 3.7kb alpha thalassemia deletion were used in a multiplex PCR assay to identify alpha thalassemia genotypes. The PCR conditions and primer sequences were as described previously.[2] The assay differentiated between normal α-globin genotype (αα/αα), heterozygous alpha+ thalassemia (-α/αα), and homozygous alpha+ thalassemia (-α/-α). DNA samples from individuals with known alpha 3.7-thalassemia status (normal, heterozygous, and homozygous α-globin deletion) served as positive controls, while a no-template reaction served as a negative control to ensure the specificity and accuracy of the PCR.

Following PCR amplification, gel electrophoresis was utilized to resolve and identify the various alpha 3.7-thalassemia deletion variants. The presence or absence of specific PCR products determined the genotype of each sample. Representative gel images of the PCR products were provided to validate the detection method and visually confirm genotype assignments. To ensure assay reliability and accuracy, each PCR run included positive controls (DNA samples with known alpha 3.7-thalassemia genotypes) and a negative control (no template DNA). The appearance of expected bands in the positive controls and the absence of amplification in the negative control confirmed the validity of the PCR results.

For clinical purposes here we will refer to heterozygous and homozygous individuals as silent carriers and alpha thalassemia trait respectively.

Data Analysis

Data were analyzed using STATA version 12 (Stata Corp, College Station, Texas, USA). Prevalence was analysed by proportions. Analysis of variants (ANOVA) was used for comparison of mean of haematological parameters between more than 2 groups whereas Student's *t*-test was used in comparing differences between two groups. A P-value < 0.05 was considered statistically significant.

Results

Enrolment Overview

The parents of 803 neonates were approached during enrolment and all 803 were screened for alpha+ thalassemia during the times the research assistants were available in the wards (Figure 1). Patients were contacted by telephone to schedule follow-up visits for receiving results and counseling. Figure 1 also includes annotations for additional screenings such as complete blood count (CBC) and polymerase-chain reaction (PCR). The screening revealed that 50.4% (405/803) of neonates had a normal genotype (αα/αα) and Alpha thalassemia was detected in 49.6% (398/803) neonates. Of the neonates, 38.6% (310/803) were heterozygous (αα/_α), and 11.0% (88/803) homozygous (α_/α_).

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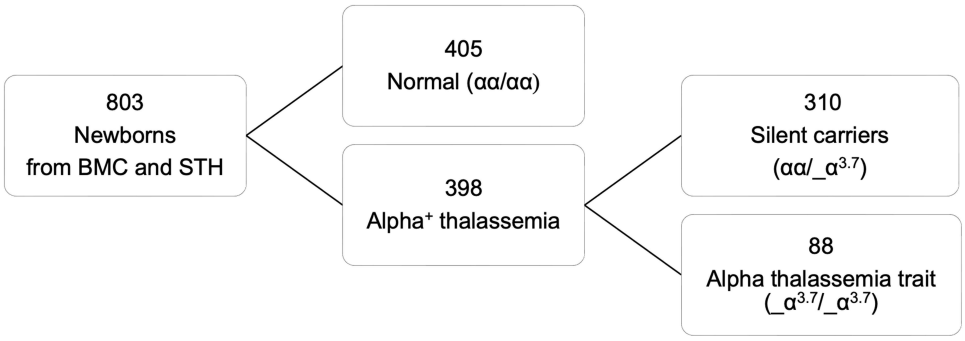

Figure 1 Enrollment figure of 803 neonates.
Abbreviations: BMC, Bugando Medical Centre; STH, Sekou Toure Hospital; CBC, complete blood count.

Clinical Characteristics at Baseline

The neonates had the median age of 2 days [IQR 1–2], with a slight male majority, 52.8% (424/803). Most neonates were born at term (≥37 weeks' gestation), comprising 97.3% (781/803) of the cohort, while preterm births were rare, 2.7% (22/803). Majority 79.2% (636/803) were not exposed to HIV, with a significant proportion with unknown HIV status 14.1% (113/803). The neonates were predominantly recruited from Mwanza region in 95.0% (763/803). Parental education varied, with more fathers than mothers having reached secondary education or higher. Majority of neonates exhibited normal activity levels. Respiratory and pulse rate abnormalities were relatively uncommon, though 17.1% (147/803) showed tachypnea. A sibling with recurrent transfusion was reported in 1.6% (13/803) of neonates (Table 1). There were no significant demographic differences across alpha-thalassemia genotypes (Table 2).

Table 1 Baseline Characteristics of Neonates Screened for Alpha Thalassemia at Bugando Medical Centre and Sekou Toure Hospital

Characteristic	Number (%) or Median [IQR]
Median age in days	2 [1–2]
Males	424 (52.8)
Neonates Gestation age	
≥37 weeks	781 (97.3)
< 37 weeks	22 (2.7)
Neonates HIV status	
Exposed	54 (6.7)
Not Exposed	636 (79.2)
Unknown	113 (14.1)
Neonates delivery place	
BMC	381 (47.4)
SekouToure	415 (51.7)
Other facility /Home/On the way to hospital	7 (0.8)
Parents residential place	
Mwanza region	763 (95.0)
Outside Mwanza region	40 (5.0)
Mother's Highest level of education	
Never went to school	45 (5.6)
Primary school attendee	466 (58.0)
Secondary school /University/ College	292 (36.4)
Father's Highest level of education	
Never went to school	14 (1.7)
Primary school attendee	379 (47.2)
Secondary (four/six)/ University/ College	410 (51.1)

(*Continued*)

Table 1 (Continued).

Characteristic	Number (%) or Median [IQR]
Siblings thought to die due to SCD/Thalassemia	1 (0.1)
Sibling history of recurrent blood transfusion	13 (1.5)
Sibling history of recurrent jaundice	13 (1.5)
Febrile condition**….Yes**	33 (3.8)
General condition	
Normal activity	769 (95.7)
Reduced activity	19 (2.2)
Unresponsive/Lethargic	18 (2.2)
Tachypnea >60 breaths/min	147 (17.1)
Pulse rate	
Normal (100–160)	214 (26.7)
Bradycardia<100	628 (75.7)
Tachycardia >160	20 (2.5)
SP02…<90% in room air	88 (11.0)
Head circumference	
>+2SD	14 (1.7)
Mean	758 (94.4)
<-2SD	31 (3.9)
Median head circumference	34.5 [34-3-35.5]
Neonatal length	50 [48–51]
Jaundice ….Yes	13 (1.6)
Pallor ….Yes	12 (1.5)
Splenomegaly	4 (0.5)
Congenital abnormalities	25 (3.1)

Abbreviations: BMC, Bugando Medical Centre, SD, Standard deviation, SPO2- Peripheral Oxygen Saturation.

Table 2 Demographic Characteristics of Neonates According to PCR Results

Characteristics	αα/αα 405	α_/αα 310	_α/_α 88	P-value Fisher's Exact Test
Age in days				
1–3 days	391 (96.5%)	302 (97.4%)	88 (100%)	0.34
4–7 days	14 (3.5%)	8 (2.6%)	0%	
Sex of neonates				
Males	225 (55.6%)	149 (48.1%)	50 (56.8%)	0.2
Females	180 (44.4%)	161 (52.0%)	38 (49.1%)	
Neonates Gestation age				
≥37 weeks	394 (97.3%)	302 (97.4%)	86 (97.7%)	0.97
< 37 weeks	11 (2.7%)	8 (2.5%)	2 (2.3%)	
Neonates HIV status				
Exposed	24 (5.9%)	27 (8.7%)	3 (3.4%)	0.17
Not Exposed	316 (78.0%)	242 (78.1%)	78 (88.6%)	
Unknown	65 (16.1%)	41 (13.2%)	7 (8.0%)	
Neonates delivery place				
BMC	194 (47.9%)	151 (48.7%)	36 (40.9%)	0.47
Sekou Toure	208 (51.4%)	155 (50%)	52 (59.9%)	
Other facility	3 (0.7%)	4 (1.3%)	0	
Region parents live				
Mwanza	389 (96.1%)	288 (93.2%)	85 (96.6%)	0.32
Outside Mwanza	16 (3.9%)	21 (6.8%)	3 (3.4%)	

(*Continued*)

Table 2 (Continued).

Characteristics	αα/αα 405	α_/αα 310	_α/_α 88	P-value Fisher's Exact Test
Mother's Highest level of education				
Never went to school	20 (4.9%)	19 (6.1%)	6 (6.8%)	0.66
Primary school lever	248 (61.2%)	173 (55.8%)	45 (51.1%)	
Secondary college/ University	137 (33.9%)	118 (29.1%)	37 (42.1%)	
Father's Highest level of education				
Never went to school	5 (1.2%)	6 (1.9%)	3 (3.4%)	0.28
Primary school lever	198 (49.0%)	136 (43.9)	45 (51.1%)	
Secondary college/ University	202 (49.8%)	168 (54.2%)	40 (45.5%)	

Abbreviation: BMC, Bugando Medical Centre.

Table 3 Prevalence of Alpha Thalassemia Observed in Neonates

Alpha Thalassemia	Clinical Effect	Observations	% of Neonates
4 copies, αα/αα	0-gene deletion, unaffected	405	50.4%
3 copies, αα/ $_{-}\alpha^{3.7}$	1-gene deletion, silent carrier	310	38.6%
2 copies, _α/ $_{-}\alpha^{3.7}$	2 gene deletion, trait	88	11%

Prevalence of Alpha Thalassemia Genotypes

The screening revealed that 50.4% (405/803) of neonates had a normal genotype (αα/αα) and Alpha thalassemia was detected in 49.6% (398/803) neonates. Of the neonates, 38.6% (310/803) were heterozygous of the alpha thalassemia (αα/_α), and 11.0% (88/803) had homozygous inheritance patten (α_/α_). This indicates a significant carrier rate within the population, which is crucial for public health awareness and genetic counselling (Table 3).

Haematological Parameters

Table 4 compares the hematological parameters among the different groups. At baseline, the heterozygous (_α/αα) and homozygous (_α/_α) alpha+ thalassemia groups showed significant differences in their erythrocyte indices. Hemoglobin (Hb) levels were slightly lower in both the heterozygous (_α/αα) group (16.42±3.62 g/dl) and the homozygous (_α/_α) group (16.04±3.37 g/dl) compared to the αα/αα group (17.03±3.35 g/dl), with a P-value of 0.02. Mean Corpuscular Volume (MCV) was also lower in the heterozygous (_α/αα) group at 99.23±9.12 μm³ and further reduced in the homozygous (_α/_α) group at 94.75±9.88 μm³ compared to the αα/αα group at 102.41±9.56 μm³ ($p < 0.0001$). Mean Corpuscular Hemoglobin (MCH) was

Table 4 Comparison of Haematological Parameters Between Silent and Alpha Thalassemia Trait

Variable	αα/ αα (a)	_α/ αα (b)	_α/ _α (c)	P-value a_vs b Student's *t*-test	P-value a_vs c Student's *t*-test	F- test ANOVA	P-value all groups ANOVA
BASELINE	383	296	84				
RBC ($\times 10^{12}$/l)	5.08±0.84	5.08±0.98	5.21±1.07	0.50	0.09	1.16	0.32
HGB (g/dl)	17.03±3.35	16.42±3.62	16.04±3.37	**0.02**	**0.01**	3.34	**0.02**
MCV (μm^3)	102.41±9.56	99.23±9.12	94.75±9.88	**<0.0001**	**<0.0001**	17.87	**<0.0001**
MCH (pg)	33.89±4.51	32.39±5.12	30.47±6.14	**0.0001**	**<0.0001**	13.45	**<0.0001**
RDW	9.71±1.10	9.57±0.79	10.03±1.22	0.07	**0.02**	4.82	**0.001**
WBC	11.26±9.76	13.91±12.14	12.60±7.91	**0.002**	0.23	3.60	**0.01**
LYMPH (#)	3.79±3.26	3.52±2.21	3.72±2.65	**0.02**	0.34	2.31	0.07
EOS (#)	0.17±0.17	0.19±0.16	0.29±1.05	0.17	**0.04**	4.19	**0.006**

Notes: Bold numbers indicate statistically significant differences with $p < 0.05$. # denotes absolute cell counts ($\times 10^9$/L) for lymphocytes (LYMPH) and eosinophils (EOS).
Abbreviations: RBC, Red Blood Cells, HGB, Hemoglobin, MCV, Mean Corpuscular Volume, MCH, Mean Corpuscular Hemoglobin, RD, Red Cell Distribution Width, WBC, White Blood Cells, LYMPH, Lymphocytes, EOS, Eosinophils, ANOVA, Analysis of Variance.

slightly lower in the heterozygous (_α/αα) group at 32.39±5.12 pg and more evident in the homozygous (_α/_α) group at 30.47±6.14 pg, while the αα/αα group had a mean of 33.89±4.51 pg ($p < 0.0001$).

The Red Cell Distribution Width (RDW) was higher in the homozygous (_α/_α) group with a mean of 10.03±1.22, compared to both the heterozygous (_α/αα) group at 9.57±0.79 and the αα/αα group ($p < 0.001$). Leucocytes were significantly higher in the heterozygous (_α/αα) group with a mean of 13.91±12.14 compared to the αα/αα group (11.26 ±9.76) and the homozygous (_α/_α) group (12.60±7.91) ($p = 0.001$). The F-test and ANOVA results indicate statistically significant differences in hematological mean parameters (HGB, MCV, MCH, RDW, WBC) across various groups of alpha+ thalassemia statuses, confirming the effect of alpha^{+} thalassemia on blood indices.

Discussion

Alpha Thalassemia Prevalence

This study revealed a high prevalence of α-thalassemia among newborns in Mwanza, Northwestern Tanzania, with nearly half of the screened neonates affected. This aligns with studies in malaria-endemic regions, where α-thalassemia confers a selective advantage against malaria.[21–23,25,31] Similar prevalence rates were observed in patients with sickle cell disease in the same area,[32] indicating a common genetic trait. The prevalence in Mwanza is higher compared to other African regions like Ghana (32%)[22] and Kenya (50%).[23] Specifically, hospital studies in Ghana reported an alpha+-thalassemia frequency of 19.9% for heterozygotes (−α/αα) and 6.8% for homozygotes (homozygous (_α/_α)),[33] lower than our findings and other studies in southern Ghana, which showed a 39.0% heterozygous and 8.2% homozygous α-thalassemia rate.[34]

In Mwanza, 38.6% of neonates were heterozygous (_α/αα), typically asymptomatic with normal hematological profiles or mild microcytosis. This form often remains undiagnosed without specific screening. Additionally, 11% of neonates had the α-thalassemia trait (_α/_α), which can combine with other forms to produce severe conditions, presenting with mild microcytic anemia and hypochromia, often misdiagnosed as iron deficiency anemia without genetic testing.

Hematological Parameters in Alpha+ Thalassemia

Hematological parameters, such as hemoglobin (Hb) concentration, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW), are critical in diagnosing and assessing the severity of α-thalassemia. Neonates with α-thalassemia consistently exhibit lower values of Hb, MCV, and MCH compared to individuals without the disorder, underscoring its profound impact on hematological profiles. These findings align with previous studies,[35] which highlight the utility of these parameters in distinguishing α-thalassemia from other forms of anemia.[36] Reduced hemoglobin levels were particularly pronounced in both heterozygous and trait individuals, consistent with earlier research that demonstrated a significant reduction in Hb concentration among alpha+-thalassemia carriers.[6] These hematological abnormalities emphasize the importance of accurate neonatal screening to identify affected individuals early.

A hallmark feature of α-thalassemia is anisocytosis,[37] as evidenced by the normal to slightly elevated RDW observed in both heterozygous and homozygous individuals compared to normal individuals. RDW serves as an indicator of red cell size variability, further supporting the diagnosis of α-thalassemia in cases where other hematological parameters point to microcytic anemia. The slight increase in RDW among affected individuals aligns with findings from other studies that have highlighted its diagnostic utility, particularly in differentiating α-thalassemia from other microcytic anemias, such as iron deficiency anemia.[1] This differentiation is crucial as it prevents the potential complications of inappropriate iron supplementation, which could occur due to a misdiagnosis.

Comprehensive hematological screening is particularly important in regions with a high prevalence of α-thalassemia, such as Mwanza, Tanzania, where neonatal health assessments can aid in identifying affected infants. Recognizing the characteristic low MCV and MCH values in α-thalassemia is essential to avoid confusion with other conditions, especially iron deficiency anemia, which presents with overlapping features. Early identification through neonatal screening programs can prevent unnecessary iron supplementation, which poses risks such as iron overload and associated complications.[1] Moreover, targeted interventions can significantly improve patient outcomes in resource-

limited settings. The integration of hematological analysis with molecular diagnostic techniques holds promise for improving the accuracy of α-thalassemia diagnosis and optimizing patient management strategies in high-burden areas.

Although red blood cell indices are the primary focus in α-thalassemia, variations in white blood cell (WBC) counts have also been observed. Some studies report mild leukocytosis or neutropenia in affected neonates, potentially reflecting stress erythropoiesis or associated inflammatory responses, though these findings remain inconsistent and warrant further investigation. In high-prevalence regions like Mwanza, Tanzania, comprehensive neonatal screening is critical. National screening practices remain limited and largely hospital-based, emphasizing the need for policy-level strategies to implement universal newborn screening for hemoglobinopathies. Integrating hematological profiles with molecular diagnostics would enhance early detection, guide appropriate management, and prevent complications associated with misdiagnosis in resource-limited settings.

Study Limitations

The study employed PCR for screening and diagnosing α-thalassemia, alongside CBC for hematological parameters. While PCR is robust for detecting specific gene deletions, it has limitations, such as the inability to detect all mutation types (eg, the kb 4.2 deletion), potentially leading to underestimation of prevalence rates that has implications for clinical mismanagement in high-prevalence areas. Also the study did not do iron profiling.

Conclusion

The prevalence of alpha+-thalassemia in Northwestern Tanzania is among the highest globally. Given the high prevalence of iron deficiency, the study emphasizes the importance of molecular diagnosis for suspected thalassemia cases, as relying solely on red cell indices can lead to unnecessary iron therapy and subsequent iron overload.

Recommendation

Investigating the interaction between α-thalassemia and other prevalent conditions like malaria and HIV could enhance comprehensive care strategies for patients with multiple health challenges. Incorporating premarital education and screening programs with neonatal screening into national newborn screening frameworks is crucial for early diagnosis. Improved availability of molecular confirmatory testing and dedicated referral pathways to experienced hematologists are also needed.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

All authors report no conflicts of interest in this work.

References

1. Kattamis A, Kwiatkowski JL, Aydinok Y. Thalassaemia. *Lancet*. 2022;399(10343):2310–2324. doi:10.1016/S0140-6736(22)00536-0
2. Liu YT, Old JM, Miles K, et al. Rapid detection of alpha-thalassaemia deletions and alpha-globin gene triplication by multiplex polymerase chain reactions. *Br J Haematol*. 2000;108(2):295–299. doi:10.1046/j.1365-2141.2000.01870.x

3. Modell B. Global epidemiology of haemoglobin disorders and derived service indicators. *Bull World Health Organ*. 2008;2008(6):480–487. doi:10.2471/BLT.06.036673
4. Williams TN, Weatherall DJ. World distribution, population genetics, and health burden of the hemoglobinopathies. *Cold Spring Harb Perspect Med*. 2012;2(9):a011692–a011692. doi:10.1101/cshperspect.a011692
5. Vichinsky EP. Clinical manifestations of-thalassemia. *Cold Spring Harb Perspect Med*. 2013;3(5):a011742–a011742. doi:10.1101/cshperspect.a011742
6. Harteveld CL, Higgs DR. Alpha-thalassaemia. *Orphanet J Rare Dis*. 2010;5:13. doi:10.1186/1750-1172-5-13
7. Galanello R, Cao A. Gene test review. Alpha-thalassemia. *Genet Med*. 2011;13(2):83–88. doi:10.1097/GIM.0b013e3181fcb468
8. Tesio N, Bauer DE. Molecular basis and genetic modifiers of thalassemia. *Hematol Oncol Clin North Am*. 2023;37(2):273–299. doi:10.1016/j.hoc.2022.12.001
9. Liebhaber SA, Cash FE, Ballas SK. Human alpha-globin gene expression. The dominant role of the alpha 2-locus in mRNA and protein synthesis. *J Biol Chem*. 1986;261(32):15327–15333. doi:10.1016/S0021-9258(18)66871-1
10. Liebhaber SA, Kan YW. Differentiation of the mRNA transcripts originating from the alpha 1- and alpha 2-globin loci in normals and alpha-thalassemics. *J Clin Investig*. 1981;68(2):439–446. doi:10.1172/JCI110273
11. Chui DHK, Fucharoen S, Chan V. Hemoglobin H disease: not necessarily a benign disorder. *Blood*. 2003;101(3):791–800. doi:10.1182/blood-2002-07-1975
12. Yuan J, Bunyaratvej A, Fucharoen S, et al. The instability of the membrane skeleton in thalassemic red blood cells. *Blood*. 1995;86(10):3945–3950. doi:10.1182/blood.V86.10.3945.bloodjournal86103945
13. Chinprasertsuk S, Wanachiwanawin W, Piankijagum A. Effect of pyrexia in the formation of intraerythrocytic inclusion bodies and vacuoles in haemolytic crisis of haemoglobin H disease. *Eur J Haematol*. 1994;52(2):87–91. doi:10.1111/j.1600-0609.1994.tb01291.x
14. Lorey F, Cunningham G, Vichinsky EP, et al. Universal newborn screening for Hb H disease in California. *Genet Test*. 2001;5(2):93–100. doi:10.1089/109065701753145538
15. El Goundali K, Chebabe M, Zahra Laamiri F, Hilali A. The determinants of consanguineous marriages among the Arab population: a systematic review. *Iran J Public Health*. 2022;51(2):253–265. doi:10.18502/ijph.v51i2.8679
16. Hamamy H, Antonarakis SE, Cavalli-Sforza LL, et al. Consanguineous marriages, pearls and perils: Geneva international consanguinity workshop report. *Genet Med*. 2011;13(9):841–847. doi:10.1097/GIM.0b013e318217477f
17. Goh LPW, Chong ETJ, Lee P-C. Prevalence of alpha(α)-thalassemia in Southeast Asia (2010-2020): a meta-analysis involving 83,674 subjects. *Int J Environ Res Public Health*. 2020;17(20):7354. doi:10.3390/ijerph17207354
18. Angastiniotis M, Vives Corrons J-L, Soteriades ES, Eleftheriou A. The impact of migrations on the health services for rare diseases in Europe: the example of haemoglobin disorders. *ScientificWorldJournal*. 2013;2013:727905. doi:10.1155/2013/727905
19. Weatherall DJ. The evolving spectrum of the epidemiology of thalassemia. *Hematol Oncol Clin North Am*. 2018;32(2):165–175. doi:10.1016/j.hoc.2017.11.008
20. Vichinsky EP. Changing patterns of thalassemia worldwide. *Ann N Y Acad Sci*. 2005;1054:18–24. doi:10.1196/annals.1345.003
21. Enevold A, Alifrangis M, Sanchez JJ, et al. Associations between alpha+-thalassemia and Plasmodium falciparum malarial infection in northeastern Tanzania. *J Infect Dis*. 2007;196(3):451–459. doi:10.1086/519390
22. Mockenhaupt FP, Ehrhardt S, Gellert S, et al. Alpha(+)-thalassemia protects African children from severe malaria. *Blood*. 2004;104(7):2003–2006. doi:10.1182/blood-2003-11-4090
23. Williams TN, Wambua S, Uyoga S, et al. Both heterozygous and homozygous alpha+ thalassemias protect against severe and fatal Plasmodium falciparum malaria on the coast of Kenya. *Blood*. 2005;106(1):368–371. doi:10.1182/blood-2005-01-0313
24. Rwezaula S, Magesa P, Mgaya J, et al. Newborn screening for hemoglobinopathies at Muhimbili National Hospital, Dar es Salaam – Tanzania. *East Afr J Public Health*. 2015;12;1:948–955.
25. Ambrose EE, Makani J, Chami N, et al. High birth prevalence of sickle cell disease in Northwestern Tanzania. *Pediatr Blood Cancer*. 2018;65(1). doi:10.1002/pbc.26735.
26. Higgs DR, Engel JD, Stamatoyannopoulos G. Thalassaemia. *Lancet*. 2012;379(9813):373–383. doi:10.1016/S0140-6736(11)60283-3
27. Piel FB, Weatherall DJ. The α-thalassemias. *N Engl J Med*. 2014;371(20):1908–1916. doi:10.1056/NEJMra1404415
28. Halim-Fikri BH, Lederer CW, Baig AA, et al. Global globin network consensus paper: classification and stratified roadmaps for improved thalassaemia care and prevention in 32 countries. *J Pers Med*. 2022;12(4):552. doi:10.3390/jpm12040552
29. Ambrose EE, Smart LR, Charles M, et al. Surveillance for sickle cell disease, united republic of Tanzania. *Bull World Health Organ*. 2020;98(12):859–868. doi:10.2471/BLT.20.253583
30. Eastburg L, Peckham A, Kawira E, et al. Extremely high birth prevalence of sickle cell disease in rural Tanzania. *Pediatr Blood Cancer*. 2020;67(11). doi:10.1002/pbc.28620.
31. Krause MA, Diakite SAS, Lopera-Mesa TM, et al. Thalassemia Impairs the Cytoadherence of Plasmodium falciparum-Infected Erythrocytes. *PLoS One*. 2012;7(5):e37214. doi:10.1371/journal.pone.0037214
32. Smart LR, Ambrose EE, Balyorugulu G, et al. Stroke prevention with hydroxyurea enabled through research and education: a phase 2 primary stroke prevention trial in Sub-Saharan Africa. *Acta Haematol*. 2023;146(2):95–105. doi:10.1159/000526322
33. Ghartey-Kwansah G, Boampong JN, Aboagye B, et al. The prevalence of α -thalassemia and its relation to plasmodium falciparum infection in patients presenting to clinics in Two Distinct Ecological Zones in Ghana. *Hemoglobin*. 2016;40(1):32–37. doi:10.3109/03630269.2015.1095207
34. Lamptey H, Ofori MF, Adu B, et al. Association between alpha-thalassaemia trait, Plasmodium falciparum asexual parasites and gametocyte carriage in a malaria endemic area in Southern Ghana. *BMC Res Notes*. 2019;12(1):134. doi:10.1186/s13104-019-4181-8
35. Williams TN, Maitland K, Ganczakowski M, et al. Red blood cell phenotypes in the alpha + thalassaemias from early childhood to maturity. *Br J Haematol*. 1996;95(2):266–272. doi:10.1046/j.1365-2141.1996.d01-1906.x
36. Raffield LM, Ulirsch JC, Naik RP, et al. Common α-globin variants modify hematologic and other clinical phenotypes in sickle cell trait and disease. *PLoS Genet*. 2018;14(3):e1007293. doi:10.1371/journal.pgen.1007293
37. Qurtom HA, al-Saleh QA, Lubani MM, et al. The value of red cell distribution width in the diagnosis of anaemia in children. *Eur J Pediatr*. 1989;148(8):745–748. doi:10.1007/BF00443100