Original Article

Thalassemia and other hemoglobinopathies among anemic individuals in Metro Manila, Philippines and their intake of iron supplements

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Background and Objectives: Iron deficiency is the most common cause of anemia worldwide. In Southeast Asia, studies showed that genetic hemoglobin disorders also contribute significantly to the burden of anemia. The study aimed to estimate the proportion of thalassemia and other hemoglobinopathies versus iron deficiency and other causes in a sample of anemic individuals; describe the characteristics of thalassemic subjects in terms of severity of anemia, adequacy of iron stores, and hematological profile; examine the intake of iron supplements among individuals with varying causes of anemia. **Methods and Study Design:** A random sample of 101 anemic individuals living in Metro Manila was examined. Hemoglobinopathy was determined using capillary electrophoresis. Iron deficiency was determined using immunoradiometric assay for serum ferritin. A questionnaire was used to obtain information on the use of iron supplements. **Results:** The most frequent underlying cause of anemia was iron deficiency (37.6%), followed by anemia due to other causes (34.7%), and hemoglobinopathy (27.8%). The most prevalent form of hemoglobinopathy was alpha-thalassemia trait (20.8%), followed by beta-thalassemia trait (5%), iron deficiency anemia with concomitant HbE (1%), and beta-thalassemia HbE interacting (1%). Thalassemic subjects exhibited mild anemia, had either normal or excessive iron stores, and did not ingest iron supplements. **Conclusion:** The majority of anemia (62.5%) in this sample was due to other causes and hemoglobinopathy, rather than iron deficiency. Genetic hemoglobin disorders appear to be common among anemic individuals. Population screening is needed to determine the real prevalence of the disease. Further investigation is needed to identify other causes of anemia among Filipinos.

Key Words: thalassemia, genetic hemoglobin disorders, Philippines, anemia, iron deficiency

INTRODUCTION

Iron deficiency caused by blood loss and inadequate iron intake is the most common cause of anemia worldwide.[1] However, recent studies suggest that in certain countries particularly those in Southeast Asia, genetic hemoglobin disorders (or hemoglobinopathies) also contribute significantly to the burden of anemia.[2-6] There are two main groups of inherited hemoglobin disorders: thalassemias and structural hemoglobin variants.[7] Thalassemic syndromes occur when gene defects cause hemoglobin synthesis disorders. Hemoglobin structure in these cases is normal but the amount of hemoglobin synthesized is limited. Abnormal (variant) hemoglobin results when gene defects cause changes in hemoglobin structure.[8] Clinical symptoms vary from mild microcytic hypochromic anemia to life-threatening anemia requiring blood transfusions, depending on the type of abnormality inherited. In Southeast Asia, the most prevalent inherited hemoglobin disorders are α-thalassemia, β-thalassemia, hemoglobin (Hb) E and Hb Constant Spring (CS).[9] More than 60 different syndromes arising from various abnormal gene combinations have been identified, making Southeast Asia a region with several complex hemoglobinopathy genotypes.[9]

Genetic abnormalities such as thalassemias cause ineffective erythropoiesis. Ineffective erythropoiesis is a condition in which large numbers of marrow erythrocyte precursors undergo apoptosis or cell death and thus fail to develop into mature erythrocytes.[10] While homozygous individuals have more severe illness, heterozygous thalassemia carriers are not completely healthy as they always

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have symptoms associated with mild, iron-refractory (i.e., not responsive to iron treatment), microcytic hypochromic anemia.[8] Homozygous major forms are accompanied by serious hypochromic hemolytic anemias and complex diseases.[8]

Population genetics of both thalassemia and abnormal hemoglobin appears to be related to the geographical distribution of malaria, stretching across the African continent, Mediterranean region, Middle East, the Indian subcontinent, and the entire Southeast Asia. An estimated 300,000 babies are born each year with a severe inherited disorder of hemoglobin and approximately 80% of these births occur in low or middle income countries.[11]When two carriers marry, there is a 25% chance that their offspring will have full blown disease.[11] It is important to identify thalassemia and other genetic blood disorders in ethnic populations for the following reasons: 1) to identify pregnancies or planned pregnancies at risk of thalassemia major so that appropriate genetic counselling can be offered; 2) to prevent unnecessary and potential harmful medical intervention and iron therapy in patients with microcytic anemia due to thalassemia.[12]

Anemia due to iron deficiency is a public health problem in the Philippines. Hence, iron fortification and supplementation programs are being implemented to address this problem. However, anemia due to hemoglobinopathy is not amenable to dietary iron intervention, and instead requires blood transfusion and iron chelation.[9]Affected individuals are at risk for iron overload which increases risk for organ damage and chronic disease such as diabetes and cardiovascular disease.[13-15]In view of current information suggesting a high prevalence of hemoglobinopathy in Southeast Asia and the potential harm that can by inflicted by high iron intake to these patients, there is an urgent need to discriminate anemic individuals with nutritional iron deficiency from those with hemoglobinopathy.

The current study investigated the prevalence of thalassemia and other hemoglobinopathies as an underlying cause of anemia among Filipinos, using data from individuals in Metro Manila who were identified as anemic. The objectives were to: 1) estimate the proportion of thalassemia and other hemoglobinopathies in a random sample of anemic individuals living in Metro Manila, Philippines; 2) describe the characteristics of thalassemic subjects in terms of severity of anemia, adequacy of iron stores, and hematological profile; 3) examine the intake of iron supplements among individuals with varying causes of anemia.

PARTICIPANTS AND METHODS

The study was done among individuals aged 6 to 59 years old living in Metro Manila (in the National Capital Region) who were screened for anemia, as part of a national survey. A randomly selected sample of anemic individuals (n=101) were tested further for serum ferritin levels and the presence of genetic hemoglobin disorders. The study was approved by the Philippine Food and Nutrition Research Institute (FNRI) Institutional Ethics Review Committee. Informed consent was obtained from all adult subjects and in the case of children, from the parent or guardian.

Sample collection

An ISO 15189 accredited laboratory was selected to conduct complete blood count (CBC) and capillary electrophoresis for determination of hemoglobinopathy. Licensed medical technologists who had undergone one-month training on blood collection techniques and proper storage under field conditions were recruited to collect venous blood samples. Samples were drawn into two purple top vacutainer tubes with ethylenediaminetetraacetic acid (EDTA) as anticoagulant and one plain blue top trace element free vacutainer tube. From the first purple top tube, 0.5 mL of whole blood was transferred into a microcentrifuge tube and kept in the FNRI laboratory in a -40°C freezer. In an accompanying interview, subjects were asked if they took iron-containing vitamin and mineral supplements.

Determination of anemia

CBC (hemoglobin and other red blood cell (RBC) parameters) was analyzed on the day of blood collection and determined using the Sysmex Automated Hematology Analyzer. Cut-offs for anemia followed WHO recommendations for hemoglobin levels to diagnose anemia at sea level:[17] children 5 to 11 yrs (<115 g/L), 12 to 14 yrs (<120 g/L), non-pregnant women 15 yrs and above (<120 g/L), pregnant women (<110 g/L), men 15 yrs and above (<130 g/L).

Determination of serum ferritin

Serum ferritin levels were determined at the FNRI Biochemical Laboratory using an immunoradiometric assay procedure. The Coat-A-Count Ferritin IRMA kit distributed by DPC was used. Cut-offs for serum ferritin followed WHO recommendations[18] – i.e., depleted iron stores (less than 5 y of age <12 µg/L; above 5 y <15 µg/L); severe risk of iron overload, adults (male >200 µg/L, female >150 µg/L).

Determination of hemoglobinopathy

Capillary electrophoresis was performed on whole blood using Sebia Fully Automated Capillary Separation System, following manufacturer's instructions. Manufacturer's recommended normal ranges for healthy adults were as follows: HbA, 96.8% or more; HbF, less than 0.5%; and HbA_2, 2.2% to 3.2%. Resulting hematograms were sent to the consulting hematologist (AM) for interpretation.

Data analysis

Data were analyzed using SPSS version 17. Individuals were categorized according to cause of anemia, severity of anemia using WHO cut-off levels for hemoglobin at sea level, iron deficiency and extent of iron stores using WHO cut-off levels for serum ferritin, and use of iron supplements. Descriptive statistics for these variables were generated. Means and 95% confidence intervals were generated for red blood cell parameters in varying causes of anemia. Due to the small sample size, data for males and non-pregnant females (excluding pregnant females) were combined to obtain RBC parameters.

RESULTS

Table 1 shows the characteristics of the study sample. Majority (68%) were females mostly adults, with a few (5%) pregnant women.

Table 2 shows the distribution of anemia by underlying cause. The most frequent cause of anemia in this group of subjects was iron deficiency (37.6%), followed by anemia due to other causes (34.7%) that were not identified in this study, and hemoglobinopathy (27.8%). The most prevalent form of hemoglobinopathy was alpha thalassemia trait (20.8%), followed by beta thalassemia trait (5%). Less prevalent were IDA (iron-deficiency anemia) with concomitant Hemoglobin E (HbE) (1%) and beta thalassemia - HbE interacting (1%). Hemoglobinopathy was more prevalent in anemic females (18.8%) than males (8.9%). Hematological values of individuals with varying causes of anemia are shown in Table 3.

Using WHO criteria for severity of anemia,[17] majority of individuals with hemoglobinopathy and those with anemia due to other causes presented with mild anemia (64.3 and 68.6%, respectively) (Table 4). This was in contrast to those with iron deficiency anemia, where moderately severe anemia was more common (46.9%) than either mild (39.5%) or severe anemia (18.8%).

Table 5 shows iron status and extent of iron stores based on serum ferritin levels by underlying cause of anemia. Among subjects with hemoglobinopathy, majority (67.9%) had normal iron stores, 28.6% had high iron stores indicating risk of iron overload, and one individual (3.6%) had depleted iron stores. A similar trend is seen among individuals with anemia due to other causes. In contrast, all individuals with iron deficiency showed depleted iron stores.

Table 6 shows the number of subjects taking iron supplements, and Table 7 shows their iron status. All of the subjects with hemoglobinopathy (100.0%) did not ingest iron supplements. Similarly, majority of subjects with iron deficiency anemia (94.7%) and those with anemia due to other causes (95%) did not take iron supplements. Among those that used iron supplements (total of 5 individuals), 2 were iron-deficient while 3 had normal iron stores (Table 7).

DISCUSSION

Results showed that hemoglobinopathy was the cause of anemia in 27.5% of anemic individuals in the present sample and that α-thalassemia was the most common type. Hemoglobinopathy was also more common among anemic females than males. Only a few studies examined hemoglobinopathies among Filipinos and these showed varying results. A pilot study by Silao et al[19] used an HPLC system to detect abnormal hemoglobins among 285 randomly selected healthy individuals and individuals suspected to have hemoglobinopathy. Results showed a 28.6% prevalence of hemoglobinopathies, comprising 12.3% β-thalassemia with high HbA_2, 6.6% β-thalassemia with normal A_2, 4.9% β-thalassemia/HbE interacting, 4 individuals (1.4%) were heterozygous E while 1 individual (0.4%) was homozygous E, and 3% were suggestive of α-thalassemia. Mirasol et al[20] examined 1488 blood donors with low mean corpuscular volume (MCV), microcytic and hypochromic red blood cell indices from two hospitals and found that 3.1% had alpha thalassemia trait, 0.6% had beta thalassemia trait, 0.5% had HbE, while 3.0% had iron deficiency. Ko et al[21,22] examined 2954 apparently healthy Filipino workers living in Taiwan and found a prevalence of 6.7% for α-thalassemia trait and 0.9% for β-thalassemia trait. Padilla's[23] analysis of the newborn screening database in California USA showed that out of 111,127 Filipino babies born between 2005 to 2011, 0.1% (n=109) had various types of hemoglobinopathies. Of these, 85.3% (n=93) had HbH disease, 4.6% (n=5) had α-thalassemia major, 2.8% (n=3) were homozygous EE, 1.8% (n=2) had HbH/Constant Spring

Table 1. Distribution of the sample of anemic individuals in Metro Manila Philippines by age group, sex, and physiological status, 2013

Age group (yrs)	Males		Females		Pregnant women		Total	
	No.	%	No.	%	No.	%	No.	%
6–18.9	5	5.0	13	12.9	0	0.0	18	17.8
19–45.9	4	4.0	28	27.7	5	5.0	37	36.6
46–59	18	17.8	28	27.7	0	0.0	42	45.5
Total	27	26.7	69	68.3	5	5.0	101	100

Table 2. Distribution of underlying causes of anemia by sex and physiological status, Metro Manila Philippines, 2013

Underlying cause of anemia	Males		Females (non-pregnant)		Pregnant females		Total	
	No.	%	No.	%	No.	%	No.	%
Iron deficiency anemia	2	2.0	33	32.7	3	3.0	38	37.6
Hemoglobinopathy	9	8.9	19	18.8	-	-	28	27.8
α – thalassemia	(7)	(6.9)	(14)	(13.9)	-	-	(21)	(20.8)
β – thalassemia	(2)	(2.0)	(3)	(3.0)	-	-	(5)	(5.0)
IDA (iron deficiency anemia)- HbE	-	-	(1)	(1.0)	-	-	(1)	(1.0)
β-thalassemia/HbE interacting	-	-	(1)	(1.0)	-	-	(1)	(1.0)
Normal HbA, HbA_2, serum ferritin (anemia due to other causes)	16	15.8	17	16.8	2	2.0	35	34.7
Total	27	26.7	69	68.3	5	5.0	101	100

Table 3. Hematological profile of individuals by underlying cause of anemia (males and non-pregnant females combined), Metro Manila Philippines, 2013

Hematological indices	Iron deficiency anemia (n=38)		Alpha-thalassemia (n=21)		Beta-thalassemia (n=5)		IDA/HbE (n=1)	Beta-thalassemia/HbE (n=1)	Anemia due to other causes (n=35)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Value	Value	Mean	95% CI
Hemoglobin (g/L)	100	95.3, 105.7	114	110.8, 117.8	112	96.3, 126.9	66.0	105	113	108.3, 118.1
MCV (fL)	72.6	69.6, 75.7	67.8	66.5, 69.0	65.4	61.5, 69.3	55.4	66.9	91.7	89.2, 94.2
MCH (Pg)	22.4	21.0, 23.7	21.3	20.8, 21.8	20.6	19.3, 21.9	14.7	23.5	30.3	23.8, 25.7
MCHC (g/dL)	30.6	29.9, 31.3	31.4	30.9, 31.9	31.5	30.3, 32.7	26.6	35.1	33.2	32.4, 33.9
HbA_2	2.2	2.1, 2.3	2.2	2.1, 2.4	6.0	5.2, 6.9	2.9	3.9	2.6	2.5, 2.7
HbA	97.8	97.7, 97.9	96.7	95.1, 98.2	92.9	91.6, 94.1	76.7	69.5	97.2	96.9, 97.3
Serum ferritin (µg/L)	3.7	2.6, 4.8	125	63.2, 186.4	205	0.0, 427	1.0	59.0	156	103, 208
RDW (%)	16.7	15.8, 17.5	15.7	14.9, 16.4	17.0	14.2, 19.7	20.2	14.8	14.2	13.3, 15.1
RBC count ($x10^{12}$/L)	4.5	4.3, 4.7	5.4	5.2, 5.6	5.4	4.5, 6.4	4.5	4.5	3.8	3.6, 3.9

Table 4. Severity of anemia by underlying cause, Metro Manila Philippines, 2013

Underlying cause of anemia	Severity of anemia†							
	Mild		Moderate		Severe		Total	
	No.	%	No.	%	No.	%	No	%
Iron deficiency	15	39.5	17	46.9	6	18.8	38	100
Hemoglobinopathy	18	64.3	9	32.1	1	3.6	28	100
α-thalassemia	(16)	(76.2)	(5)	(23.8)	(0)	(0.0)	(21)	(100)
β-thalassemia	(2)	(40.0)	(3)	(60.0)	(0)	(0.0)	(5)	(100)
IDA-HbE	(0)	(0.0)	(0)	(0.0)	(1)	(100)	(1)	(100)
β-thalassemia HbE interacting	(0)	(0.0)	(1)	(100)	(0)	(0.0)	(1)	(100)
Normal HbA& HbA_2, Ferritin (anemia due to other causes)	24	68.6	9	25.7	2	5.7	35	100
Total	57	56.4	35	34.7	9	8.9	101	100

†Based on WHO cut-offs.[17]

Table 5. Adequacy of iron stores by underlying cause of anemia, Metro Manila Philippines, 2013

Underlying cause of anemia	Serum ferritin level†							
	Normal iron stores		Depleted Iron stores		Severe risk of iron overload		Total	
	No.	%	No.	%	No.	%	No.	%
Iron deficiency	0	0.0	38	100	0	0.0	38	100
Hemoglobinopathy	19	67.9	1	3.6	8	28.6	28	100
α-thalassemia	(16)	(76.2)	(0)	(0.0)	(5)	(23.8)	(21)	(100)
β-thalassemia	(2)	(40.0)	(0)	(0.0)	(3)	(60.0)	(5)	(100)
IDA-HbE	(0)	(0.0)	(1)	(100)	(0)	(0.0)	(1)	(100)
β-thalassemia HbE interacting	(1)	(100)	(0)	(0.0)	(0)	(0.0)	(1)	(100)
Anemia due to other causes	24	68.6	0	0.0	11	31.4	35	100
Total	43	42.6	39	38.6	19	18.8	101	100

†Based on WHO cut-offs.[18]

disease, 1.8% (n=2) had sickle cell C disease, 0.9% (n=1) had β-thalassemia major, 0.9% (n=1) had HbE/β + thalassemia, 0.9% (n=1) had Hb variant/β+ thalassemia, and 0.9% (n=1) had sickle cell anemia.

Non-transfusion-dependent thalassemia and accompanying disease risk

In the present study, most of the subjects (68%) with hemoglobinopathy presented with mild anemia (shown in Table 3), and it was not known if the severely anemic female with IDA-HbE was undergoing transfusion therapy. There are two categories to describe thalassemia patients based on disease management: non-transfusion-dependent thalassemias (NTDT) and transfusion-dependent thalassemia (TDT). NTDT are thalassemic patients that do not require regular blood transfusions for survival, have a very mild phenotype, and exhibit normal growth.[14,24] NTDT individuals are primarily found in Southeast Asia, stretching into the Middle East and Mediterranean region to sub-Saharan Africa. It has now been established that morbidity in NTDT patients is more common and serious than previously thought.[14] Although NTDT patients do not depend on regular transfusions to address anemia, their intestinal iron absorption from a standard diet is increased by as much as 3 to 4 times those of a normal person,[25] making them susceptible to iron overload. In a study among Thai women, Zimmerman etal[26] found that iron absorption in α- and β-thalassemia heterozygotes was significantly higher compared with control groups having normal hemoglobin.

Iron accumulation in NTDT is a slow process, compared with TDT. The rate of iron loading in NTDT patients is approximately 0.01 mg Fe/kg/day, compared with 0.30-0.60 mg Fe/kg/day among TDT patients.[27] NTDT patients may accumulate a total of 3 to 4 mg Fe/day or as much as 1000 mg Fe/year.[14] The hepatic peptide hepcidin which regulates iron absorption is disproportionately low in thalassemic individuals, allowing iron to be absorbed from the gut even in the presence of severe overload. By the third or fourth decade, the iron load in NTDT adults may be similar in magnitude to that of transfusion-dependent patients in their teens.[28] Liver iron concentration is the gold standard indicator of body iron stores, measured using magnetic resonance imaging (MRI) methods. It has been shown that NTDT patients eventually accumulate clinically significant liver iron concentration (LIC) levels and start experiencing iron-related morbidity beyond 10 years of age.[14,27]

Iron accumulation in NTDT with advancing age results in high levels of "free iron" in plasma, capable of reacting with reactive oxygen species (ROS) such as peroxide and superoxide (by-products of aerobic metabolism) to produce damaging free radicals. Increased free radical formation is linked to pathological processes such as inflammation and subsequent organ damage. Complications in NTDT due to iron overload include pulmonary hypertension, endocrine complications such as delayed puberty, leg ulcers, osteoporosis, vascular disease, and renal damage.[27] It was shown that an LIC increase of 1 mg Fe/g dry weight was independently and significantly associated with higher odds of thrombosis, pulmonary hypertension, hypothyroidism, osteoporosis, and hy-

pogonadism. LIC of ≥7 and 6 mg Fe/g dry weight were associated with established vascular and endocrine/bone morbidity, respectively.[29]

Compared with LIC, serum ferritin is considered an alternative and less expensive measure of body iron stores. In the absence of inflammation, the concentration of serum ferritin is positively correlated with the size of total body iron stores. A low serum ferritin value reflects depleted iron stores, whereas high serum ferritin concentrations indicate iron overload in the absence of inflammation or liver disease.[18] In this study, inflammation was not examined. Majority of subjects with hemoglobinopathy had either normal serum ferritin levels or high levels suggesting risk of iron overload. Only one subject exhibited depleted iron stores (Table 3). Since serum ferritin acts as an acute phase protein, increasing in the presence of inflammatory disorder, long-term monitoring of ferritin is recommended to gain additional information for thalassemia diagnosis.[30] It should also be noted however that studies demonstrated that serum ferritin underestimates iron burden in patients with NTDT. At similar LIC, patients with NTDT show considerably lower serum ferritin levels compared with TDT patients.[30]

Hematological profile of Filipino thalassemic and non-thalassemic subjects

Complete blood count (CBC) is a primary screening test for thalassemia.[31] Table 3 shows that CBC hematological values tend to overlap in patients with thalassemia trait and those with iron deficiency. It has been suggested that in geographic regions where iron deficiency is high, the cut-offs for routinely derived hematological values for thalassemia interpretation should be adjusted to more suitable values by using a receiver operator characteristic (ROC) curve, to better differentiate thalassemic microcytosis from non-thalassemic conditions (e.g., iron deficiency) in a specific population.[31] However, a bigger sample size than in the present study is needed to provide reliable cut-off values. A proposed alternative is the use of discriminant functions (Df) using a number of red blood cell indices to distinguish between thalassemia trait and iron deficiency.[32] These formulae include among others, England and Fraser index, Mentzer's index, and Shine and Lal index. The limitation is that these criteria may result in diagnostic errors in populations where the prevalence of iron deficiency is higher than that of thalassemia, although Dfs may help determine which patients need further screening tests.[32]

Diet for thalassemia patients

Due to their high rates of intestinal iron absorption and tendency to develop iron overload, dietary iron reduction is the focus of nutritional intervention in patients with thalassemia.[33] Hence the use of iron-containing supplements and iron-fortified foods should be avoided. For transfused patients, a daily multivitamin mineral supplement without iron is suggested, while folate supplementation is suggested for non-transfused patients.[33]

Fortunately, in the present study, all subjects with hemoglobinopathy did not ingest iron supplements, although there is no information regarding their intake of iron-rich or iron-fortified foods. In the Philippines, a law (RA 8976) has been passed requiring mandatory iron fortification of all rice (except brown rice and locally produced glutinous rice) and wheat flour. Rice is fortified with ferrous sulfate (60-90 mg Fe/kg raw rice) while wheat flour is fortified with elemental iron (70-105 mg Fe/kg) or ferrous sulfate or ferrous fumarate (50-75 mg Fe/kg).[34] While the law may have reduced the numbers of iron-deficient individuals, studies are needed to determine the amount of iron ingested from these food sources by individuals with thalassemia trait and its health effects on this population, both in the short- and long-term.

For NTDT patients where the main contributor to total iron burden is increased intestinal iron absorption,[24] it seems reasonable that dietary modification may help reduce iron burden although few studies have been undertaken. Elmoneim et al[25] examined the effect of modifying the diet of thalassemic patients to one containing foods with less iron and foods that inhibit iron absorption (e.g., dairy foods that contain calcium, high fiber foods with phytate, coffee and tea, curcumin and other polyphenol-containing cereals, vegetables, spices). Lower serum ferritin levels were observed after intervention compared to baseline ($p<0.002$) indicating that limiting foods containing iron and increasing intake of those that inhibit iron

Table 6. Intake of iron supplement by cause of anemia, Metro Manila Philippines, 2013

Cause of anemia	No iron supplement taken		Iron supplement taken		Total	
	No.	%	No.	%	No.	%
Iron deficiency	36	94.7	2	5.3	38	100
Hemoglobinopathy	28	100	0	0.0	28	100
Anemia due to other causes	32	91.4	3	8.6	35	100
Total	96	95.0	5	5.0	101	100

Table 7. Intake of iron supplement by adequacy of iron stores, Metro Manila Philippines, 2013

Serum ferritin concentration (µg/L)	No iron supplement taken		Iron supplement taken		Total	
	No.	%	No.	%	No.	%
≥15 (normal iron stores)	40	93.0	3	7.0	43	100
<15 (depleted iron stores)	37	94.9	2	5.1	39	100
Male >200; Female >150 (severe risk of iron overload)	19	100	0	0.0	19	100
Total	96	95.0	5	5.0	101	100

absorption can be an adjunct to the use of chelating agents in the treatment of thalassemia.

While iron should be avoided, it is recommended that patients should ensure adequate intake of other micronutrients including antioxidants since they are prone to high levels of oxidative stress.[35-37] Antioxidant compounds that have been isolated from various Asian foods and examined for use in thalassemia include curcuminoids from turmeric, catechins from tea, mangiferin and other phytochemicals from mango, pheophytin, catechin derivatives, and other antioxidant compounds from rice bran and rice grass.[38]

There is currently no data regarding dietary iron and other nutrient intakes of Filipino thalassemic individuals. A recent study[36] showed that thalassemia patients residing in the US and Canada consume inadequate amounts of vitamin A, D, E, folate, calcium, magnesium, and that adults were more likely than children to have inadequate intake. Fung[36] noted depressed circulating levels of nutrients despite seemingly adequate dietary intake, indicating that thalasssemic patients may have increased needs for certain nutrients due to either poor nutrient absorption, elevated losses or increased nutrient turnover. Examining the dietary intake and nutritional status of Filipino NTDT patients is a gap that needs to be addressed.

The present study showed that the proportion of individuals with anemia due to genetic hemoglobin disorders is at a level that cannot be ignored. Weatherall[11] stated that micro-mapping studies (i.e., studies involving analysis of samples taken from many different centers in a particular country or region) revealed significant heterogeneity in the distribution of hemoglobin disorders, often within short geographical distances. Genetic micro-mapping studies are needed to determine the real prevalence of the disease, and these should include all individuals regardless of anemia status.

Conclusion and recommendations

The study showed that genetic hemoglobin disorders are common among anemic individuals in Metro Manila, although less common than iron deficiency anemia and anemia due to other causes. Interventions that help prevent transmission include educating the public about thalassemia and hemoglobinopathy, screening couples prior to marriage, and providing genetic counselling to thalassemia carriers. Due to the hazards of high body iron levels, health monitoring should include not only iron deficiency but also excess iron stores. The government should re-examine its mandatory iron fortification program for rice and wheat flour and the distribution of iron supplements, evaluate their effects on thalassemic populations, and monitor these programs to ensure that patients who carry the trait and those with adequate iron stores are not exposed to excess iron intake, while those with depleted iron stores receive the fortified foods and supplements. Further studies are needed to examine dietary intakes and nutritional status of thalassemic individuals and to establish cut-offs for thalassemia screening among Filipinos. Also importantly, other causes of anemia in the Philippines need to be identified so that appropriate interventions can be implemented.

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Disclaimer

The views expressed in this paper are those of the authors and do not reflect the views of their respective institutions. All authors read and approved the final report.

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