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Research article

Magnitude and morphological types of anemia differ by age among under five children: A facility-based study

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ABSTRACT

Background: World Health Organization recently acknowledged the proportion of anemia attributable to iron deficiency among under-five children could be lower than the previously assumed 50%. Ethiopia reported 8.6% and 12.3% prevalence of iron deficiency anemia by serum ferritin and soluble transferrin receptor respectively. However, evidence generated from large samples on the magnitude of different types of anemias is limited. We aimed to determine the prevalence and morphological types of anemia in relation to age.

Methods: A retrospective analysis was conducted using electronic records of hemoglobin and red blood cell indices of 4739 children of 6–59 months of age who visited Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019. Microcytic hypochromic morphology combined with high red cell distribution width was used to estimate the prevalence of iron deficiency.

Results: About 44.7% of the children were anemic. Anemia affected 6–23 months old children (53.1%) more than 24–59 (37.2%) months ($p < 0.001$) with no difference among boys and girls. Iron deficiency and iron-deficiency anemia, as explained by microcytic hypochromic morphology with high red cell distribution width combined model, were estimated to be 38.6% and 24.1%, respectively. About 54% of anemic children had iron deficiency which was higher among 6–23 months (63.5%) than 24–59 months (41.8%) ($P < 0.001$; $X^2 = 98.883$). Regardless of anemia status, iron deficiency was two-fold higher among 6–23 months old children than 24–59 months of age. On the contrary, normocytic normochromic anemia affected significantly 24–59 months old children (23.1%) compared to 6–23 months. Less than 6% of the total anemia was macrocytic showing no significant relation with age. About 96% of macrocytic anemia was coupled with high red cell distribution width, indicating folate and vitamin B_{12} deficiency.

Conclusions: Microcytic hypochromic anemia with high red cell distribution width was the most prevalent type affecting primarily under two children. Normocytic normochromic anemia was significant among 24–59 months while macrocytic anemia had no age-related pattern. An in-depth study of causes of anemia other than iron deficiency particularly among 24–59 months children is essential.

1. Introduction

Anemia is a significant public health problem affecting nearly half of children under five years of age (under-5) globally with the highest burden in regions of Central and West Africa, South Asia and East Africa in their ranking order (Stevens et al., 2013; Kassebaum et al., 2014; Lopez et al., 2016). Anemia impairs physical growth, brain development as well as immunity, contributing to increased morbidity and mortality of under five children with far reaching negative impact of poor school performance and productivity. Its effect is exacerbated by the co-occurrence of a higher degree of malnutrition in the aforementioned regions (Development Initiatives, 2018).

The 2016 National Demographic and Health Survey of Ethiopia revealed that six out of ten preschool children were anemic with a significant increasing trend from 2011 to 2016 (CSA and ICF, 2016). However, little was known about the types of anemia the children were suffering from. Information is also limited on the contribution of the different types of anemia to the total magnitude. The micronutrient survey is the sole source of comprehensive information in Ethiopia that determined the prevalence of iron deficiency and iron deficiency anemia

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among preschool children and women of reproductive age at national level.

Iron deficiency is estimated to contribute to 50% of the total anemia among women (pregnant and non-pregnant) and 42% of cases in children aged under five years (Stevens et al., 2013). However, In its most recent nutritional anemias prevention and control tool, World Health Organization acknowledged the proportion of anemia attributable to ID could be lower than the previously assumed 50% (World Health Organization, 2017). Evidence derived from robust research is limited on how much of the anemia among preschool children is caused by iron deficiency particularly in developing countries (Lopez et al., 2016). Recently, studies have reported that the contribution of iron deficiency is by far less than half, challenging the previous estimation. A systematic analysis of national surveys of different countries reported that estimation of 50% of total anemia as attributable to iron deficiency is too high and it should no longer be used. The study also suggested estimation of iron deficiency as causing 25% and 37% of total anemia among preschool children and women of reproductive age respectively if there is no representative national data on iron deficiency anemia (Petry et al., 2016). This suggestion agrees with the finding of the national micronutrient survey of Ethiopia that reported the magnitude of iron deficiency among preschool children to be 18% and 30% using serum ferritin and soluble transferrin receptor biomarkers respectively. The survey also found 8.6% and 12.3% prevalence of iron deficiency anemia among the children with the respective biomarkers indicating that the contribution of iron deficiency anemia to total anemia among preschool Ethiopian children is lower than what has been previously thought (Ethiopian Public Health Institute, 2016).

Understanding the prevalence of the different types of anemia across each age group of under five children is essential to be able to formulate prevention strategies. Red blood cell indices are part of the routine complete blood count carried out in hospitals using different automated machines. They measure size, shape and color and other physical characteristics of red blood cells. Thus, red cell indices are very important in identification of different types of anemia by categorizing based on size and color of red blood cells (Singh and Gautam, 2015). This study determined the types and magnitude of anemia in relation to age among under five children visiting Hawassa University Comprehensive and Specialized Hospital (HUCSH) using red blood cell indices.

2. Materials & methods

This was a facility-based retrospective study using existing electronic hematological records of all under five children who visited Hawassa University Comprehensive and Specialized Hospital for health service and medical care between May 2017 and May 2019; thus, informed consent was not required. The study was ethically cleared by the Institutional Review Board of Hawassa University (Ref No: IRB/156/14). The hospital management provided access to the data after making an official request through a letter written by the School of Nutrition, Food Science and Technology of Hawassa University and verbal explanation about objective of the study. Retrieved in June 2019, the data received from the hospital lab was only age, sex, name of town/city of residence and hematological profiles without patient name, physical address and other identifiable data. In addition, there was no biological sample collected and no offensive procedure was carried out in the whole process.

Complete Blood Count (CBC) tests were conducted using CELL-DYN Ruby, SYSMEX and Mindray hematology analyzers. The hematological data included date and time of test, age, sex and address of the patient without names and results of CBC tests including hemoglobin and red blood cell indices. Statistical analysis was made using SPSS version 25.

Hemoglobin (Hgb) values were adjusted for altitude and cut off values for anemia set by WHO were used (WHO, 2011). Red blood cell indices used to classify anemia were mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and red cell distribution width (RDW). Reference ranges of red cell indices set by Hawassa University Comprehensive and Specialized Hospital laboratory quality control unit were used for analysis. They were derived from the ranges set by the manufacturers of the hematology analyzers used in the hospital lab.

In this study, a combined low MCV, low MCH and high RDW was taken as the best model to predict iron deficiency (ID) and iron deficiency anemia (IDA) prevalence considering the outputs as '*estimated true prevalence*'. The model used in this study is also supported by Tong et al. (2017) who combined MCV, MCHC and RDW to diagnose IDA and found 94% sensitivity and 90% specificity.

Because of increased demand for nutrients, high physical and brain development, low immunity and other factors, children of under two years of age are more vulnerable to and hence, affected by anemia than older children (CSA and ICF, 2016). Therefore, participants in this study were grouped by age as 6–23 and 24–59 months for statistical purposes. The age groups were compared for magnitude and morphological patterns of anemia. Comparisons of magnitude of anemia and morphological patterns were made between age groups of children of 6–23 and 24–59 months old. Similarly, comparison of anemias caused by micronutrient deficiencies (iron, folate and cobalamin) as estimated by combining MCV, MCH and RDW variables was made between children of 6–23 months and 24–59 months. Cross tabulation was carried out and Pearson chi square was used to compare groups. P-value of less than 0.05 was taken as statistically significant.

3. Results

3.1. Demographic characteristics and hematological profile of study children

Out of the total 80,096 people who were examined for hematological tests in the above specified time period, 4785 (6%) were children under the age of five years (6–59 months). Excluding extreme high and low values, a total of 4739 children were selected for analysis (Figure 1). Among these children, there were fewer females (41.2%) than males ($p < 0.001$; 95% CI = −0.10, −0.07). Similar trend of having few females was seen in both age groups of children of 6–23 months and 24–59 months old (40.2% and 42.2% respectively). However, difference in gender distribution among the age groups was not found ($p = 0.165$).

About 57.7%, 66.6% and 65.1% of the total children had low MCV, low MCH and high RDW RBC profiles, respectively (Table 1). These parameters were seen decreasing as age increased from 6 months to four years. Children of 6–23 months age had significantly higher prevalence of microcytic (70.6%) and hypochromic (76.7%) RBCs as well as high RDW (77.6%) when compared to children of 24–59 months who had 46.2%, 57.3% and 54.0% rates of the indices in their respective order ($p < 0.001$) (data not shown). On average, 4.7% of the children had macrocytic red cells with insignificant variation across the age groups (Table 1).

3.2. Prevalence of anemia

About 44.7% of the children were anemic (<11.0 g/dl of Hgb) out of which mild, moderate and severe anemia constituted 34.1%, 47.9% and 18.1%, respectively, based on WHO classification (WHO, 2011) (Table 1). Anemia was found to decrease as age increased (Figure 2). Children of 6–23 months of age were significantly more affected by anemia (53.1%) than 24–59 months old children (37.2%) ($X^2 = 121.592$; $p < 0.001$). No difference was seen between males and females in terms of anemia prevalence ($p = 0.444$).

3.3. Morphologic classification of anemia

Among the total anemic children (N = 2117), 66.4% were microcytic, 5.7% were macrocytic, 27.9% were normocytic, 74.8% were hypochromic and 81.8% had higher RDW (Table 2). Children of 6–23 months age had significantly higher microcytic (75.2%), hypochromic (81.6%) and

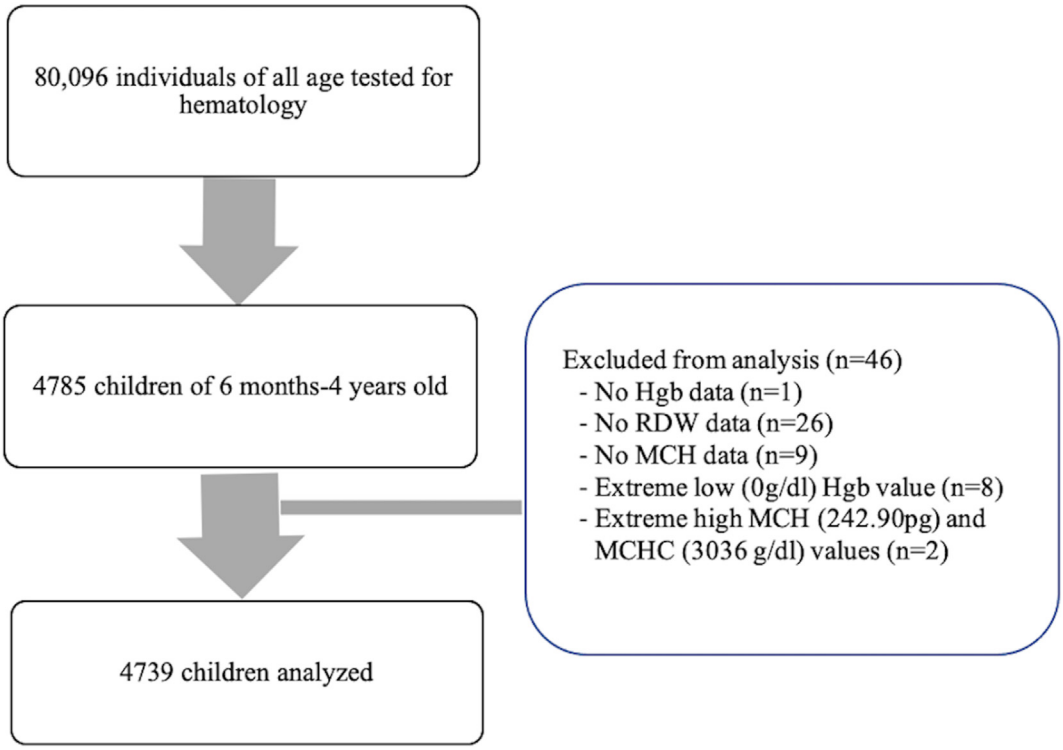

Figure 1. Flow diagram for selection of 6–59 months of age children visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

Table 1. Demographic characteristics and hematological profile of 6–59 months of age children visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

Characteristic	Description	N (%)
Child Sex	Male	2785 (58.8)
	Female	1954 (41.2)
Age category	6–23 months	2231 (47.1)
	24–59 months	2508 (52.9)
Hemoglobin (Hgb)	Anemia, total (<11.0 g/dl)	2117 (44.7)
	Mild anemia (10.0–10.9 g/dl)	721 (34.1)
	Moderate anemia (7.0–9.9 g/dl)	1013 (47.9)
	Severe anemia (<7.0 g/dl)	383 (18.1)
Mean Corpuscular Volume (MCV)	Low (Microcytic) (<80 fl)	2736 (57.7)
	High (Macrocytic) (>97fl)	224 (4.7)
Mean Corpuscular Hemoglobin (MCH)	Low (Hypochromic) (<26 pg)	3154 (66.6)
	High (Hyperchromic) (>32 pg)	161 (3.4)
Mean Corpuscular Hemoglobin Concentration (MCHC)	Low (<31 g/dl)	2357 (49.7)
	High (>36 g/dl)	52 (1.1)
Red cell Distribution Width (RDW)	Low width (<11.5%)	122 (2.6)
	High width (>14.5%)	3083 (65.1)

higher RDW (86.9%) anemia when compared to those 24–59 months old with 55.2%, 66.2% and 75.2% rates of the indices in the respective order ($p < 0.001$). In contrast, 24–59 months old children had two times higher normocytic (39.2%), normochromic (31.0%) and normal RDW (23.5%) anemia than children of 6–23 months of age ($p < 0.001$).

3.4. Prevalence of iron deficiency and iron deficiency anemia

About 28.2% of the children had microcytic and hypochromic anemia. The prevalence of ID and IDA as explained by combined low MCV, low MCH and high RDW (and Hgb of <11 g/dl for IDA) model was estimated to be 38.6% and 24.1%, respectively among all children visiting HUCSH from may 2017 to May 2019. As age increased from 6 to 59 months, the number of children with microcytic, hypochromic and high RDW RBCs (with or without Hgb <11 g/dl) decreased. About 53.5% of under two children had RBCs of low MCV, low MCH and high RDW (estimated ID) which was 2.1 times higher than that of children of 24–59 months old (25.4%) ($p < 0.001$; $X^2 = 394.981$). Moreover, 33.8% of under two children had microcytic, hypochromic anemia with high RDW (estimated IDA) which was 2.2 times higher than that of children of 2–4 years old (15.6%) ($p < 0.001$; $X^2 = 213.727$). Among the non-anemic group, 6–23 months old children were 2.7 times more affected by ID (estimated) than children of 24–59 months old (Table 3).

About 54.0% of anemic children had ID as estimated by low MCV, low MCH and high RDW combined model. Anemic children of 6–23 months age (63.5%) were significantly affected by ID (estimated) compared to 24–59 months old children (41.8%) ($p < 0.001$; $X^2 = 98.883$) (Table 3). To the contrary, normocytic normochromic anemia was higher among 24–59 months old children (23.1%) than 6–23 months (9.9 %) ($p < 0.001$; $X^2 = 68.693$). ID (estimated) was also found to be significantly higher among under three children than three years and above children ($p < 0.001$; $X^2 = 75.064$).

Microcytic hypochromic anemia and normocytic normochromic anemia showed a trend opposite to each other particularly in the period between 6 and 47 months of age: the former decreased and the later went up. Iron deficiency anemia (estimated as low MCV, low MCH and high RDW with Hgb <11 g/dl) showed insignificant fluctuation at two age periods: 6–23 months with prevalence rate ranging between 64.3 and 63% and 36–59 months with rates ranging from 37.7 to 38.1%. The age 24–35 months lied between these two age periods with a prevalence of 47.2%. Iron deficiency (estimated prevalence) was significantly higher among 6–23 months old anemic children than 24–35 months ($p < 0.001$; $X^2 = 32.803$) who in turn had significantly higher rate than that of 36–59 months old children ($p = 0.004$; $X^2 = 8.180$).

Normocytic normochromic anemia also showed a trend of little change between the age of 6–23 months ranging from 8.3% to 11.1%

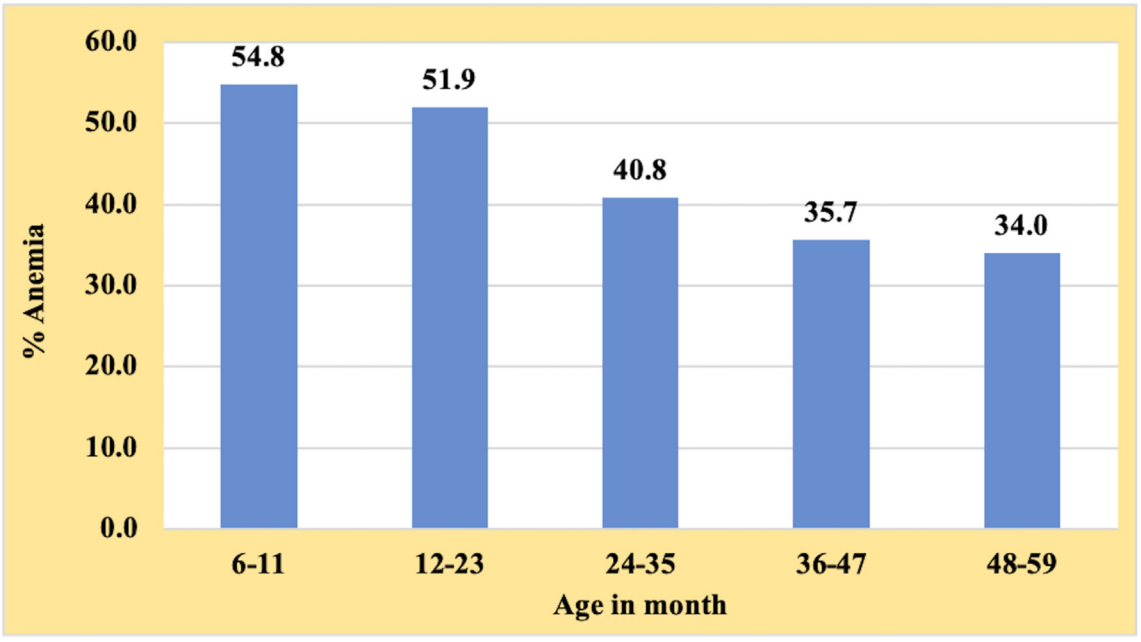

Figure 2. Magnitude of anemia by age among 6–59 months old children visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

Table 2. Morphological classification of anemia among 6–59 months of age anemic children visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

RBC indices		Total (N = 2117)	6–11 months (N = 518)	12–23 months (N = 667)	24–35 months (N = 396)	36–47 months (N = 276)	48–59 months (N = 260)
MCV	Microcytic	1405 (66.4%)	401 (77.4%)	490 (73.5%)	233 (58.8%)	147 (53.1%)	134 (51.5%)
	Macrocytic	121 (5.7%)	27 (5.2%)	41 (6.1%)	21 (5.3%)	15 (5.4%)	17 (6.5%)
	Normocytic	591 (27.9%)	90 (17.4%)	136 (20.4%)	142 (35.9%)	114 (41.3%)	109 (41.9%)
MCH	Hypochromic	1584 (74.8%)	438 (84.6%)	529 (79.3%)	275 (69.4%)	175 (63.4%)	167 (64.2%)
	Hyperchromic	66 (3.1%)	18 (3.5%)	22 (3.3%)	11 (2.8%)	7 (2.5%)	8 (3.1%)
	Normochromic	467 (22.1%)	62 (12.0%)	116 (17.4%)	110 (27.8%)	94 (34.1%)	85 (32.7%)
MCHC	Low MCHC	1242 (59.3%)	295 (57.4%)	415 (62.8%)	237 (60.9%)	150 (55.1%)	145 (56.0%)
	High MCHC	21 (1.0%)	4 (0.8%)	11 (1.7%)	2 (0.5%)	2 (0.7%)	2 (0.8%)
	Normal MCHC	832 (39.7%)	215 (41.8%)	235 (35.6%)	150 (38.6%)	120 (44.1%)	112 (43.2%)
RDW	Low RDW	18 (0.9%)	2 (0.4%)	4 (0.6%)	2 (0.5%)	4 (1.4%)	6 (2.3%)
	High RDW	1731 (81.8%)	445 (85.9%)	585 (87.7%)	315 (79.5%)	202 (73.2%)	184 (70.8%)

followed by a significant increase at the age of 24–35 months (21.5%) ($p < 0.001$; $X^2 = 35.784$) that continued with rates varying insignificantly till the age of 59 months ($p = 0.998$; $X^2 = 0.318$). Microcytic hypochromic anemia (with or without high RDW) and normocytic normochromic anemia did not show significant change of trend between 36 and 59 months of age period. Macrocytic anemia showed very little fluctuation of prevalence across ages of the children. About 96% of macrocytic anemia was coupled with high RDW (Figure 3).

4. Discussion

This study determined the magnitude and trend of different types of anemias classified based on red blood cells morphology among under five children who visited HUCSH from May 2017 to May 2019. Parameters of RBC indices have been used individually or in combination to measure nutrient deficiencies and different types of anemias including ID and IDA though they do lack specificity. For this study, it was essential to develop scientifically meaningful model by combining the different parameters of RBC indices rather than using a single index for better estimation of the magnitude of ID and IDA. Low MCV (microcytic) and low MCH (hypochromic) red blood cells are typical features of ID and IDA. However, inflammation can also cause microcytic anemia. Higher RDW is a characteristics observed more commonly in ID/IDA than infection particularly among pediatrics population (Novak, 1987; Silva Litao and Kamat, 2018). Studies reported elevated RDW mainly in adults with chronic illnesses particularly cardiovascular and pulmonary diseases as well as related syndromes (Ozsu et al., 2012; Li et al., 2017; Al-Kindi et al., 2017; Schepens et al., 2017). An efficiency trial in India reported the use of RDW of >15 and Hgb of <10 in combination to diagnose IDA in children of 1–3 years old yielding a sensitivity of 99% and specificity of 90% without the need of iron status markers (Sazawal et al., 2014). In addition, the use of RDW was reported to be a reliable and useful parameter for detection of ID during pregnancy (Sultana et al., 2011; Bibi et al., 2018). Therefore, combining the three indices, we defined ID as low MCV (<80fl), low MCH (<26pg) and high RDW (>14.5%) and IDA as low MCV, low MCH, high RDW and low Hgb (<11 g/dl) for our analysis which is very similar model used by (Tong et al., 2017).

The prevalence of all anemia cases found in Hawassa University Comprehensive and Specialized Hospital (44.7%) was lower than the national average (57%) reported by demographic health survey (DHS) of Ethiopia (CSA and ICF, 2016) but higher than that of the micronutrient survey (34.4%) (Ethiopian Public Health Institute, 2016). This might be

Table 3. Magnitude of microcytic-hypochromic red blood cell morphology among 6–59 months of age children visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

Age in month	All children							Anemic children					Non-anemic children		
	Number of children	Low MCV and MCH	Low MCV + High RDW	Low MCV and MCH + High RDW	Low MCV and MCH + Hgb <11 g/dl	Low MCV + High RDW + Hgb <11 g/dl	Low MCV and MCH + High RDW + Hgb <11 g/dl	Number of children	Low MCV and MCH	Low MCV + High RDW	Low MCV and MCH + High RDW		Number of children		Low MCV and MCH + High RDW
	N	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)		N (%)		N (%)
6–11	946	684 (72.3)	540 (57.1)	525 (55.5)	394 (41.6)	338 (35.7)	333 (35.2)	518 (54.8)	394 (76.1)	338 (65.3)	333 (64.3)		428 (45.2)		192 (44.9)
12–23	1285	812 (63.2)	699 (54.4)	669 (52.1)	470 (36.6)	434 (33.8)	420 (32.7)	667 (51.9)	470 (70.5)	434 (65.1)	420 (63.0)		618 (48.1)		249 (40.3)
24–35	970	447 (46.1)	349 (36.0)	315 (32.5)	221 (22.8)	195 (20.1)	187 (19.3)	396 (40.8)	221 (55.8)	195 (49.2)	187 (47.2)		574 (59.2)		128 (22.3)
36–47	773	281 (36.4)	195 (25.2)	172 (22.3)	129 (16.7)	112 (14.5)	104 (13.5)	276 (35.7)	129 (46.7)	112 (40.6)	104 (37.7)		497 (64.3)		68 (13.7)
48–59	765	256 (33.5)	163 (21.3)	149 (19.5)	122 (15.9)	102 (13.3)	99 (12.9)	260 (34.0)	122 (46.9)	102 (39.2)	99 (38.1)		505 (66.0)		50 (9.9)
6–23	2231	1496 (67.1)	1239 (55.5)	1194 (53.5)	864 (38.7)	772 (34.6)	753 (33.8)	1185 (53.1)	864 (72.9)	772 (65.1)	753 (63.5)		1046 (46.9)		441 (42.2)
24–59	2508	984 (39.2)	707 (28.2)	636 (25.4)	472 (18.8)	409 (16.3)	390 (15.6)	932 (37.2)	472 (50.6)	409 (43.9)	390 (41.8)		1576 (62.8)		246 (15.6)
Total	**4739**	**2480 (52.3)**	**1946 (41.1)**	**1830 (38.6)**	**1336 (28.2)**	**1181 (24.9)**	**1143 (24.1)**	**2117 (44.7)**	**1336 (63.1)**	**1181 (55.8)**	**1143 (54.0)**		**2622 (55.3)**		**687 (26.2)**

due to the clinical nature of patients presenting at a hospital compared to national survey data that included both healthy and unhealthy subjects, as well as differences in target population, geographical location, and laboratory tests used to determine hemoglobin level. However, the prevalence was comparable with the findings of facility based studies in North East Ethiopia (41.1%) (Gebreweld et al., 2019), South West Ethiopia (46%) (Getaneh et al., 2000), Nigeria (49.2%) (Ughasoro et al., 2015), Nepal (49.5%) (Joshi et al., 2015) and Ghana (47.5%) (Parbey et al., 2017). In addition, a retrospective study from Ghana which is methodologically similar with ours reported very comparable levels of mild, moderate and severe anemia among under five children (Adu-A-mankwaah et al., 2018).

Historically, as reported in the last three demographic and health surveys, anemia among under five Ethiopian children has had a decreasing trend as age increased being under two children the most affected group (CSA and ORC Macro, 2006; CSA and ICF International, 2012; CSA and ICF, 2016). The same trend was found in our study that 6–23 months old children were disproportionately affected (1.43 times higher) by anemia compared to 24–59 months. This may imply that infants and young children are always most affected group among under five Ethiopian population regardless of clinical status. A Ethiopian Public Health Institute (2016) retrospective study from Ghana reported an opposite trend which might be due to the small sample size per each age group and factors related with feeding practices (Adu-Amankwaah et al., 2018).

Microcytic hypochromic anemia was the most common type of anemia which was comparable with the Ghana retrospective study (Adu-A-mankwaah et al., 2018). Both ID (38.6%) and IDA (24.1%) (estimated prevalence) were a bit higher than what was reported by the Ethiopian micronutrient survey which can be explained by the effect of infection related with the target population of our study and the lack of specificity of RBC indices in determining ID (Ethiopian Public Health Institute, 2016). However, comparable findings were reported by facility-based studies in Nigeria (42.3% of ID) (Ughasoro et al., 2015) and Ghana (28.8% of IDA) (Adu-Amankwaah et al., 2018). Lopez et al. (2016) reported the magnitude of IDA to be 23% among hospitalized population in a seminar paper that summarized prevalence of anemia among different population group.

Our model showed that ID (low MCV, low MCH and high RDW) was more prevalent at an early age among under five children. It was two-fold higher among 6–23 months old children than 24–59 months of age who visited HUCSH regardless of their anemia status. Among the non-anemic group, children of 6–23 months age were 2.7 times more affected by ID than 24–59 months. Other studies have also reported similar findings (Hinchliffe et al., 2013; Lopez et al., 2016; Adu-Amankwaah et al., 2018). Higher physiological demand for iron and other nutrients, recurrent infection and inadequate iron intake and other factors put infants and young children at higher risk of ID (WHO, 2016).

About 54% of children with anemia had morphological expression of microcytic hypochromic RBCs with higher distribution width that provided an estimation of more than half of the anemia among 6–59 months old children visiting HUCSH is attributed to ID. This estimated prevalence of ID among anemic children was higher than that of WHO's approximation of 42% contribution of ID to total anemia (World Health Organization, 2017). It was also higher than that of Ethiopian Public Health Institute report that attributed 35.7% of the anemia among children of 6–59 months old was due to iron deficiency (ID measured by elevated soluble transferrin receptor) (Ethiopian Public Health Institute, 2016). This can be partly due to effect of inflammation as our target children are referral hospital visitors in addition to low specificity of RBC indices in diagnosing ID.

The contribution of different types of anemia to the total anemia showed significant difference among age groups suggesting the need of preventive and curative interventions designed systematically. Anemia with low MCV, low MCH and high RDW attributed nearly two thirds of the total anemia among 6–23 months old children which was significantly higher than that of children of 24–59 months age (41.8%). This

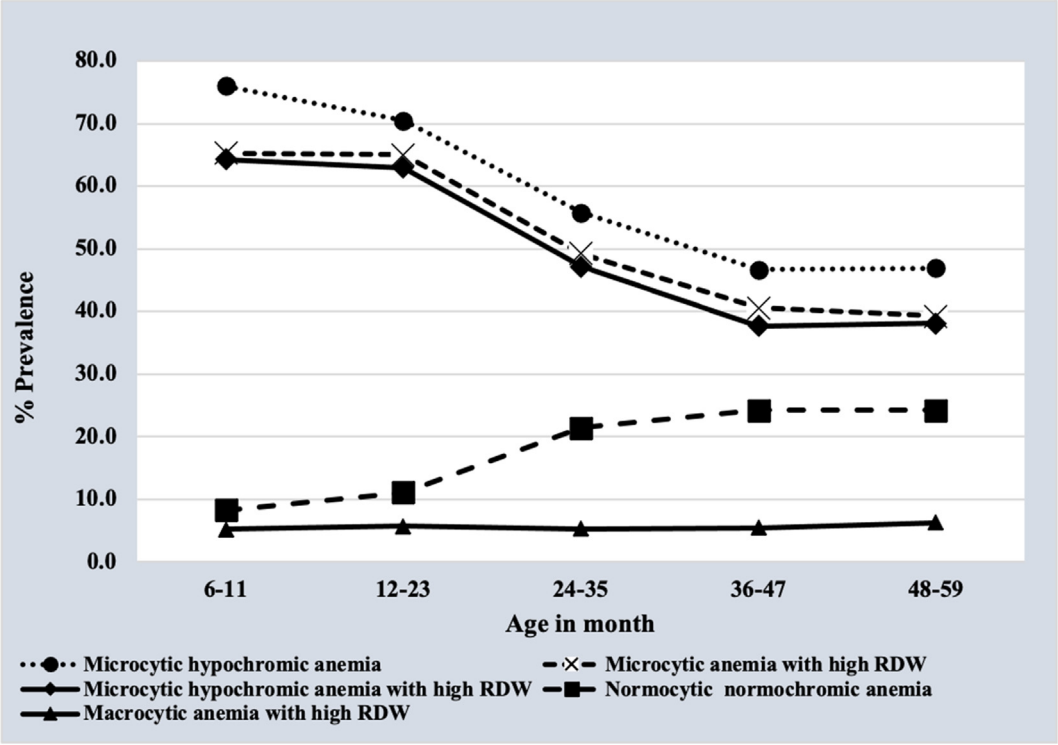

Figure 3. Prevalence and trend of normocytic, microcytic and macrocytic anemia among anemic children of 6–59 months old visiting Hawassa University Comprehensive and Specialized Hospital from May 2017 to May 2019.

finding strengthens the fact that under two children are disproportionately affected by IDA (Lopez et al., 2016; World Health Organization, 2017). Trend analysis revealed that children of all age groups were affected by anemia of low MCV, low MCH and high RDW (IDA). Though the prevalence showed significant differences in relation to age, the magnitude was high in all age groups to the level of public health concern. Even among the least affected group (36–59 months old), nearly 4 out of 10 children had low MCV, low MCH and high RDW anemia (IDA). Supporting our finding is the report of Ethiopian food consumption survey that revealed iron intake of under five children is considerably low even though there is high prevalence of excessive intake of iron among the adult population (63.6% in women and 89% in urban males). Dairy foods constituted above 50% of diet of the children which is low in iron that followed by cereals/grains (less than 20%) (Ethiopian Public Health Institute, 2013). Strengthening implementation of interventions including maternal iron folate supplementation, promotion of maternal iron rich foods intake (Menon et al., 2016), delayed cord clamping (World Health Organization, Nutrition for Health and Development & World Health Organization. 2014), malaria and intestinal parasite control and nutrition education that enable prevention of IDA at an early age is very essential to reduce the burden even at later age. Community-based nutrition interventions should promote iron rich complementary foods including animal source foods, iron absorption enhancers and techniques known to increase bioavailability of iron. WHO also recommends daily iron supplementation with different doses for infants and young children (6–23 months old) and preschool age children (24–59 months old), living in areas where anemia is 40% and above for three consecutive months in a year to prevent ID and anemia (WHO, 2016).

Normocytic normochromic anemia, the second most common, contributed to nearly a quarter of the total anemia among children aged 24–59 months which was significantly higher than that of 6–23 months. Similarly, Adu-Amankwaah et al. (2018) reported children of 24–59 months were more affected by normocytic normochromic anemia than 6–23 months. Our finding indicated that there are important causes of anemia other than ID that are affecting significant number of children of under-five years, particularly those two years old and above, that need to be addressed for effective treatment and meaningful reduction of anemia in this age group. Normocytic anemia has multiple causes including nutritional deficiencies, acute blood loss, and diseases like hemolysis and renal disease (Lanzkowsky, 2005; Adamson and Longo, 2010). In depth study of etiological factors is required to design remedial action strategically.

Important to note in the trend of microcytic hypochromic and normocytic normochromic anemias was their magnitude at the age of 24–35 months. Both types of anemia were significantly high in this group of children because of two reasons. Normocytic anemia which was relatively low at earlier ages started a remarkable increase at this age. The second reason is that even though microcytic anemia which was at its highest rate at earlier ages showed the first decrease at this time, the prevalence was still significantly higher than the one seen at later ages. This finding indicated both ID and other causes of anemia are important to be considered in preventive and curative interventions that targeted this age group suggesting rigorous study for better understanding of the types and causes of anemias specifically.

Macrocytic anemia constituted less than 6% of the total anemia among children of 6–59 months who visited HUCSH from May 2017 to 2019 affecting all ages almost equally. Compared to our finding, lower prevalence of macrocytosis (4.1%) and higher prevalence (18%) was reported by a study in Turkey (Sarbay and Ay, 2018) and India (Singh and Gautam, 2015) respectively which might be due to factors including differences in target age group, sample size and geography. Macrocytic anemias are classified as megaloblastic or non-megaloblastic. Megaloblastic anemias are characterized by impaired DNA synthesis and the presence of megaloblasts in the bone marrow mainly caused by folate and vitamin B_{12} deficiency (Lanzkowsky, 2016a). In non-megaloblastic anemias, there is no DNA synthesis impairment and megaloblastic change of the bone marrow. Chronic liver disease, alcohol abuse and drugs are the common causes of non-megaloblastic anemia (Manchanda, 2020).

About 96% of the macrocytosis in this study was coupled with high red cell distribution width which is a morphological feature of folate and

vitamin B_{12} deficiency (Lanzkowsky, 2016b). Vitamin B_{12} (15.1%) and folate deficiencies (17.3% as measured by serum folate and 32% by RBC folate) are significant nutritional problems among non-pregnant Ethiopian women of reproductive age (Ethiopian Public Health Institute, 2016). Animal source food and vegetable intake is very low particularly among under five children (Ethiopian Public Health Institute, 2013; CSA and ICF, 2016). Taking the above facts together and considering the presence of recurrent infections among under five Ethiopian children, folate and cobalamin deficiency might be the primary cause of the macrocytosis found in our target group. The ongoing efforts of iron folate supplementation for pregnant women and promotion of vegetables and animal source food intake by mothers and children should be strengthened as a prevention strategy. The lack of data on folate and vitamin B_{12} deficiency among under five Ethiopian children calls for a national survey.

As a limitation of this study, findings of this study could not be inferred to the general population as the target children were those visiting a referral hospital for any health and medical care. Medical condition of the children could have affected our estimation of the magnitude of iron and folate and cobalamin deficiency. The other limitation is related with the parameter we used to determine prevalence of some types of anemias among the pediatric population. Magnitude of ID, IDA and folate and cobalamin deficiency presented in this study should be treated carefully as they were estimated using red cell indices. The electric records retrieved from the hospital lab lack results of biomarkers important for differential diagnosis of anemia. Even if we used combined models for the best estimate, red cell indices lack specificity to determine nutritional deficiencies and identify other causes of anemia.

5. Conclusions

Anemia was prevalent to the level of public health concern among children of 6–59 months visiting HUCSH from May 2017 to May 2019 with the highest burden in infants and young children. Microcytic hypochromic anemia with high RDW, characteristic feature of ID, was the most prevalent type contributing to more than half of the total of anemia. Children of 6–23 months old were disproportionately more affected than 24–59 months by microcytic hypochromic anemia with high RDW. A quarter of the total anemia among children of 24–59 months was normocytic normochromic showing the importance of considering other causes of anemia apart from ID in prevention and curative interventions particularly in this age group. Unlike microcytic and normocytic anemias, macrocytosis did not show age related difference. Nearly all macrocytic anemia was seen with high red cell distribution width, which is indicative of folate and cobalamin deficiency. Large scale surveys engaging biomarkers are recommended for in-depth study of the types of anemia affecting children of under-five years of age.

Declarations

Author contribution statement

Anteneh Omer: Conceived and designed the experiments; Performed the experiments; Analysed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Afework Mulugeta: Conceived and designed the experiments; Analysed and interpreted the data; Wrote the paper.

Dejene Hailu: Performed the experiments; Analysed and interpreted the data; Wrote the paper.

Gezahegn Nigusse: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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