Review Article

Prevalence and Management of Anemia in Adolescents in Primary Care Settings

Abstract:

Anemia is defined as a drop in haemoglobin (Hb), hematocrit (HCT), or red blood cell (RBC) count.Anemia is a widespread issue in primary care, and primary care physicians are generally the first to notice its symptoms.Anaemia is a prevalent clinical concern among the adolescents. It is widely known that haemoglobin levels drop with age increase.Anemia has been linked to a variety of negative effects, including higher mortality, hospitalisation, and a worse quality of life. epidemiological reporting of anaemia is fragmented. Anemia is diagnosed in part by symptoms reported in general practice/family medicine (GP/FM). Management of anemia relies on the type of anemia and underlying cause, in this review we will be looking at Prevalence, etiology, classification and management of Anemia.

Introduction:

Anemia is defined as a drop in haemoglobin (Hb), hematocrit (HCT), or red blood cell (RBC) count. It is a symptom of a more serious underlying illness that might be classified as macrocytic, microcytic, or normocytic. Patients with anaemia usually have nonspecific symptoms such lethargy, weakness, and exhaustion. Syncope, shortness of breath, and impaired activity tolerance are all symptoms of severe anemia. [1]

Anaemia is a prevalent clinical concern among the adolescents. It is widely known that haemoglobin levels drop with age, and this is frequently observed in the presence of multimorbidity. The most recent estimates of anaemia in older populations show a prevalence of 10% , likewise contain figures are inevitably influenced by the classifications employed and the groups investigated. Although there are no age-specific reference values, the WHO classifies males with haemoglobin below 13.0 g/dL and women with haemoglobin below 12.0 g/dL as anemic. In a clinical environment, these cut-offs are often employed to emphasise aberrant laboratory results.It is unknown if these limits are suitable in adolescents populations when levels below these thresholds are frequent, or whether age-adjusted thresholds would be better. [2,3-8]

Anemia is a widespread issue in primary care, and primary care physicians are generally the first to notice its symptoms. Anemia is defined by the World Health. It affects people of all ages, although it is most common among the adolescents. Anemia appears to have more significant implications in older individuals, including an increased risk of morbidity, functional decline, and death. Despite this, anemia's importance in the adolescents population is underrated, and the illness frequently goes undetected and untreated. [9]

The principal activator of red blood cell (RBC) synthesis is erythropoietin (EPO), which is produced in the kidney. EPO synthesis is primarily stimulated by tissue hypoxia, and EPO levels are inversely proportional to haemoglobin concentrations. In other words, someone who is anaemic and has low haemoglobin has high EPO levels. In anaemic individuals with renal failure, however, EPO levels are lower than predicted. EPO levels are frequently raised in anaemia of chronic disease (AOCD), but not as high as they should be, indicating an EPO insufficiency.[1]

Anemia has been linked to a variety of negative effects, including higher mortality, hospitalisation, and a worse quality of life, according to research. However, it's unclear how much treating anaemia in adolescents individuals improves outcomes and reverses the identified negative connections. Randomized controlled studies have had conflicting results, and a recent comprehensive review found that oral or intravenous iron supplementation had no effect on mortality in adults. [2,10-17]

The normal ranges for haemoglobin (Hgb) vary significantly depending on the laboratory, but in general, the usual ranges are as follows: [1]

- Men's blood levels range from 13.5 to 18.0 g/dL.
- Women's blood levels range from 12.0 to 15.0 g/dL.
- Children's blood levels range from 11.0 to 16.0 g/dL.
- In pregnancy, it varies depending on the trimester, although it is usually larger than 10.0 g/dL.

Although anaemia diagnosis is vital in primary care, in a changing and uncertain world where health-care finances are more challenged, the necessity for a low-cost, reliable diagnostic tool is becoming a viable choice. Although the use of near-patient testing (point-of-care devices) is still a polarizing issue with opposing viewpoints from clinical practitioners and laboratory specialists, academic and laboratory researchers are interested in the topic. It appears that the use of such diagnostic techniques might lead to the discovery of new instances of anaemia or other diseases sooner than is normally the case. [18]

Etiology and Classification:

The cause of anaemia is determined by whether it is hypoproliferative (corrected reticulocyte count less than 2%) or hyperproliferative (corrected reticulocyte count greater than 2%). Microcytic anaemia (MCV less than 80 fl), normocytic anaemia (MCV 80-100 fl), and macrocytic anaemia (MCV more than100 fl) are the three types of hypoproliferativeanaemia based on the mean corpuscular volume.[1]

Anemia has a variety of causes, all of which may be traced back to one of three processes:

- Reduced red blood cell (RBC) production: Because RBCs have a short lifespan of 90 to 120 days, hematopoiesis must be a continuous process to keep up with natural attrition. Any hematopoiesis-disrupting action might result in a net decrease of RBC mass over time, resulting in anaemia.
- Increased RBC destruction: Anemia is caused by any process that degrades RBCs or severely shortens the lifespan of the cell to the point that hematopoiesis cannot keep up with the destruction.

- Anemia is caused by any loss of blood, whether microscopic or macroscopic, that surpasses hematopoiesis. [19]

These are types of anemia with its most causing factors: [1]

- Microcytic Anemia Hypoproliferative (MCV80 less than fl)Anemia due to a lack of iron
- Anemia caused by a long-term illness (AOCD)
- Sideroblastic anaemia (may be associated with an elevated MCV as well, resulting in a dimorphic cell population)
- Thalassemia
- Poisoning with lead

1- Anemia with Hypoproliferative Normocytic Cells (MCV 80-100 fL)

- Anemia caused by a long-term illness (AOCD)
- Failure of the kidneys
- Aplastic anaemia
- Aplasia of the red blood cells (pure red cell aplasia)
- Myelofibrosis or myelophthisis
- Multiple myeloma

2- Hypoproliferative Macrocytic Anemia (MCV>100 fL)

- Alcohol
- Liver disease
- Hypothyroidism
- Folate and Vitamin B12 deficiency
- Chronic myelomonocytic leukemia (CMML)
- Diuretics
- Chemotherapeutic agents
- Hypoglycemic agents
- Antiretroviral agents
- Antimicrobials
- Anticonvulsants

3- Hemolytic anemiaHemolytic anemia (HA) is divided into extravascular and intravascular causes.

- Extravascular hemolysis: The liver and spleen remove red blood cells from circulation too soon. The majority of HA instances are caused by this.
    - Hemoglobinopathies (sickle cell, thalassemias)

    - Enzyemopathies (G6PD deficiency, pyruvate kinase deficiency)
    - Membrane defects (hereditary spherocytosis, hereditary elliptocytosis)
    - Drug-induced
- Intravascular hemolysis: red cells lyse within the circulation, and is less common.
    - PNH
    - AIHA
    - Transfusion reactions
    - MAHA
    - DIC
    - Infections
    - Snake bites/venom

Epidemiology:

Because distinct diagnostic criteria are utilised in the United States vs WHO standards in the rest of the globe, epidemiological reporting of anaemia is fragmented. There are also demographic, genetic, and regional subtypes of anaemia prevalence. According to best estimates, anaemia prevalence is statistically comparable throughout the United States, Canada, and northern Europe, with roughly 4% of males and 8% of females in these regions meet anaemia diagnosis. The rest of the globe has far less information. [19,20-22]

Estimates based on current data are inexact, but they show that anaemia is 2 to 5 times more common worldwide than in the United States, Canada, and northern Europe.

The following are some of the areas where anaemia is more common:

- Sickle cell disease is more widespread in the African, Indian, and Mediterranean basins.
- Thalassemia is more frequent in Mediterranean basin regions.
- Anemia from chronic disease is widespread in areas where malaria/protozoal sickness is endemic.
- There is an increased risk of nutritional anaemia in impoverished communities.

In a study A total of 151 473 complete blood counts were collected from 53 890 participants, with 29.6% of the patients being anaemic. The bulk of the subjects had normocytic anaemia (82.4%), and 46.0 percent of those who had anaemia had no further tests done. The mean haemoglobin in the anaemic group that received further inquiry was lower than in the control group (Hb 10.68 g/dl versus 11.24 g/dl, P0.05): 33.2 percent of patients with microcytic anaemia (mean cell volume 80) had no iron status indicators assessed. [2]

Diagnosis:

Anemia is diagnosed in part by symptoms reported in general practice/family medicine (GP/FM). Anemia is associated with fatigue, palpitations, dyspnoea on exercise, and poor attention; however, these symptoms can also be associated with cancer, thyroid diseases, angina pectoris, and depression. Anemia has been linked to clinical indications such as cheilitis, hair loss, nail fragility, and even cognitive impairment in certain cases. Weight loss that isn't explained, persistent bone discomfort, and other unusual symptoms should be evaluated to rule out cancer or inflammation. [18]

Research Data:

In a study that looked at recommendation by physicians in primary care for patients with anemia:A complete blood count once a year was considered 'acceptable' for patients with an underlying chronic illness, men over 50 years old, and all women without a chronic condition once every five years. Five anaemia care approaches were given specific recommendations (observation, referral, empiric trial of iron, transfusion, and erythropoietic growth factors). Age, gender, and haemoglobin level were used to provide recommendations for observation only. In all situations, an immediate referral to a gastroenterologist or haematologist for a check-up was considered 'inappropriate.'For women over 40 and all males, an empiric trial of iron was considered 'inappropriate.' The administration of erythropoietic growth factors was recommended based on haemoglobin levels and anaemia symptoms ('suitable' if Hb was less than 9.5 g/dL or if Hb was 9.5-11.0 g/dL with anaemia symptoms). Finally, transfusion recommendations were based on the severity of anaemia and the existence of cardiovascular illness ('suitable' in patients over the age of 70 and those with either anaemic symptoms or underlying cardiovascular disease). Anemia caused

by dietary inadequacies, cancer/chemotherapy, or chronic renal failure were not addressed in the recommendations. [23]

Research done in Crete Island: For 10 consecutive working days, all patients attending the rural primary health care facilities of 12 GPs on the island of Crete were examined. Portable analyzers were used to measure haemoglobin levels. According to, 131 out of 541 patients had a low Hb level. Anemia was verified in 45 (45.5%) of the 99 patients who completed laboratory testing. The mean Hb levels in the group with confirmed anaemia, as identified by the portable analyzer, were 11.1 g/dl, whereas the mean Hb levels acquired by the whole blood count were 11.4 g/dl. Sixteen of the 45 patients with anaemia (35.6%) had IDA, meaning their ferritin levels were less than 30 ng/ml. [18]

In research done by Gandhi SJ, et al: Electronic medical records of 499 adult patients who had at least one haemoglobin value and did not have moderate to high-risk surgery were analyzed in a suburban internal medicine clinic.Anemia affected nearly one-fifth of the patients (21.1%). The average age of anaemia patients was 62.6 years. Males made up 20.3 percent of all anaemia patients, while females made up 79.6%. 60.1 percent of the patients had mild anaemia (haemoglobin 11 - 12.9 g/dL), whereas 39.8% had moderate anaemia (haemoglobin 8 - 10.9 g/dL). Anemia was found to be 5.2 times more common among African-Americans than in Caucasians.Anemia was shown to be 3.2 times more common in Hispanics than in Caucasians. When compared to individuals without anaemia, those with anaemia had a higher average number of comorbidities. When compared to the non-anemic population, the anaemic group had a significantly higher number of individuals with essential hypertension, hypothyroidism, chronic renal disease, malignancy, rheumatologic illness, congestive heart failure, and coronary artery disease. Additional diagnostic tests were performed on 41 percent of patients with mild anaemia and 62 percent of individuals with significant anaemia. [24]

Management:

The first thing to determine if the patient is bleeding and, if so, how much. This will aid in determining the necessity for immediate action. The American Trauma Life Support System (ATLS) lays forward precise criteria for treating trauma-related bleeding. Gastrointestinal (GI), gynecologic (GYN), and genitourinary (GU)

bleeding are the most prevalent non-traumatic sources of haemorrhage. The patient's hemodynamic stability is a key factor in determining the best course of action. Anticoagulation and occult chest, abdominal, or pelvic bleeding or hematoma development might reveal more modest haemorrhage. The goal of therapy, as usual, is to restore blood volume while also addressing the source of the bleeding. [19]

For patients with iron deficiency anemia the clear treatment option is iron supplements. However only When intestinal absorption is intact, oral iron supplementation is beneficial. Because repletion is delayed, it should only be used in individuals with mild anaemia (Hb, 11.0-11.9 g/dL in non-pregnant women and 11.0-12.9 g/dL in males). Intravenous injection is used when rapid repletion is required. Oral iron, on the other hand, is commonly available, affordable, and easy, making it a feasible therapeutic choice. [25]

If acute bleeding is ruled out, anaemia should be classified based on cell size and haemoglobin density, as well as the shape of red blood cells on a peripheral smear. Depending on RBC size, anaemia is classified as macrocytic, microcytic, or normocytic, and hypo or normochromic based on relative haemoglobin content. On a blood smear, specific cell dysmorphisms may be seen. Hemoglobin electrophoresis may be used to describe the cell structure at the level of the amino acid chains binding the heme moiety, providing another perspective on red cell dysmorphism. [19]

In chronic iron deficiency anaemia, blood transfusions should be avoided. It may be considered for patients who are hemodynamically unstable due to active bleeding, as well as individuals who have serious anaemia (Hb level less than 7 g/dL), acute myocardial ischemia, or if all previous therapies have failed to rectify the anaemia. Higher cutoff levels (Hb fewer than 8 g/dL) may be used in patients with substantial cardiovascular disease.Transfusions are merely a quick and temporary approach; comprehensive care should entail identifying and treating the underlying cause. In addition, intravenous iron (and, if necessary, erythropoiesis-stimulating drugs) should be given concurrently to correct and maintain the Hb level and iron storage, avoiding the need for further transfusions. [25]

Conclusion:

Anemia is one of the most prevalent disease in primary care, specially affecting elder patients, diagnosing of the anemia should rely on CBC analysis following the criteria set by WHO, treatment of the anemia depends on the underlying cause behind the anemia and thus further tests may be required, supplements such as oral or intravenous iron can be used for iron deficiency anemia, transfusion can be used for most severe cases.

References:

1. Turner J, Parsi M, Badireddy M. Anemia. [Updated 2021 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499994/
2. McCartney D, Shine B, Hay D, Lasserson DS. The evaluation of anaemia in an older primary care population: retrospective population-based study. BJGP Open. 2017 Oct 4;1(4):bjgpopen17X101157. doi: 10.3399/bjgpopen17X101157. PMID: 30564686; PMCID: PMC6181094.
3. Beghé C, Wilson A, Ershler WB. Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. Am J Med. 2004;116 Suppl 7A:3S–10. doi: 10.1016/j.amjmed.2003.12.009.
4. Nilsson-Ehle H, Jagenburg R, Landahl S, et al. Blood haemoglobin declines in the adolescents: implications for reference intervals from age 70 to 88. Eur J Haematol. 2000;65(5):297–305. doi: 10.1034/j.1600-0609.2000.065005297.x.
5. Tettamanti M, Lucca U, Gandini F, et al. Prevalence, incidence and types of mild anemia in the adolescents: the 'Health and Anemia' population-based study. Haematologica. 2010;95(11):1849–1856. doi: 10.3324/haematol.2010.023101.
6. Nutritional anaemias Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1968;405:5–37.
7. Nissenson AR, Goodnough LT, Dubois RW. Anemia: not just an innocent bystander? Arch Intern Med. 2003;163(12):1400–1404. doi: 10.1001/archinte.163.12.1400.
8. Andrès E, Serraj K, Federici L, et al. Anemia in adolescents patients: new insight into an old disorder. GeriatrGerontol Int. 2013;13(3):519–527. doi: 10.1111/ggi.12017.
9. Eisenstaedt RS. The prevalence of anemia in primary care. Postgrad Med. 2004 Nov;116(5 Suppl Anemia):7-11. doi: 10.3810/pgm.11.2004.suppl36.248. PMID: 19667678.
10. Riva E, Tettamanti M, Mosconi P, et al. Association of mild anemia with hospitalization and mortality in the adolescents: the Health and Anemia population-based study. Haematologica. 2009;94(1):22–28. doi: 10.3324/haematol.13449.

11. Lucca U, Tettamanti M, Mosconi P, et al. Association of mild anemia with cognitive, functional, mood and quality of life outcomes in the adolescents: the 'Health and Anemia' study. PLoS One. 2008;3(4):e1920. doi: 10.1371/journal.pone.0001920.
12. Wu WC, Rathore SS, Wang Y, et al. Blood transfusion in adolescents patients with acute myocardial infarction. N Engl J Med. 2001;345(17):1230–1236. doi: 10.1056/NEJMoa010615.
13. Swedberg K, Young JB, Anand IS, et al. Treatment of anemia with darbepoetin alfa in systolic heart failure. N Engl J Med. 2013;368(13):1210–1219. doi: 10.1056/NEJMoa1214865.
14. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med. 2006;355(20):2085–2098. doi: 10.1056/NEJMoa065485.
15. Solomon SD, Uno H, Lewis EF, et al. Erythropoietic response and outcomes in kidney disease and type 2 diabetes. N Engl J Med. 2010;363(12):1146–1155. doi: 10.1056/NEJMoa1005109.
16. Macdougall IC, Provenzano R, Sharma A, et al. Peginesatide for anemia in patients with chronic kidney disease not receiving dialysis. N Engl J Med. 2013;368(4):320–332. doi: 10.1056/NEJMoa1203166.
17. Gurusamy KS, Nagendran M, Broadhurst JF, et al. Iron therapy in anaemic adults without chronic kidney disease. Cochrane Database Syst Rev. 2014;12: CD010640
18. Lionis C, Symvoulakis EK, Duijker G, Anastasiou F, Dimitrakopoulos S, Kladou C, Ladoukaki E, Makri K, Petraki C, Sivaropoulos N, Sasarolis S, Stefanaki A, Vasilaki A, Vasilopoulos T. Reporting new cases of anaemia in primary care settings in Crete, Greece: a rural practice study. Asia Pac Fam Med. 2012 Apr 25;11(1):4. doi: 10.1186/1447-056X-11-4. PMID: 22533879; PMCID: PMC3353223.
19. Freeman AM, Rai M, Morando DW. Anemia Screening. [Updated 2021 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499905/
20. Zúñiga C P, Martínez G C, González R LM, Rendón C DS, Rojas R N, Barriga C F, Wietstruck P MA. [Sickle cell disease: A diagnosis to keep in mind]. Rev ChilPediatr. 2018 Aug;89(4):525-529.

21. Mohandas N. Inherited hemolytic anemia: a possessive beginner's guide. Hematology Am Soc Hematol Educ Program. 2018 Nov 30;2018(1):377-381.
22. Bartels M, Bierings M. How I manage children with Diamond-Blackfananaemia. Br J Haematol. 2019 Jan;184(2):123-133.
23. Dubois RW, Goodnough LT, Ershler WB, Van Winkle L, Nissenson AR. Identification, diagnosis, and management of anemia in adult ambulatory patients treated by primary care physicians: evidence-based and consensus recommendations. Curr Med Res Opin. 2006 Feb;22(2):385-95. doi: 10.1185/030079906X89720. PMID: 16466611.
24. Gandhi SJ, Hagans I, Nathan K, Hunter K, Roy S. Prevalence, Comorbidity and Investigation of Anemia in the Primary Care Office. J Clin Med Res. 2017 Dec;9(12):970-980. doi: 10.14740/jocmr3221w. Epub 2017 Nov 6. PMID: 29163729; PMCID: PMC5687900.
25. Jimenez K, Kulnigg-Dabsch S, Gasche C. Management of Iron Deficiency Anemia. Gastroenterol Hepatol (N Y). 2015 Apr;11(4):241-50. PMID: 27099596; PMCID: PMC4836595.