Original Article

Micro and Macrocytic Anemia – A Population Based Cross-Sectional Study

Micro and Macrocytic Anemia

Ayeshah Zaib-Un-Nisa[1], Iyad Naeem Muhammad[2], Sheikh Abdul Khaliq[3] and Agha Umer Draz Khan[4]

ABSTRACT

Objective: The main objective of current study was to determine age-standardized point prevalence of iron, folic-acid and vitamin B-12 deficiency anemia.

Study Design: A population based cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pharmacy Practice, Hamdard University and University of Karachi from January-2023 and ended on April-2023.

Methods: Data collected from blood banks. Collected blood samples were analyzed by Hematology Analyzer, Sysmex XP-100 and XN–1000. Analysis of data was done by Statistical Package for Social Sciences version-22. Main outcome measures: Levels of hemoglobin, hematocrit, microcytosis, macrocytosis

Results: Among 8,134 patients and donors data; male 37% (N=3043) and female 63% (N=5091). Age range for the majority of population was 18-28 years. In female; hemoglobin and hematocrit were lower-than normal in 39% (N=1984) and 53% (N=2685) respectively; microcytosis found in 31% (N=1554) and macrocytosis in 7% (N=325). In male; hemoglobin and hematocrit were lower-than normal in 33% (N=994) and 34% (N=1048) respectively; microcytosis reported in 25% (N=739) and macrocytosis in 8% (N=223). In both genders; significant (p=0.0001) differences are noted in the mean values of RBC indices versus the mean value of standard.

Conclusion: Evaluation of data reveals that hypochromic-microcytic anemia highly prevailed in the society. Majority of such population is in between 18-28 years old. Mean values of RBC indices in both gender were significantly lower than standard.

Key Words: Anemia; prevalence; iron; folic-acid; vitamin B-12; microcytosis.

Citation of article: Zaib-Un-Nisa A, Muhammad IN, Khaliq SA, Khan AUD. Micro and Macrocytic Anemia – A Population Based Cross-Sectional Study. Med Forum 2024;35(1):104-108. doi:10.60110/medforum.350123.

INTRODUCTION

Anemia should not be underestimated; it may significantly increases the risk of cardiovascular diseases (CVD) and renal disease (RD) in hypertensive individuals.[1] Cardio-renal Anemia Syndrome (CRAS) patients when treated with iron supplements and erythropoietin; heart failure and kidney injury were addressed.[2] Similarly among children; iron deficiency anemia may retard their psychomotor development.[3]

[1.] Department of Pharmacy Practice, Hamdard University and University of Karachi.
[2.] Department of Pharmacy Practice, University of Karachi.
[3.] Department of Pharmacy Practice, Hamdard University, Karachi.
[4.] Department of Pathology and Hematology, Hussaini Hematology & Oncology Trust, Karachi.

Correspondence: Sheikh Abdul Khaliq, Pharmacy Practice, Hamdard University, Karachi.
Contact No: 0345-2670820
Email: drsheikh1974@gmail.com

Received: August, 2023
Accepted: November, 2023
Printed: January, 2024

Among women; despite high prevalence of iron deficiency anemia, it is under-diagnosed and under-treated; which results in adverse health consequences pertaining to emotional and physical health.[4] Poor clinical prognosis also reported in patients of Acute Coronary Syndrome (ACS) having hemoglobin less than normal.[5]

According to the World Health Organization (WHO); the adult individual will be considered anemic; if hemoglobin levels is less than 13 g/dL in men and 12 g/dL in women.[6] However; based on unique apparatus; techniques employed and the characteristics of patient population; each laboratory must establish their own reference values.[7] Anemia is an important global health issue. Roughly one-third of people on the planet (32.9%) are anemic.[8] According to Global age-standardized point prevalence rate of anemia is 23,176.20 per 100,000 and years of healthy life lost due to disability (YLD) rates is 672.4per 100,000.[9] South Asia has the greatest frequency of age-standardized YLD from anemia (1358.2 per 100,000 people).[9] Anemia can be caused by inadequate erythropoesis by dietary deficiencies, inflammation, or hereditary hemoglobinopathies (thalassemia, sickle-cell-trait); or excessive erythrocyte loss (due to blood-loss, hemolysis, or both).[10] Anemia is usually

categorized according to the erythrocyte morphology (e.g. microcytic, macrocytic, normocytic); and/or underlying etiology (e.g. iron deficiency, inflammation and hemolysis).[10] Nutritional deficiencies and chronic illnesses are often the most frequent etiologies of anemia in children and young adults.[11]

The main objective of current study was to determine age-standardized point prevalence of iron, folic-acid and vitamin B12 deficiency anemia. For this purpose after collection of blood samples; hematological indices of individuals were determined along with demography of individuals.

METHODS

Design of Study, Place and Duration: The study design was population based cross-sectional. Study began on 15th January-2023 and Ended on 29th April-2023 in the city of Karachi.

Ethical Statement/Approval: Ethical approval of study has been taken before initiating study from Institutional Bioethical Committee (Reference No. IBC KU-300/2023), University of Karachi. Prior to initiating the study; all researchers ensured the maintenance of patient data confidentiality in compliance with the Declaration of Helsinki[12] and also taken written informed consent before data collection.

Data Collection Method: Data has been collected from the well know blood banks and blood transfusion centers of the Karachi city. Precision analysis technique was used for the determination of sample size of study.[13] The study includes around 8,134 patients and donors of blood from different centers; male 3043 (37%) and female 5091 (63%). Age range of population was neonatal (less than one month) to 95 years in both genders.

Procedure: After taken written informed consent; blood samples were collected through veni-puncture by professional staff into a 3mL vacutainers-tube with EDTA. Hemoglobin (Hb), hematocrit (Hct), mean-corpuscular-volume (MCV), mean-corpuscular-hemoglobin (MCH), mean-corpuscular-hemoglobin-concentration (MCHC) and red-blood-cell count (RBC) were determined by using Hematology Analyzer, Sysmex XP - 100 and XN – 1000.

Inclusion criteria: No co-morbidity in the selected subjects.

Exclusion criteria: Subjects having malignancy, infection, inflammation, any chronic disease that may affect the analyzing parameters, blood transfusion in last three months or received iron therapy.

Assessment of Data: The data for study was analyzed by SPSS (Statistical Package for Social Sciences) version-22. Descriptive (Frequency distribution, histograms) and inferential statistics (Student t-test) applied. Blood indices were compared by student t-test versus standard after keeping significance value of probability (p) <0.05.

RESULTS

Age range for the majority of population was 18-28 years. Among females, anemia is reported in 1984 (39%); 2685 (53%) has Hematocrit (Hct) value lower than normal; microcytosis reported in 1554 (31%) and macrocytosis in 325 (7%). (Table No. 1)

In male gender; anemia is reported in 994 (33%); 1048 (34%) has hematocrit value lower than normal; microcytosis reported in 739 (25%); macrocytosis in 223 (8%). (Table No. 2)

Descriptive statistical findings of total population for age and RBC (Red Blood Cells) indices mentioned in Table No. 3; however, in both genders significant differences are noted in the mean values of RBC indices versus the mean value of standard.[15] (Table 4)

Table No. 1: CBC* parmeters reporting Anemia in Female Gender

CBC* Parameters	Normal Range[15]	N (%)	Mean± SD
Hemoglobin	<11g/dL	1984 (39%)	9.27±1.48
	11-14.5g/dL	2887 (57%)	12.35±0.89
	>14.5g/dL	220 (4%)	19.84±4.77
Hematocrit	<34.5%	2685 (53%)	29.2±3.30
	34.5-45.4%	2251 (44%)	38.36±2.55
	>45.4%	155 (3%)	63.33±13.72
MCV (Mean Corpuscular Volume)	<78.1 fL	1554 (31%)	70.06±6.48
	78.1-95.3 fL	3073 (62%)	85.19±4.17
	>95.3 fL	325 (7%)	124.47 ±34.15
MCHC (Mean Corpuscular Hemoglobin Concentration)	<30.3 g/dL	815 (16%)	28.48±1.88
	30.3-34.4 g/dL	3858 (78%)	32.27±1.02
	>34.4 g/dL	279 (6%)	47.73±15.28
MCH Mean Corpuscular Hemoglobin)	<25.3 pg	1761 (36%)	21.58±2.97
	25.3-31.7 pg	2920 (59%)	27.95±1.55
	>31.7 pg	271 (5%)	42.42±11.02
RBC (Red Blood Cells) Count	<3.61 $x10^{12}$/Lit.	482 (10%)	3.101±0.51
	3.61-5.2 $x10^{12}$/Lit.	3949 (80%)	4.41±0.39
	>5.2 $x10^{12}$/Lit.	521 (11%)	6.306±1.56

*Complete blood Count

Table No. 2: CBC* parmeters reporting Anemia in Male Gender

CBC* Parameters	Normal Range[15]	N (%)	Mean± SD
Hemoglobin	<12.3 g/dL	994 (33%)	9.98±1.93
	12.3-16.6 g/dL	1855 (61%)	14.38±1.14
	>16.6 g/dL	194 (6%)	20.203±4.97
Hematocrit	<38.4%	1048 (34%)	32±5.45
	38.4-50.7%	1845 (61%)	43.88±3.05
	>50.7%	150 (5%)	63.88±15.96
MCV (Mean Corpuscular Volume)	<78.7 fL	739 (25%)	70.15±26.84
	78.7-96.3 fL	2010 (68%)	86.4±26.13
	>96.3 fL	223 (8%)	118.32±31.83
MCHC (Mean Corpuscular Hemoglobin Concentration)	<30 g/dL	217 (7%)	27.84±2.11
	30-35.5 g/dL	2661 (90%)	32.86±1.20
	>35.5 g/dL	94 (3%)	53.47±16.16
MCH Mean Corpuscular Hemoglobin)	<25.1 pg	647 (22%)	21.19±3.21
	25.1-31.6 pg	2027 (68%)	28.32±1.61
	>31.6 pg	298 (10%)	37.7±9.57
RBC (Red Blood Cells) Count	<4.25 $x10^{12}$/Lit.	509 (17%)	3.50±0.69
	4.25-6.02 $x10^{12}$/Lit.	2261 (76%)	5.04±0.43
	>6.02 $x10^{12}$/Lit.	202 (7%)	7.27±1.68

*Complete blood Count

Table No. 3: Descriptive statistics of total population for age and RBC (Red Blood Cells) indices

Parameters Mean±SD	Male	Female
Age (years)	31.57±20.58	31.98±16.92
Hemoglobin (g/dL)	13.34±3.28	11.51±3.76
Hematocrit (%)	40.85±9.25	36.15±8.01
MCH (pg)	27.71±5.71	26.48±5.91
MCHC (g/dL)	33.15±4.99	32.52±5.50
MCV (fL)	84.75±15.49	83.03±16.39
RBC (10^{12}/Lit) Count	4.93±1.07	4.49±0.97

Table No. 4: Statistical comparison of mean values of RBC indices versus the mean value of standard in both genders

CBC* Parameters	Gender	Mean of Standard[15]	Mean of Sample	p-value**
Hemoglobin (g/dL)	Male	14.45	13.34	p = 0.001
	Female	12.75	11.51	p = 0.0034
Hematocrit (%)	Male	44.55	40.85	p = 0.01
	Female	39.95	36.15	p = 0.015
MCH (pg)	Male	28.35	27.71	p = 0.01
	Female	28.5	26.48	p = 0.022
MCHC (g/dL)	Male	32.75	33.15	p = 0.0001
	Female	32.35	32.52	p = 0.028
MCV (fL)	Male	87.5	84.75	p = 0.001
	Female	86.7	83.03	p = 0.0122
RBC (10^{12}/Lit)	Male	5.13	4.93	p = 0.039
	Female	4.40	4.49	p = 0.01

*Complete blood Count; **p-value is significant at <0.05

DISCUSSION

Anemia remains a serious worldwide health issue especially in developing countries. The current study focused on the prevalence of anemia, its causative factors and available therapeutic options. According to the criteria set-forth by the largest private sector of JCI (Joint Commission International) accredited tertiary-care hospital of the city; anemia was reported in 39% (N=1984) female and 33% (N=994) male population. This indicates that high prevalence of anemia among females of reproductive age. Studies condcuted in different countries revealed that anemia is linked to higher rates of morbidity and mortality,[14] poor birth outcomes,[15] and delays in children's cognitive and behavioral development.[16]

Therefore, the World Health Organization recommends a daily 30–60 mg elemental iron supplementation for the women of reproductive age; while for infants and children (6 months to 12 years of age), WHO recommends consumption of fortified foods with folic acid, zinc, vitamin A as multiple micronutrients. Despite overall beneficial effects, there is limited adoption by high risk population.[17] Reasons could be poor socio-economic standing and poverty. Therefore, the 1,000 Days initiative has drawn the attention of numerous countries and efforts are required to increase intake of iron-rich foods.[18]

Microcytic, hypochromic anemia is a condition, where RBC size is less than normal and also decreased in red color.[19] In the current study; based upon MCV; microcytic anemia prevailed in both the genders; male 25% (N=739) and female 31% (N=1554), while hypochromic-microcytic anemia was found in 7% (N=217) male and 16% (N=815) female. In case of microcytosis; Iron deficiency anaemia (IDA), thalassemia and anaemia of chronic diseases (ACD) are the three basic diagnostic options.[24] The most common type of microcytic anaemia is iron deficiency anaemia.[20] Therefore, assessment is necessary by the findings of ferritin levels, serum iron, total iron binding capacity and haemoglobin. Fortunately in the findings of current study; normocytic condition was found in 62% (N=3073) female and 68% (N=2010) male, while normochromic condition was found in 78% (N=3858) female and 90% (N=2661) male. Normochromic-normocytic anemia is basically caused by nutritional deficiencies, renal insufficiency and hemolytic anaemia.[21] Current study found clinically small number of cases of normochromic-normocytic anemia, that is 8% (N=407) female and 8% (N=243) male.

Megaloblastic or Macrocytic anemia is usually caused by deficiencies of foilc-acid and/or vitamin B-12 (Cobalamin); in this situation, usually MCV is >100fL.[22] Deficiencies of folic-acid and/or vitamin B-12 may results in ineffective erythropoesis.[22] Megaloblastic anemia in the current study was found in 8% (N=223) male and 7% (N=325) female population. However, nonmegaloblatis macrocytic anemia also occurs due to other causes, such as abuse of ethanol, aplastic anemia, myelo-dysplastic syndrome, liver disease, hypothyroidism and drugs,[22] for differential diagnosis; folic acid and vitamin B-12 serum levels should be determined. Sometimes vitamin B-12 deficiency occurs due to positive antibodies to intrinsic factor; which confirms the diagnosis of pernicious anemia.[22]

The alarming situation is that; when mean values of RBC indices (Hb, Hct, MCV, MCH, MCHC, RBC count) in both gender were statistically compared with standard; indices were significantly lower than standard (Table No. 4); which concluded that most of the population in Karachi is either anemic or there is a need to develop new standards for the normal ranges of these indices.

Based upon findings of current study; it is highly recommended to follow international guidelines to resolve the issue. According to a recent comprehensive analysis, supplementing with just 10 mg/day of elemental iron can improve the levels of hemoglobin.[23] In another reference; 60 randomized controlled studies involving 27402 women from 30 different nations across all continents; overall risk of low-birth weight newborns among women taking daily iron supplements was reduced; mean birth weight of children whose mothers took iron during pregnancy was 30.81g higher. Daily iron supplementation of 8.88 gm decreased the risk of maternal anemia at term by 70% and the risk of iron deficiency at term by 57%. Supplementation of zinc with iron salts also tend to reduce anemia.[24] The role of vitamin B-12 and/or folic-acid for the treatment of megaloblastic anemia cannot be overlooked; it is found in literatures three injections of 1,000 mcg of vitamin B-12 and 5 mg of folic-acid daily rose Hb from 11.24 to 13.12 g/dL (p=0.001), MCV reduced from 95.50 to 89.64.[25] If anemia is induced due to chemotherapy; ethropoetin stimulating hormones (epoetin-alpha, darbepoetin-alpha) are highly recommended.[26]

CONCLUSION

Evaluation of data of more than 8,000 male and female population reveals that hypochromic-microcytic anemia highly prevalied in the society. Majority of such population is in between 18-28 years old. Mean values of RBC indices in both gender were significantly lower than standard.

Limitations and Recommendations: Since mean values of RBC indices in both gender were significantly lower than standard; it is recommended to address anemia or there is a need to develop new standards for the normal ranges of these indices in this population. To enhance anaemia control and prognosis, currently reported factors should be further investigated to develop preventive as well as treatment strategies acoording to patient's needs.

Author's Contribution:

Concept & Design of Study:	Ayeshah Zaib-Un-Nisa
Drafting:	Iyad Naeem Muhammad
Data Analysis:	Sheikh Abdul Khaliq, Agha Umer Draz Khan
Revisiting Critically:	Ayeshah Zaib-Un-Nisa, Iyad Naeem Muhammad
Final Approval of version:	Ayeshah Zaib-Un-Nisa

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No.IBCKU-300/2023 dated 23.01.2023

REFERENCES

1. Kim-Mitsuyama S, Soejima H, Yasuda O, Node K, Jinnouchi H, Yamamoto E, et al. Anemia is an independent risk factor for cardiovascular and renal events in hypertensive outpatients with well-controlled blood pressure: a subgroup analysis of the ATTEMPT-CVD randomized trial. Hyperten Res 2019;42(6):883-91.
2. McCullough PA. Anemia of cardiorenal syndrome. Kidney Int Suppl 2021;11(1):35-45.

3. Zavaleta N, Astete-Robilliard L. Effect of anemia on child development: Long-term consequences. Rev Peruana De Med Experiment Sal Publ 2017;34(4):716-22.
4. Mirza FG, Abdul-Kadir R, Breymann C, Fraser IS, Taher A. Impact and management of iron deficiency and iron deficiency anemia in women's health. Exp Rev Hematol 2018;11(9):727-36.
5. Mamas MA, Kwok CS, Kontopantelis E, Fryer AA, Buchan I, Bachmann MO, et al. Relationship between anemia and mortality outcomes in a national acute coronary syndrome cohort: insights from the UK myocardial ischemia national audit project registry. J Am Heart Ass 2016;5(11):1-19.
6. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. The Lancet Glob Healt 2013;1(1):16-25.
7. Fristsma GA. Laboratory Evaluation of Hemostasis. 6th ed. In: Keohane E, Otto CN, Walenga J, editors. St. Louis; Missouri 63043: Elsevier Health Sciences; 2020.p.765-92.
8. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. J Am Soc Hemat 2014;123(5): 615-24.
9. Safiri S, Kolahi AA, Noori M, Nejadghaderi SA, Karamzad N, Bragazzi NL, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990–2019: results from the Global Burden of Disease Study 2019. J Hematol Oncol 2021;14(1):1-16.
10. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci 2019;1450(1):15-31.
11. Pincelli A, Cardoso MA, Malta MB, Johansen IC, Corder RM, Nicolete VC, et al. Low-level Plasmodium vivax exposure, maternal antibodies, and anemia in early childhood: Population-based birth cohort study in Amazonian Brazil. P Neglect Trop Dis 2021;15(7):01-22.
12. Shrestha B, Dunn L. The Declaration of Helsinki on Medical Research involving Human Subjects: A Review of Seventh Revision. J Nepal Health Res Counc 2019;17(45):548-52.
13. John P. Bentley. Sample Size and Power Analysis; Chapter 13. In: Aparasu RR, editor. Principles of Research Design and Drug Literature Evaluation. 2nd ed. USA: McGraw-Hill Education;2020.p.139-50.
14. Scott SP, Chen-Edinboro LP, Caulfield LE, Murray-Kolb LE. The impact of anemia on child mortality: an updated review. Nutrients 2014; 6(12):5915-32.
15. Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. BMJ 2013;346(1):01-19.
16. Luo R, Yue A, Zhou H, Shi Y, Zhang L , Martorell R, et al. The effect of a micronutrient powder home fortification program on anemia and cognitive outcomes among young children in rural China: A cluster randomized trial. BMC Pub Healt 2017;17(1):1-16
17. de Barros SF, Cardoso MA. Adherence to and acceptability of home fortification with vitamins and minerals in children aged 6 to 23 months: a systematic review. BMC Pub Heal 2016;16(1): 1-11.
18. Harding KL, Aguayo VM, Namirembe G, Webb P. Determinants of anemia among women and children in Nepal and Pakistan: An analysis of recent national survey data. Mat Chil Nut 2018;14(S4):01-13.
19. Salama MA, Kamal MY, Younan DN, Henish GA. Hypochromic microcytic anemia: a clincopathological cross-sectional study. Alexan J of Pediatr 2017;30(1):37-43.
20. Elstrott B, Khan L, Olson S, Raghunathan V, DeLoughery T, Shatzel JJ. The role of iron repletion in adult iron deficiency anemia and other diseases. Eur J Haematol 2020;104(3):153-61.
21. Newhall D, Oliver R, Lugthart S. Anaemia: A disease or symptom. Neth J Med 2020;78(3): 104-10.
22. Socha DS, DeSouza SI, Flagg A, Sekeres M, Rogers HJ. Severe megaloblastic anemia: Vitamin deficiency and other causes. Clevel Clin J Med 2020;87(3):153-64.
23. Casgrain A, Collings R, Harvey LJ, Hooper L, Fairweather-Tait SJ. Effect of iron intake on iron status: a systematic review and meta-analysis of randomized controlled trials. The Am J Cl Nut 2012;96(4):768-80.
24. Barffour MA, Hinnouho GM, Kounnavong S, Wessells KR, Ratsavong K, Bounheuang B, et al. Effects of daily zinc, daily multiple micronutrient powder, or therapeutic zinc supplementation for diarrhea prevention on physical growth, anemia, and micronutrient status in rural Laotian children: a randomized controlled trial. The J Pediatr 2019;207(1):80-9.
25. Nozari E, Ghavamzadeh S, Razazian N. The Effect of Vitamin B12 and Folic Acid Supplementation on Serum Homocysteine, Anemia Status and Quality of Life of Patients with Multiple Sclerosis. Clinic Nut Res 2019; 8(1):36-45.
26. Zhao F, Wang Y, Liu L, Bian M. Erythropoietin for cancer-associated malignant anemia: a meta-analysis. Molecul Cl Oncol 2017;6(6):925-30.