Original Research Article

Macrocytosis is highly prevalent in Raebareli district, Uttar Pradesh, India

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ABSTRACT

Background: Anemia is a most common health issue in Indian population mainly due to nutritional deficiencies. A number of factors contribute in anemia which is further categorized based on various parameters in hematological indices and microscopic examination.

Methods: A retrospective study has been carried out on the patients (n = 1332) in a retrospective study on the patients (n = 1332) in Raebareli district to determine prevalence of anemia and subsequent categorization into normocytic, microcytic and macrocytic based on complete blood count (CBC) profile and blood smear.

Results: This study demonstrates 15.54% patients were diagnosed for anemia and more than half of the total anemic patients (55.07%) were found to be suffered from macrocytosis which was found significantly more prevalent among male (65.17%) compare to female (38.38%) patients.

Conclusions: Several factors may contribute to macrocytosis among male population including alcoholism in Raebareli region. However, female patients were found almost equally susceptible to all three forms of anemia: normocytic, microcytic and macrocytic. This study provides a key insight into prevalence and possible causes of different types of anemia in this region which may be useful for implementation of government health programs to counter this problem and provide better treatment plans.

Keywords: Anemia, Hemoglobin, Macrocytosis, Mean corpuscular volume, Microcytic

INTRODUCTION

Anemia is a global public health issue that affects 1.6 billion populations in the world.[1] Among all, India has highest prevalence (around 40% of total world population) of anemia and 51% of women with all reproductive ages have anemia in Indian continent.[2] Iron deficiency is considered as one of the prominent causes of anemia due to low iron intake which is more prevalent in the case of young and pregnant women however, multiple clinical reasons are also found to be associated with it.

Hematological indices is a direct way to define blood profile and type of anemia based on various parameters (Hb, MCV, MCH, MCHC and RDW), those are further confirmed by peripheral blood smear study. Mean corpuscular volume (MCV) defines an average size of RBCs in a sample. Whereas, Mean corpuscular hemoglobin (MCH) measures an average content or weight of hemoglobin (Hb) in RBC and mean corpuscular hemoglobin concentration (MCHC) refers to an average concentration of Hb in RBCs present in a sample. RBC distribution width (RDW-CV) measures a variation of different size RBCs in the sample.

Anemia is defined by low Hb content (Hb <13 gm/dl in males and Hb <12 gm/dl in females) according to WHO guidelines.[3]

Anemia is further categorized into normocyctic, microcytic and macrocytic based on red blood cell (RBC) morphology or size. Normal size RBCs with low Hb is considered as normocytic anemia, which is mainly caused by chronic disease, haemolysis and bone marrow disorders. Microcytic anemia is reflected by the smaller size RBCs those may be due to iron deficiency. Whereas, macrocytic anemia has larger size RBCs as evident in case of vitamin B12 and folic acid deficiency along with alcoholism.

Low values of MCV, MCH, MCHC parameters represent microcytic anemia that is further confirmed by microscopic examination of peripheral blood smear.[4] Microcytic anemia may be resulted from defect in globin genes (thalassemias), defective heme biosynthesis, impaired iron availability and its acquisition by developing erythrocytes.[5]

High MCV values are indicative of macrocytic anemia followed by the further confirmation through peripheral blood smear.[4] Macrocytic anemia is further categorized into pernicious and megaloblastic anemia based on low levels of vitamin B12 or folic acid. Megaloblastic anemia is resulted from acquired deficiency of vitamin B12 or folic acid due to poor intake whereas pernicious anemia is resulted from defective absorption of vitamin B12 due to lack of intrinsic factor in gastric secretions.[6,7]

Here, authors have carried out a retrospective study for determining prevalence of anemia and its types in Raebareli district of Uttar Pradesh, India and tried to explore the possible causes for proper medication. This study includes complete blood count (CBC) profile followed by the microscopic examination of peripheral blood smear of the OPD patients at All India Institute of Medical Sciences (AIIMS), Raebareli, Uttar Pradesh, India

METHODS

Authors performed a retrospective study based on the patient's records; those visited All India Institute of Medical Sciences (AIIMS), Raebareli OPD for regular check-up examination. The complete blood profiling (CBC) was performed at hospital laboratory during the month of December, 2018 to February, 2019.

For this study, authors have included a number of patients (n = 1332) based on clinical symptoms and diagnosis (CBC profile and blood smear examination) and excluded patients with a history of fever e.g. malaria, viral or bacterial infections resulting into altered CBC profile. This study was carried out in accordance with recommendations made by institutional ethics committee (IEC).

CBC and microscopy

Authors have collected fresh blood samples of OPD patients in K2-EDTA vaccutainers and performed CBC test using Sysmex XP-100 machine. In addition, authors have performed microscopy on blood smears for each sample using Magnus MLX plus microscope.

Authors defined Hb lower than 11gm/dl as anemia, MCV <80 fl as microcytic and MCV >100 fl as macrocytic anemia.[4]

Statistical analysis

Authors have used Student's t-Test and one-way ANOVA for determining significance for this analysis. A p-value of less than 0.01 was considered significant for this study.

RESULTS

Prevalence of anemia among local population

Anemia was diagnosed in 15.54% of total patients out of which 48.4% male (mean age = 42±22 years) and 51.6% female (mean age = 34±16 years) were found susceptible to anemia based on CBC profile and microscopy (Figure 1A).

Table 1: Mean±SD (standard deviation) values of various CBC parameters with age and number in identified normocytic anemic patients.

Parameters	Mean±SD	
	Males	Females
N	11	31
Age (year)	41±17	44±17
Hb (g/dl)	8.4±1.7	9.5±1.3
RBC count (x10^6/μl)	3.4±0.9	3.7±0.6
HCT (%)	27±5.8	30±4.5
MCV (fl)	80±6.0	80±3.8
MCH (pg)	26±3.6	25±2.0
MCHC (g/dl)	31±3.4	32±1.6
RDW-CV (%)	17±4.2	16±2.3
Platelets (x10^3/μl)	3.0±1.3	2.7±1.5

More than half of the total anemic patients were detected for macrocytic anemia (55.07%) as compare to normocytic (24.64%) and microcytic (20.29%) anemia (Figure 1B).

Prevalence of macrocytic anemia was found significantly (p-value=0.004, n = 3) higher in males (65.17%) than females (38.38%) (Figure 1C). However, females were found equally prone to all three types (Normocytic, Microcytic and Macrocytic) of anemia (Figure 1D).

Normocytic anemia

Authors have analyzed 42 samples, out of which 11 samples in male (mean age = 41±17 years) and 31 samples in female (mean age = 44±17 years) were diagnosed for normocytic anemia with mean MCV values of 80±6.0 fl and 80±3.8 fl respectively (Figure 1E and Table 1).

Table 2: Mean±SD values of various CBC parameters with age and number in identified microcytic anemic patients.

Parameters	Mean±SD	
	Males	**Females**
n	14	27
Age (year)	32±28	35±14.4
Hb (g/dl)	8.3±1.7	8.0±2.0
RBC count (x10^6/µl)	4.3±1.0	4.0±0.9
HCT (%)	27.8±5.4	27±5.5
MCV (fl)	66±5.9	68±4.4
MCH (pg)	19.4±2.6	20±2.1
MCHC (g/dl)	29±2.3	29±2.0
RDW-CV (%)	18.2±3.1	18.6±2.5
Platelets (x10^3/µl)	2.0±2.0	3.5±1.9

Table 3: Mean±SD values of various CBC parameters with age and number in identified patients with macrocytosis.

Parameters	Mean±SD	
	Males	**Females**
n	55	36
Age (year)	42±20	32±18
Hb (g/dl)	13.8±2.3	11.1±2.8
RBC count (x10^6/µl)	3.9±0.7	3.1±0.9
HCT (%)	39.4±6.5	31.8±8.0
MCV (fl)	102±7.3	104±8.0
MCH (pg)	35.8±3.1	36.1±3.0
MCHC (g/dl)	35±1.0	34.8±1.0
RDW-CV (%)	14.5±2.2	16.5±4.2
Platelets (x10^3/µl)	2.1±1.0	1.8±0.8

Microcytic anemia

Authors have diagnosed 14 samples in male (mean age = 32±28 years, mean MCV = 66±5.9 fl) and 27 samples in females (mean age = 35±14.4 years, mean MCV = 68±4.4 fl) out of total 41 samples, for microcytic anemia (Figure 1F and Table 2).

Macrocytic anemia

Macrocytosis was detected in 55 samples of males (mean age = 42±20 years) and 36 samples of females (mean age = 32±18 years) out of total 96 samples (Figure 1G and Table 3).

Table 4: Prevalence (%) of Megaloblstic anemia and non-megaloblastic macrocytosis among male and female patients based on various factors/clinical features.

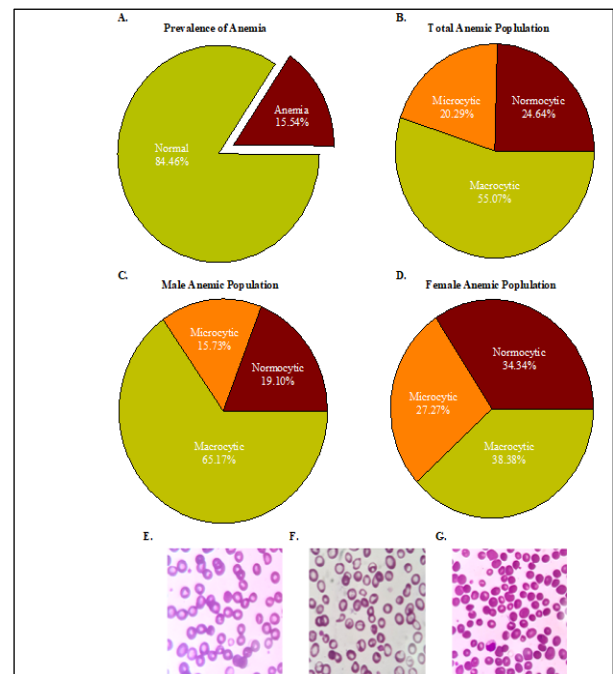| Macrocytosis			
	Male	Female	Clinical feature/ associated factors
Megaloblastic anemia	6.90%	23.70%	Hb <11 gm/dl , RDW-CV > 15%
Non megaloblastic anemia	93.10%	76.30%	Pregnancy (31.57% females), Alcoholism, smoking etc (89.65% males)

Figure 1: Prevalence of anemia among population at Raebareli district. (A) Pie chart representing % of normal and anemic patients. (B) Distribution (%) of three forms of anemia among total anemic patients based on diagnosis. (C) Prevalence of three forms of anemia among male and (D) Female anemic patients. Microscopic image of blood smear of (E) Normocytic (F) Microcytic and (G) Macrocytic anemia patients after CBC profile.

Interestingly, only 23.7% females and 6.9% males were found positive for megaloblastic anemia (Hb < 11gm/dl) and macrocytosis (mean MCV = 102±7.3 fl for males and 104±8.0 fl for females) (Figure 2A, 2C and Table 3, 4).

Low Hb with high RDW-CV (more than 15%) values were reported in case of megaloblastic anemia, therefore

authors also looked for RDW-CV of these macrocytic anemia patients.[8,9] RDW-CV was found significantly higher (p-value = 0.003, n = 36-55) in case of females (Mean RDW-CV = 16.4±4.1%) than males (Mean RDW-CV = 14.4±2.1%) suggesting these patients mostly females were susceptible to megaloblastic anemia and nutritional deficiencies that may be a prominent cause for it.[9] Additionally, this data also showed that majority of the cases with macrocytosis were non-megaloblastic or non-anemic with Hb >11mg/dl (76.3% females and 93.1% males) (Figure 2A, 2C and Table 4).

Factors associated with non-anemic macrocytosis

A number of factors contribute to non-anemic macrocytosis e.g. alcoholism, chronic liver disease, smoking, reticulocytosis and pregnancy etc. Here, authors looked for some of these factors to get an insight into its possible causes in population at Raebareli district. Interestingly, authors have found that alcohol or tobacco abuse, smoking etc. appeared as a major cause for non-megaloblastic/non-anemic macrocytosis in case of 89.65% males (Figure 2B) whereas, pregnancy was found associated with this in case of 31.57% females in this region (Figure 2D and Table 4).
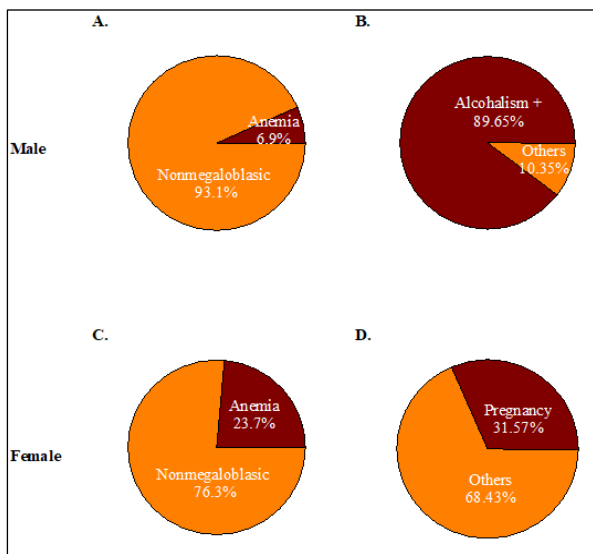

Figure 2: Prevalence of macrocytosis among anemic population at Raebareli district. (A) Pie chart representing % of suspected megaloblastic and non-megaloblastic anemia patients in total diagnosed (based on Hb and RDW-CV values etc.) male and (C) female patients with macrocytosis. (B) Factors associated such as alcoholism+ (+ represents other causes e.g. smoking, tobacco/opium abuse etc.) in male and pregnancy in (D) female patients with non-megalobalstic macrocytosis.

DISCUSSION

This retrospective observational study was carried out during winter season (December, 2018 to February,

2019) therefore it excludes the impact of other factors influencing CBC blood profile e.g. malaria, bacterial infections such as typhoid etc which are found highly prevalent during summers and rainy season. In this way, authors tried to study key factors e.g. socioeconomic, habits, nourishment etc. responsible for causing different types of anemia (normocytic, microcytic and macrocytic) in the population living at Raebareli district.[9]

This is a novel study carried out in Raebareli district, Uttar Pradesh, India implicating high prevalence of macrocytosis especially in males due to bad habits e.g. alcohol and tobacco abuse. Macrocytic anemia is further subcategorized into megaloblastic and nonmegaloblastic conditions based on bone marrow examination, CBC profile, peripheral blood smear and detection of erythrocyte morphology etc. clearly provide clues towards such forms of macrocytic anemia.[10] Macrocytosis is reported in terms of elevated MCV (more than 100 fl) where RBCs are larger than the normal.[10] Similarly elevated levels of RDW-CV were also reported in case of patients with megaloblastic anemia.[9] Large and oval shaped erythroblast cells with immature nucleus are characteristic features of megaloblasts those are found in bone marrow of megaloblastic anemia patients primarily due to vitamin B12 and folate deficiency. Due to limited resources, authors did not examined patient's bone marrow samples but categorized them as megaloblastic anemia based on only low Hb and high RDW-CV levels (Table 4).

Surprisingly, authors found that males in this region are more prone to non-anemic and non-megaloblastic macrocytosis compare to females. A number of studies suggest that alcoholism and smoking particularly in young and middle aged men is responsible for macrocytosis.[11,12]

This study also demonstrated that mostly males of younger to middle age are susceptible to non-anemic macrocytosis due to bad habits such as alcohol, tobacco and smoking in this region, whereas, pregnancy was appeared as a major factor contributing in macrocytosis in females due to folic and vitamin B12 deficiency in that stage (Figure 2B, 2D).[11-15]

This is an important retrospective study carried out in Raebareli region indicating towards the prevalence of macrocytosis in the population.

Here, authors tried to explore the possible causes of macrocytosis in this region. These findings will unravel some of interesting insights into prevalence of macrocytosis and helpful for implementing ongoing government health schemes for proper medication.

CONCLUSION

This study indicated that macrocytosis is highly prevalent among population living in Raebareli district of Uttar

Pradesh, India. In addition, authors found that alcohol abuse and smoking appeared as a main cause contributing in non-anemic macrocytosis among male population whereas, pregnancy related malnutrition was found as a major factor for it in females in Raebareli region.

REFERENCES

1. De Benoist B, Cogswell M, Egli I, McLean E. Worldwide prevalence of anaemia 1993-2005; WHO Global Database of anaemia. 2008:1-40.
2. Hawkes C. Global nutrition report 2017: Nourishing the SDGs. 2017:1-21.
3. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? Blood. 2006;107(5):1747-50.
4. Maner BS, Moosavi L. Mean corpuscular volume (MCV). Stat Pearls. 2019;25:3976-82.
5. Iolascon A, De Falco L, Beaumont C. Molecular basis of inherited microcytic anemia due to defects in iron acquisition or heme synthesis. Haematologica. 2009;94(3):395-408.
6. Wangel AG, Callender ST, Spray GH, Wright R. A family study of pernicious anaemia. II. Intrinsic factor secretion, vitamin B12 absorption and genetic aspects of gastric autoimmunity. Br J Haematol. 1968;14(2):183-204.
7. Whittingham S, Ungar B, Mackay IR, Mathews JD. The genetic factor in pernicious anaemia. A family study in patients with gastritis. Lancet. 1969;1(7602):951-4.
8. Khanduri U, Sharma A. Megaloblastic anaemia: prevalence and causative factors. National Med J India. 2007;20(4):172-5.
9. Veda P. Evaluation of macrocytosis in routine hemograms. Indian J. Hematol. Blood Transfus. 2013;29(1):26-30.
10. Aslinia F, Mazza JJ, Yale SH. Megaloblastic anemia and other causes of macrocytosis. Clin Med Res. 2006;4(3):236-41.
11. Seppä K, Laippala P, Saarni M. Macrocytosis as a consequence of alcohol abuse among patients in general practice. Alcohol. Clin. Exp. Res. 1991;15(5):871-6.
12. O'Reilly MA, Buckley CM, Harrington JM, O'Shea S, Perry IJ, Cahill MR. Cigarette smoking is an under recognised cause of macrocytosis. 2013;122(21):4660.
13. Seppä K, Sillanaukee P, Saarni M. Blood count and hematologic morphology in nonanemic macrocytosis: differences between alcohol abuse and pernicious anemia. Alcohol. 1993;10(5):343-7.
14. Chanarin I, McFadyen IR, Kyle R. The physiological macrocytosis of pregnancy. BJOG. 1977;84(7):504-8.
15. Buckle AE, Shaw S. Macrocytic anaemia of pregnancy. J Obstet Gynaecol Br Emp. 1957;64(3):396-404.