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Assessment of pattern, risk factors and treatment of Iron Deficiency and Megaloblastic Anemia in Adult and Pediatric population in a tertiary care hospital in South India

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Assessment of pattern, risk factors and treatment of Iron Deficiency and Megaloblastic Anemia in Adult and Pediatric population in a tertiary care hospital in South India.

A Project Report Submitted to
MANIPAL ACADEMY OF HIGHER EDUCATION
In partial fulfilment for the degree of Doctor of Pharmacy (Pharm D)

Submitted by

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Declaration

We hereby declare that the project entitled **"Assessment of pattern, risk factors and treatment of Iron Deficiency and Megaloblastic Anemia in Adult and Pediatric population in a tertiary care hospital in South India."** was carried out under the guidance of **Dr. Leelavathi D Acharya**, M.Pharm, PhD, Associate Professor, Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal, co-guidance of **Dr. Girish Thunga,** M.Pharm, PhD, Assistant Professor (Selection Grade), Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal, **Dr. Sneha Seshadri**, Assistant Professor, Department of General Medicine, KMC, Manipal and **Dr. Shrikiran A Hebbar**, Professor & HOD, Department of Pediatrics, KMC, Manipal. The extent and source of information derived from the existing literature have been indicated throughout the project work at appropriate places. The work is original and has not been submitted in part or full for any diploma or degree purpose for this or any other university.

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Assessment of pattern, risk factors and treatment of Iron Deficiency Anemia in Adult and Pediatric population in a tertiary care hospital in South India

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LIST OF ABBREVIATIONS

1. IDA- Iron Deficiency Anemia
2. SPSS- Statistical Package for the Social Sciences
3. CRF – Case Record form
4. WHO - World Health Organization
5. GI- Gastric Intestinal
6. NSAID- Non Steroidal Anti Inflammatory Drug
7. SOB- Shortness of breath
8. SD- Standard deviation
9. Hb- Haemoglobin
10. MCV- Mean Cell Volume
11. MCHC- Mean corpuscular hemoglobin concentration
12. MCH- Mean cell hemoglobin
13. PCV- Packed cell volume
14. TIBC- Total iron binding capacity
15. RBC- Red blood cell
16. RDW- Red blood cell distribution width
17. MMA- methylmalonic acid

ABSTRACT

Introduction

Iron Deficiency Anemia (IDA) is a major nutritional problem globally which is especially true in developing countries like India. IDA is associated with worsened quality of life, impaired physical & cognitive performance. Even though treatment patterns are simple & effective, there is a high prevalence of IDA. The reason for this is partly due to non-compliance of the patients & partly due to ineffective/incomplete treatment by physicians.[4] Due to the risks associated with blood transfusions, alternative treatments of anemia in the critically ill are being explored.[5]

Objectives

To assess the pattern, risk factors and treatment of IDA in adult and pediatric population in a tertiary care hospital in South India.

Methodology

A retrospective observational study conducted in Kasturba Hospital on patients with Iron Deficiency Anemia admitted during the year 2017 after ethical committee approval. Medical records of these patients were reviewed and relevant data was recorded in the CRF. Demographic information of patients, family and social history, risk factors of each patient, and their treatment pattern were estimated and recorded. Collected Data was documented and analyzed using SPSS version 20.

Results

A total of 894 patients' data diagnosed as IDA in the year 2017 was included for the study, out of which 401(44.8%) were pediatric and 493 (55.1%) were adult patients. It was observed that the highest distributed risk factor in pediatrics was age below 2 years (54.6%) and in adults it was Female gender (55.9%). It was also seen that pallor (pediatric- 41.39% and adults-49.08%) was the highest observed clinical manifestation in both the groups. The standard treatment for IDA was provided to 30.1% pediatric patients and 40.3% adult patients.

Conclusion

Study concludes that it helps in identifying the various risk factors and clinical manifestation of IDA which will in turn help in prevention of the disease by early assessment of the disease based on these factors. It also gives us an idea of the changes to be made in the treatment pattern and/or to provide counselling to patients regarding medication and food habits for better outcome of the disease.

INTRODUCTION

1. Introduction

The WHO defines Anemia as a condition in which the number of red blood cells or their oxygen-carrying capacity is insufficient to meet physiological needs, which vary by age, sex, altitude, smoking, and pregnancy status. [6] According to WHO, the normal haemoglobin values for children (6-59 months of age) is 11mg/dL or higher, for children (5-11 months of age) is 11.5mg/dL or higher, children (12-14 years of age) is 12mg/dL or higher, for women (15 years and above) is 12mg/dL or higher and for men (15years and above) is 13mg/dL or higher. [9,10] Anemia is one of the most common health problem in India, [7]. Out of the various different kinds of anemia Iron deficiency anemia (IDA) is thought to be the most common cause of anaemia globally [8] which is reduced Iron concentration in the body[11], although other conditions, such as folate, vitamin B12 and vitamin A deficiencies, chronic inflammation, parasitic infections and inherited disorders can all cause anemia. Majority of the patients with IDA have severe IDA (58%), followed by moderate IDA (36%). [8] In its severe form, it is associated with fatigue, weakness, dizziness, drowsiness and various other clinical manifestations. [6] The normal TIBC levels are 250-400 mcg/dl and the normal ferritin levels for age group 2-18 years are 7-140ng/ml and for 18-49 years are 15-200ng/dl for males and 12-150ng/dl for females. The TIBC value above the normal range and ferritin value below the normal range causes IDA. [13]

The risk factors for anemia include Social determinants- race/ethnicity, poverty, food in- security; behavioural determinants- Tobacco use, Nutritional intake, Body mass index, physical activity; Reproductive history- Years since menarche, usage of oral/IV contraception, Older women only (live births, time on oral contraceptive) and various others. For women with risk factors like menstrual or other blood loss, low iron intake, previous diagnosis of anemia are recommended for annual objective screening while adolescents can't quantify blood loss or iron intake hence, guidelines do not advise how many years after menarche to start screening. It was found that adolescent risk factors are not the same as for older reproductive age women. [3] Worm infestation is also one of the major problems in India for causing IDA, especially for females over males. [29]

The high risk groups for anemia include pregnant women and children. [6] The prevalence of anemia in adults was found to be 53% and about 204997 children aged between 6-59 months were diagnosed with anemia [1] Most of the patients who suffer from anemia are female (71%) and are usually more than 15 years of age. This could be attributed to the low nutrition intake in the females and menstrual blood loss that occurs every month. [1]

Need for the Study

According to NFHS-4 (National Family Health Survey), 2015-16, the prevalence of anemia in adults was found to be 53% and about 204997 children aged between 6-59 months were diagnosed with anemia. [1] Study by Rakesh et al. stated that the prevalence of Anemia is not known in the South Indian population. There are many reports and surveys that cannot be combined, due to non-uniform haemoglobin estimation methods. [2]

Shekhar et al. studied the risk factors for anemia which included Social determinants- race/ethnicity, poverty, food insecurity; behavioral determinants- Tobacco use, Nutritional intake, Body mass index, physical activity; Reproductive history- Years since menarche, usage of oral/IV contraception, Older women only (live births, time on oral contraceptive) and various others.[3]

In Kasturba Hospital, Manipal which is a 2000 bedded tertiary care hospital with various specialties; there were more than 2000 different types of anemic patients admitted per year in Medicine and Pediatric wards. hence, there is a need to assess the risk factors in this population. Hence, we are carrying out this study to compare the prevalence of anemia in adult and pediatric population in a tertiary care hospital in South India along with the treatment pattern, risk factors and clinical manifestations associated with IDA.

OBJECTIVES

2.OBJECTIVES

- To assess the pattern, risk factors and treatment of Iron Deficiency Anemia in adult and pediatric population in a tertiary care hospital in South India.
- To study the demographic and clinical characteristics of IDA in patients.
- To assess the severity of IDA.
- To compare various study parameters in adult and pediatric population with respect to IDA.

METHODOLOGY

3. METHODOLOGY

3.1 Study Site: Kasturba Hospital, Manipal.

3.2 Study Design: Retrospective Observational Study

3.3. Study Period: August 2018 to March 2019

3.4 Ethical Clearance: Obtained from the Institutional Ethics Committee, Kasturba Hospital, Manipal MAHE. (Appendix 1) (471/2018)

3.5 Sample Size: A total number of 974 (801-IDA | 83-IDA+MEGALOBLASTIC ANEMIA) subjects diagnosed with IDA in the year 2017 were included in the study.

3.6 Study Criteria:

Inclusion Criteria: All in-patients with final diagnosis of IDA admitted in Kasturba Hospital, Manipal during January 2017-December 2017
Exclusion Criteria: Patient files with incomplete data and/or other types of Anemia.

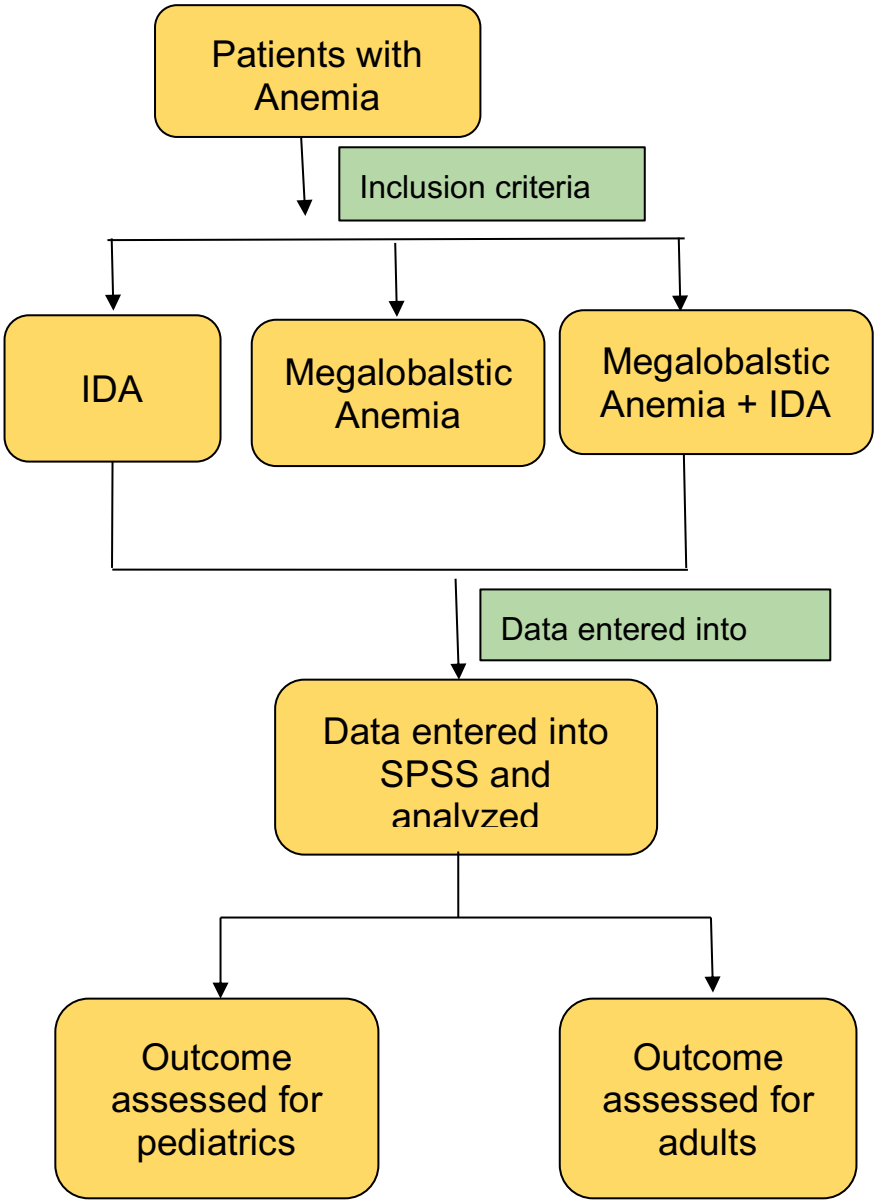
3.7 Sources for Data Collection:

Patient Case Records which contained the following data:
-Patient Demographics
-Patient History notes
-Patient risk factors
-Laboratory tests
-Drug treatment charts
-Outcomes
-Discharge Medications and follow up.

3.8 Materials Used: Case Record Form (CRF). (Appendix 2)

3.9 Operation Modality:

All patients satisfying the inclusion criteria admitted in the year 2017 in a tertiary care hospital with the final diagnosis as IDA were included in the study. The medical records of these patients were obtained from the medical record department (MRD). The data from the patients' file were reviewed and documented in the CRF individually for each patient. The data was analysed using SPSS 20 and the distribution of all the particulars were checked in pediatric (0-18 years) and adult (>18 years) patients.



3.10 Collection of Data:

The medical records of all IDA patients were reviewed and the details of the patient were entered in a case record form. Demographic details like age, gender, occupation and social history were noted. Information regarding the presence of any risk factors or chronic illness, medical history and type of admission were retrieved from the files on a structured CRF. The various Laboratory values were noted down and the severity classified based on the WHO classification (Table 1) .

Table 1; Haemoglobin levels to diagnose anaemia at sea level (mg/dl) .[9,10]

Population	Non-anemia	Mild	Moderate	severe
Children 6-59 months of age	11 or higher	10-10.9	7-9.9	7 or lower
Children 5-11 months of age	11.5 or higher	11-11.4	8-10.9	8 or lower
Children 12-14 years of age	12 or higher	11-11.9	8-10.9	8 or lower
Non-pregnant women (15 years of age and above)	12 or higher	11-11.9	8-10.9	8 or lower
Pregnant women	11 or higher	10-10.9	7-9.9	7 or lower
Men (15 years and above)	13 or higher	11.12.9	8-10.9	8 or lower

3. 11 Data Analysis and Statistics:

The obtained data from the medical records of patients with IDA were analysed for various parameters like demographic data, gender ratio, risk factor distribution, clinical manifestation, prescription pattern, discharge medications, laboratory values, outcomes and severity for pediatrics (age below 18 years) and adults (age above 18 years), etc. using SPSS version 20. The results of pediatrics and adults were compared and represented as descriptive statistics.

The various risk factors for IDA were assessed as follows:

Age below 2 years and above 60 years [20][21], Child bearing age [19], Female gender [1], Low socio economic group (occupation, geographical area) , Alcohol, Smoking, Chronic Disease, Pregnancy, History of blood loss, History of taking NSAID or Aspirin, Diet, Worm infestation, Haemorrhoids, Nose Bleeding, Postpartum Haemorrhage [13]

The various clinical manifestations for IDA were assessed as follows:

Chest Pain, Pallor, Fatigue, Dizziness, Irritability, Weakness, Palpitations, vertigo, Tingling, Shortness of breath, Decreased exercise tolerance and tachycardia [13]

RESULTS

4. RESULTS

A total of 995 patients' data were collected during the study period out of which 811 were diagnosed with IDA, 101 were diagnosed with Megaloblastic anemia and 83 were diagnosed as IDA and Megaloblastic anemia. In this study we are focusing on the patients diagnosed with IDA, that is 894 patients.

4. 1 Demographic characteristics of patients with IDA

Total of 894 patients were admitted and diagnosed with IDA in the year 2017. Among them 401 were pediatric and 493were adult patients.

Gender wise distribution:
Out of 401 pediatric patients 229 (57.1%) patients were male and 172 (42.8%) were female and out of 493 (55.1%) adult patients 213 (43.2%) were male and 280 (56.8%) were female which is shown in Table 2.

Food Habit wise distribution:
Amongst 401 pediatric patients 109 (26.1%) were vegetarians, 34 (8.4%) were non vegetarians and the data was not available for 258 (64.3%) patients and out of 493 adult patients 71 (14.3%) were vegetarians, 180 (36.4%) were non vegetarians and the data was not available for 242 (48.9%) patients as shown in table 2.

Geographical area wise distribution:
From the 401 pediatric patients 348 (86.7%) were from rural areas and 53 (13.2%) were from urban areas and among 493 (85.6%) adult patients 423 (85.6%) were from rural areas and 70 (14.1%) were from urban areas.

Table 2; General characteristics of patients with IDA

	GENDER-Number of patients (%)		FOOD HABITS- Number of patients (%)		
	MALE	Female	VEG	NON VEG	NOT MENTIONED
PEDIATRIC (N=401)	229 (57.1)	172 (42.8)	109 (26.1)	34 (8.4)	258 (64.3)
ADULTS (N=493)	213 (43.2)	280 (56.8)	71 (14.3)	18 (36.4)	242 (48.9)

Age group wise distribution in IDA patients:

Depicted in Table 3 is the distribution of the various kinds of anemia in different age groups. In pediatrics Infants (28 days to 12 months) are in majority who have IDA and in adults young adults (19-30 years) are in majority who have IDA.

Table 3; Age group wise distribution in IDA patients.

Age group	No. of Patients (%) (N=894)
Infancy (28 days to 12 months)	142 (35.4)
Toddler (13months-2 years)	87 (21.6)
Early Childhood (2-5years)	81 (20.1)
Middle childhood (6-11 years)	52 (12.1)
Early Adolescence (12-18 years)	39 (9.7)
Young adult (19-30 years)	207 (41.9)
Middle aged adults (31-59 years)	158 (32)
Geriatrics (>60 years)	128 (25.9)

4.2 Distribution of Various Risk Factors for IDA in Adults and Pediatrics

The various risk factors for Anemia based on studies include Age below 2 years and above 60 years, female gender, occupation, child bearing age (15-44 years) , alcohol, smoking, chronic disease, low absorption in IDA, pregnancy, GI Bleeding, history of blood loss, history of taking aspirin or NSAID, food habits-veg, place-rural, worm infestation, hemorrhoids, nose bleeding, postpartum hemorrhage and various drug use.

Risk factor distribution in pediatric IDA patients:

Out of 401 pediatric patients 219 (54.6%) patients were below the age of 2 years, 164 (40.9%) patients were female, 19 (4.7%) patients were of the child bearing age, 5 (1.2%) pediatric patients had a history of blood loss, 2 (0.5%) patients had GI bleeding, 1 (0.2%) patient had a family history of IDA, 1 (0.2%) patient had chronic diseases, and 1 (0.2%) patient used methotrexate which is associated with increased risk of Iron Deficiency Anemia.

Risk factor distribution in adult IDA patients:

Among 494 adults **,** 276 (55.9%) patients were female, 188 (38.1%) patients were of the child bearing age, 128 (25.9%) patients were above the age of 60 years, 103 (20.8%%) patients had chronic diseases, 42 (8.5%) adult patients had a history of blood loss, 29 (5.8%) adult patients had a history of alcohol use, 18 (3.6%) adult patients had a history of smoking, 16 (3.2%) adult patients had a history or using NSAID/ aspirin. There were 13 (2.6%) pregnant women. 14 (2.8%) adult patient had a family history of IDA, 10 (2%) adult patients had GI bleeding, 5 (1%) adult patients used a drug associated with anemia which were Sulfasalazine, methotrexate and corticosteroid, 4 (0.8%) adult patients had an occupation which were risk factors to anemia, those being-farmer, field worker and fishermen, 3 (0.6%) adult patients had low absorption in IDA, 3 (0.6%) adult patients had worm infestation and 1 (0.2%) adult patient had a previous medical history of IDA which is represented in figure 1.

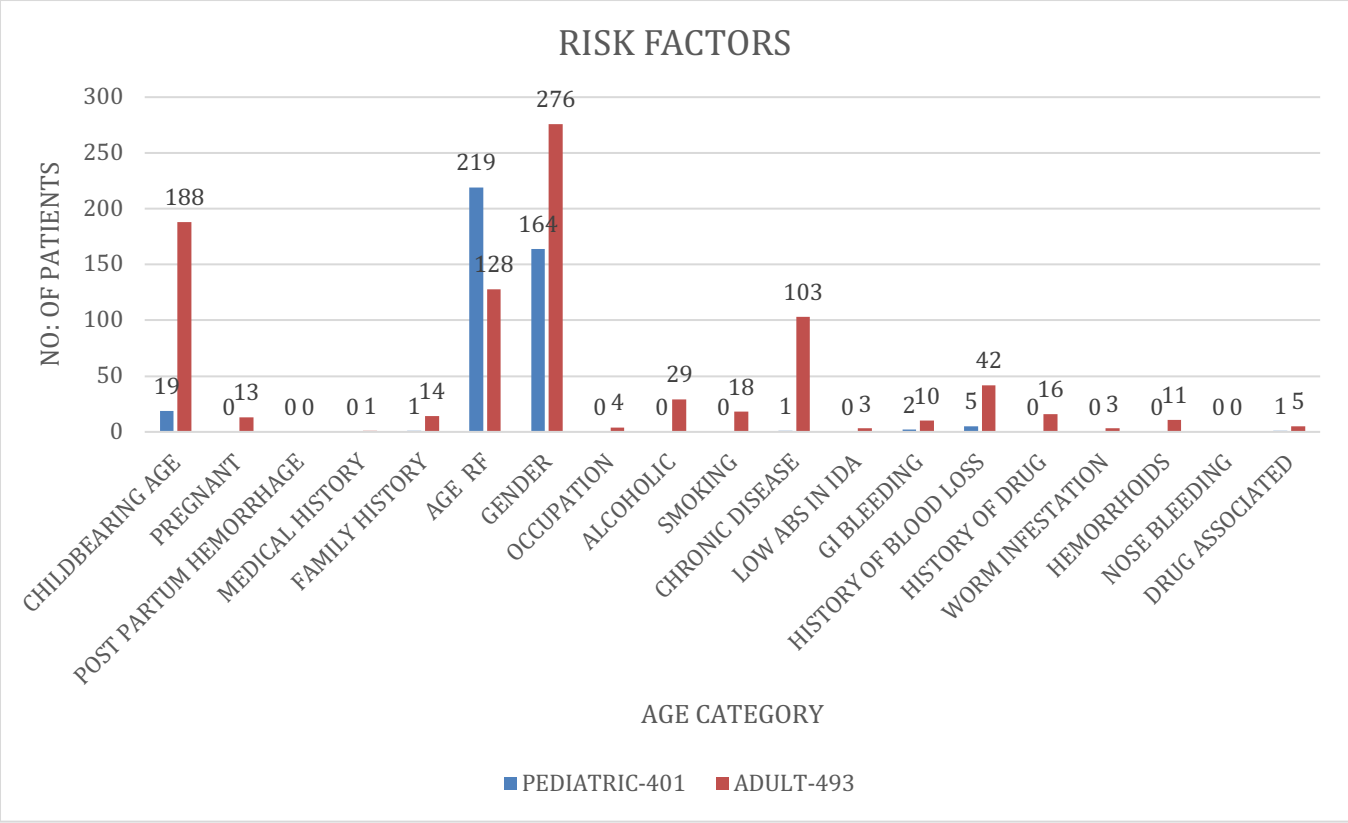


Figure 1; Distribution of various risk factors in Adults and Pediatrics

4.3 Presence of Clinical Manifestations of IDA in patients

Among 401 pediatric patients 194 (48.4%) patients had clinical manifestations of IDA present and 207(51.6%) patients had no clinical manifestations present.

Out of 493 adult patients 348 (70.5%) patients had clinical manifestations present and 145 (29.4%) patients had no clinical manifestations present.

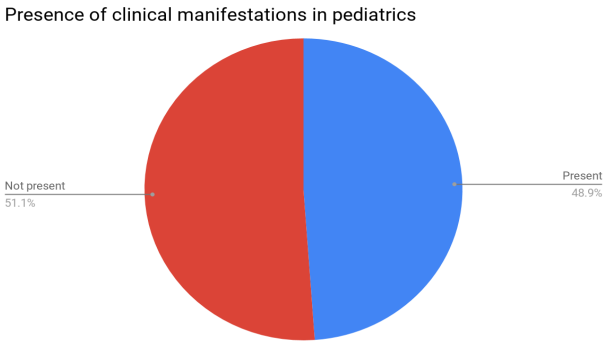


Figure 2; Presence of clinical manifestations in pediatrics

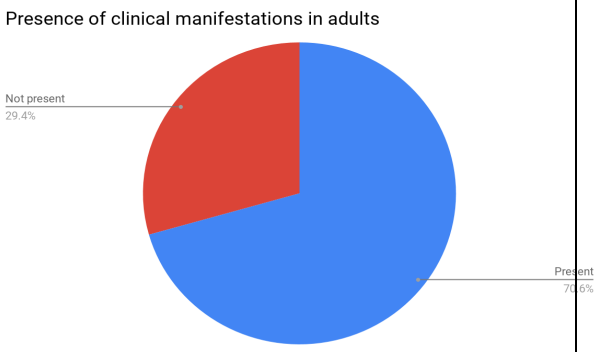


Figure 3; Presence of clinical manifestations in adults

4.4 Distribution of Clinical Manifestations

The various clinical manifestations associated with anemia are chest pain, fatigue, dizziness, irritability, weakness, palpitations, vertigo, tingling, shortness of breath, decreased exercise tolerance, tachycardia and pallor.

Distribution of clinical manifestations in pediatric patients:

Out of 401 pediatric patients 166 (41.39%) patients had pallor, 12 (2.9%) patients felt fatigued, 9 (2.24%) patients were weak, 8 (1.9%) patients had shortness of breath, 4 (0.9%) patients were irritable, 3 (0.7%) patients were dizzy, 1 (0.2%) patient had palpitation, 1 (0.2%) patient had chest pain and 1 (0.2%) patient had tachycardia which is shown in figure 4.

Distribution of clinical manifestations in adult patients:

Out of 493 adult patients 242 (49.08%) patients had pallor, 96 (19.47%) patients felt fatigued ,80 (16.2%) patients had shortness of breath, 52 (10.54%) patients were weak, 24 (4.86%) patient had chest pain, 10 (2.01%) patients had decreased exercise tolerance, 5 (1.01%) patient had palpitation, 5 (1.01%) patients had tingling, 4 (0.81%) patients were irritable, 3 (0.6%) patients were dizzy, 2 (0.4%) patients had vertigo and 1 (0.2%) patient had tachycardia which is also shown in figure 4.

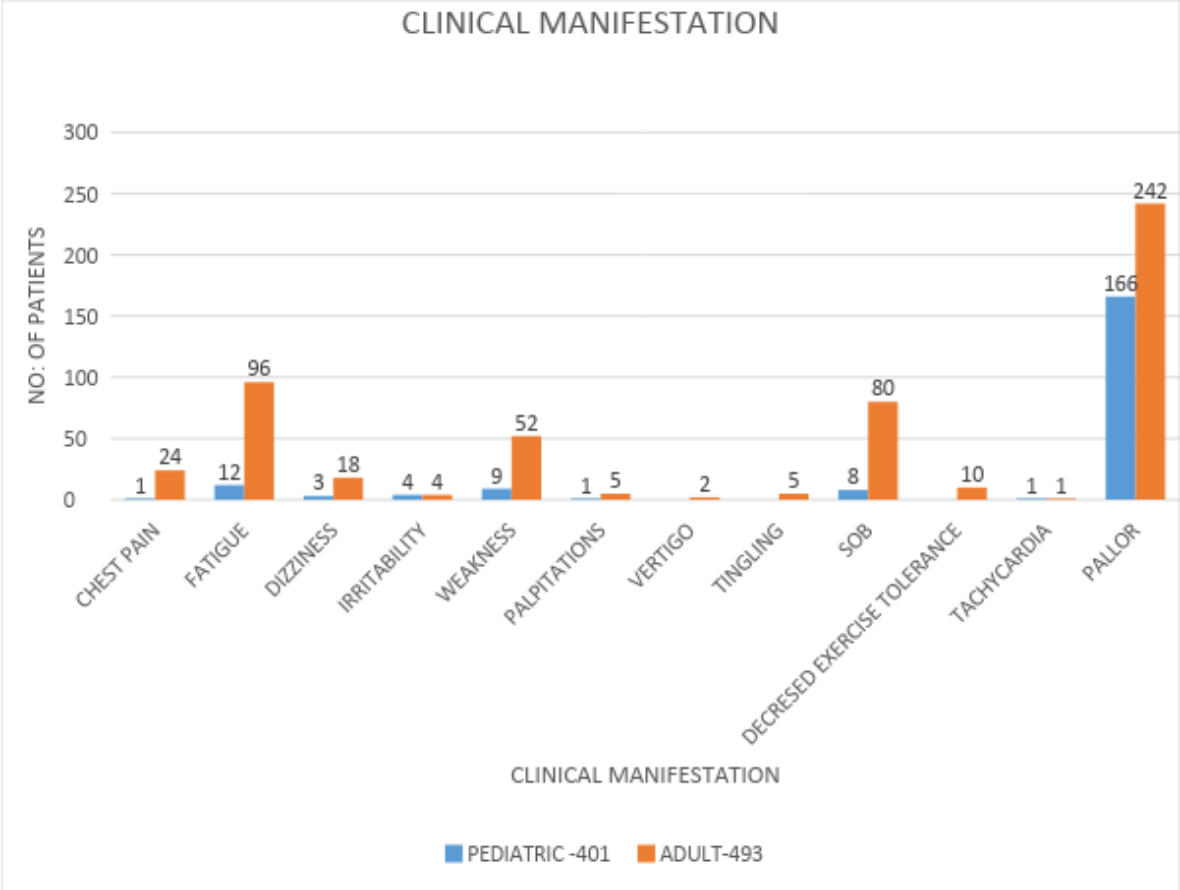


Figure 4; Distribution of clinical manifestations in pediatrics and adults.

4.5 Severity

The severity was categorised based on the WHO classification depicted in Table 1 and in this study the laboratory values were not assessed for 5 (1.2%) pediatric patients and 11 (2.2%) adult patients due to which their severity could not be classified.

Classification of severity of anemia in pediatric patients:

Out of 401 pediatric patients 77 (19.2%) had mild anemia, 269 (67.1%) had moderate anemia and 31 (7.7%) had severe anemia. The values were normal for 19 (4.7%) pediatric patients.

Classification of severity of anemia in adult patients:

and of 493 adult patients 61 (12.4%) patients had mild anemia, 243 (49.3%) had moderate anemia and 167 (33.9%) patients had severe anemia. The value were normal for 11(2.2%) adult patients.

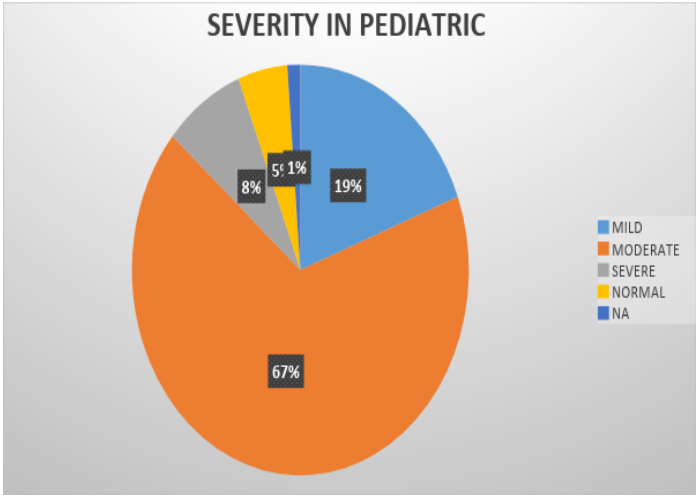


Figure 5; Severity in Pediatrics

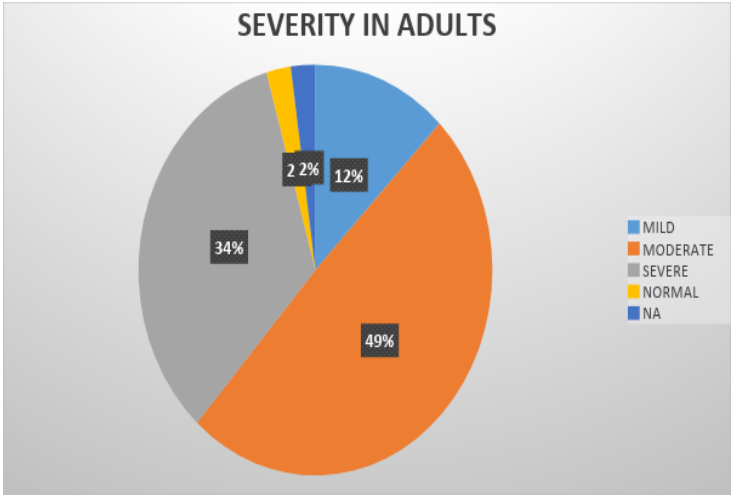


Figure 6; Severity in Adults

4.6 Outcome

The outcome of the treatment varied for adults and pediatrics as shown in figure 7.

Outcome of therapy for pediatric patients:

Out of 401 pediatric patients, 93 (22.3%) patients' laboratory values and condition improved after treatment, 66 (17.2%) patients' values did not improved and data was not available for 242 (60.4%) patients.

Outcome of therapy for adult patients:

Out of 478 adult patients, 246 (49.8%) patients' laboratory values and condition improved after treatment, 86 (17.4%) patients' values did not improve and data was not available for 146 (29.6%) patients.

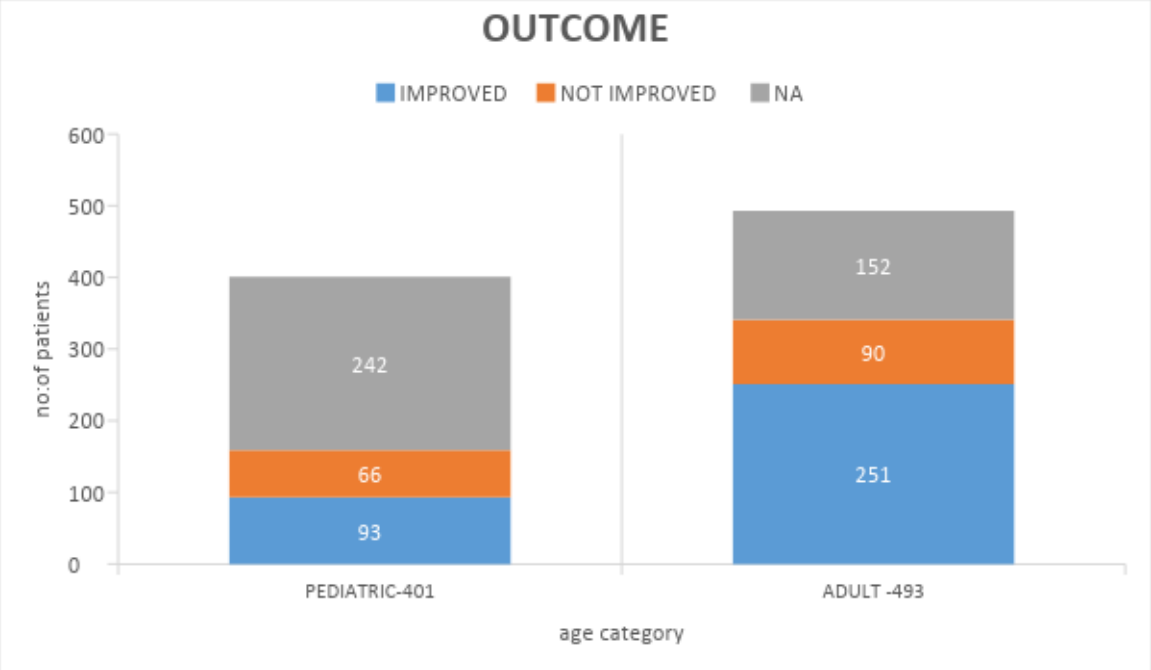


Figure 7; Outcome of treatment

4.7 Comparison of Laboratory values before and after treatment.

Although the data was not available for all the patients, in table 6 and table 7 the laboratory values for pediatrics and adults are depicted during admission and follow up respectively.

Table 4; Laboratory parameters on admission and during discharge in pediatric patients.

PEDIATRIC (N=401)		
DURING STAY		DURING FOLLOW UP
	MEAN ± STANDARD DEVIATION	
HB (g/dl)	10.07±1.71	10.07±4.81
MCV (fl)	68.40±34.53	73.60±54.07
MCHC (g/dl)	34.30±25.11	33.89±24.27
MCH (pg)	22.19±3.98	23.20±7.36
PCV (%)	31.10±14.52	30.60±5.21
TIBC (mcg/dl)	183.35±192.15	34.7±0
RBC (cells/µL)	$4.94*10^6$±$3.83*10^6$	$4.91*10^6$ ±$2.74 *10^6$
FERRITIN (ng/mL)	55.04±76.28	0
VITAMIN B12 (pg/ml)	569.30±603.28	0
FOLIC ACID (µg)	15.50±.4242	0
RDW (%)	18.07±9.35	18.9±5.73
IRON (mcg/dl)	32.90±48.60	0
TRANSFERRIN (mg/dL)	0	0
INTRINSIC FACTOR (AU/mL)	0	0
MMA (mmol/L)	0	0
HOMOCYSTEINE <(mg/dl)	0	0

Table 5 ; Laboratory parameters on admission and during discharge in adults

ADULT (N=493)		
DURING STAY		DURING FOLLOW UP
	MEAN ± STANDARD DEVIATION	
HB (g/dl)	9.46±1.98	8.42±2.37
MCV (fl)	74.57±41.97	76.40±38.26
MCHC (g/dl)	31.21 ±2.50	33.4±23.74
MCH (pg)	23.57±12.7	25.25±15.64
PCV (%)	27.72±17.97	30.24±16.70
TIBC (mcg/dl)	334.59±166.8	232.42±147.70
RBC (cells/µL)	$3.87*10^6$ ±$1.74 *10^6$	$4.28*10^6$ ±$2.52*10^6$
FERRITIN (ng/mL)	112.76±262.98	124.40±162.98
VITAMIN B12 (pg/ml)	701.11±728.49	1163.6±767.69
FOLIC ACID (µg)	11.60±8.03	0
RDW (%)	19.67±11.1	21.6±7.42
IRON (mcg/dl)	38.02±55.17	83.50±75.05
TRANSFERRIN (mg/dL)	0	0
INTRINSIC FACTOR (AU/mL)	0	0
MMA (mmol/L)	0	0
HOMOCYSTEINE <(mg/dl)	0	0

4. 8 Treatment pattern during hospital stay and discharge

The treatment pattern during hospital stay and discharge was recorded. Although not all the patients were given treatment during hospital stay and discharge.

Treatment pattern for IDA in pediatric patients:

Out of 401 pediatric patients 121 (30.1%) patients received treatment during hospital stay and 280 (69.8%) patients did not receive treatment during hospital stay, the details of which is represented in table 6.

Treatment pattern for IDA in adult patients:

493 adult patients with IDA 199 (40.3%) patients received treatment and 194 (39.3%) patients did not receive treatment during hospital stay, the details of which is represented in table 7.

Table 6; Pattern of treatment during hospital stay for pediatrics.

DRUG	FREQUENCY	NO. OF PATIENTS (%) (N=401)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.1MG	ONCE A DAY	6 (1.4)
IRON HYDROXIDE+FOLIC ACID+VIT B12 25MG+500MCG+5MCG	ONCE A DAY TWICE A DAY NA	293 (73) 6 (1.4) 17 (4.2)
IRON+FOLIC ACID+ZINC SULPHATE 100MG+1.5MG+22.5MG	ONCE A DAY	1 (0.2)
CYANOCOBALAMIN+ELEMENTAL COPPER+ELEMENTAL MANGANESE +FERROUS AMMONIUM CITRATE +FOLIC ACID 7.5MCG+3MCG+30MCG+160MG+0.5 MG	ONCE A DAY	1 (0.2)
FERROUS FUMARATE +MULTIVITAMINS 30 MG	NA	1 (0.2)

INJ IRON SUCROSE 100 MG	NA	3 (0.7)
NO ANEMIC DRUG	NA	280 (69.8)

Table 7; Pattern of treatment on discharge for pediatrics

PEDIATRIC		
DRUG	FREQUENCY	NO . OF PATIENTS (%) (N=401)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.1MG	ONCE A DAY	6 (1.4)
IRON HYDROXIDE+FOLIC ACID+VITB12 25MG+500MCG+5MCG	ONCE A DAY	297 (74)
	TWICE A DAY	2 (0.4)
	NA	17 (4.2)
CYANOCOBALAMIN+ELEMENTAL COPPER+ELEMENTAL MANGANESE +FERROUS AMMONIUM CITRATE +FOLIC ACID 7.5MCG+3MCG+30MCG+160MG+0.5MG	1-0-1	1 (0.2)
NO ANEMIC DRUG	NA	78 (19.4)

Table 8; Pattern of treatment during hospital stay for adults

DRUGS	FREQUENCY	NO. OF PATIENTS (%) (N=493)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.1MG	ONCE A DAY	51 (10.3)
	TWICE A DAY	1 (0.2)
	THRICE A DAY	1 (02)
	NA	4 (0.8)
IRON HYDROXIDE+FOLIC ACID+VIT B12 25MG+500MCG+5MCG	ONCE A DAY	2 (0.4)
VIT C/ FOLIC ACID+FERROUS FUMERATE+VITB12	ONCE A DAY	4 (0.8)

IRON+FOLIC ACID+ZINC SULPHATE 100MG+1.5MG+22.5MG	ONCE A DAY	37 (7.5)
	NA	4 (0.81)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.5MG	ONCE A DAY	2 (0.4)
FERROUS FUMERATE+FOLIC ACID 152MG+1.5MG	ONCE A DAY	7 (1.4)
	NA	3 (0.60)
FERROUS FUMERATE+FOLIC ACID+ZINC SULPHATE 100MG+1500MCG+61.8MG	ONCE A DAY	25 (5.07)
	NA	1 (0.2)
CYANOCOBALAMIN+ELEMENTAL COPPER+ELEMENTAL MANGANESE +FERROUS AMMONIUM CITRATE +FOLIC ACID 7.5MCG+3MCG+30MCG+160MG+0.5MG	ONCE A DAY	13 (2.63)
IRON+FOLIC ACID+CYANOCOBALAMIN+NIACINAMIDE+PYRIDOXINE. 150MG+1MG+15MCG+2MG+50MG	ONCE A DAY	15 (3.04)
FERROUS FUMARATE +MULTIVITAMINS 30 MG	ONCE A DAY	9 (1.82)
ELEMENTAL IR0N+ELEMENTAL SULPHATE+FOLIC ACID+METHYCOBALAMIN 60MG+15MG+1MG+500MCG	ONCE A DAY	1 (0.2))
ELEMENTAL IRON+FERROUS AMMONIUM CITRATE+FOLIC ACID+LIVER FRACTION+PEPTONE 3.95MG+34MG+0.17MG+40MG+20MG	ONCE A DAY	1 (0.2)
ELEMENTAL IRON+ L METHYLFOLATE+MECOBALAMIN 100MG+300MCG+1500MCG	ONCE A DAY	5 (1.01)
FERROUS ASCORBATE+ L METHYL FOLATE+ZINC+METHYLCOBALAMIN 100MG+ 500MCG+ 61.8MG	ONCE A DAY	1 (0.2)
INJ IRON SUCROSE 100 MG	NA	3(.60)
	ONCE A DAY	2 (0.4)

ELEMENTAL IRON+ FOLIC ACID+ VIT B12+ ZINC SULPHATE 152MG+1.5MG+15MCG+15MG	NA	2 (0.4)
NO ANEMIC DRUG	NA	299 (60.6)

Table 9; Pattern of treatment on discharge for adults

ADULT		
DRUG	FREQUENCY	NO. OF PATIENTS (%) (N=493)
VITC+FOLIC ACID+FERROUS FUMERATE+VITB12 150 MG+1.5MG+350MG+15MCG	ONCE A DAY	6 (1.21)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.1MG	ONCE A DAY	57 (11.56)
	TWICE A DAY	1 (0.2)
IRON HYDROXIDE+FOLIC ACID+VITB12 25MG+500MCG+5MCG	ONCE A DAY	6 (1.21)
	NA	1 (0.2)
IRON+FOLIC ACID+ZINC SULPHATE 100MG+1.5MG+22.5MG	ONCE A DAY	50 (10.1)
	NA	1 (0.2)
FERROUS ASCORBATE+FOLIC ACID 100MG+1.5MG	ONCE A DAY	1 (0.2)
FERROUS FUMERATE+FOLIC ACID 152MG+1.5MG	ONCE A DAY	6 (1.21)
	NA	2 (0.4)
FERROUS FUMERATE/FOLIC ACID/ZINC SULPHATE 100MG+1500MCG+61.8MG	ONCE A DAY	12 (2.4)
	TWICE A DAY	16 (3.24)
CYANOCOBALAMIN+ELEMENTAL COPPER+ELEMENTAL MANGANESE +FERROUS AMMONIUM CITRATE +FOLIC ACID 7.5MCG+3MCG+30MCG+160MG+0.5MG	ONCE A DAY	13 (2.63)
IRON+FOLIC ACID+CYANOCOBALAMIN+NIACINAMIDE+PYRIDOXINE 150MG+1MG+15MCG+2MG+50MG	ONCE A DAY	2 (0.4)
	TWICE A DAY	11 (2.23)
	THRICE A DAY	1 (0.2)

DISCUSSION

5. Discussion

This study was conducted in a tertiary health care hospital in South India and it was a retrospective observational study. IDA patients demographics, risk factors, clinical manifestations and treatment pattern during stay and on discharge were assessed. A total of 894 patients' data (out of which 401 (44.8%) were pediatrics and 493 (55.1) were adults) diagnosed with IDA in the year 2017 were included for evaluation. In this study out of 995 patients, 894 were diagnosed with Iron Deficiency anemia, 101 patients were diagnosed with Megaloblastic anemia and 83 patients were diagnosed with both Megalobalstic and Iron deficiency anemia. Natarajan et al. stated that out of the various different kinds of anemia Iron deficiency anemia (IDA) is thought to be the most common cause of anaemia globally [8]

It was found that 493 (55.1%) adult patients and 401 (44.9%) pediatric patients had anemia among 894 patients.

In our study it was observed that 160 (40.9%) were female and in adults it was found that the female gender was the highest distributed risk factor where 276 patients (55.9%) patients were female, which was similar to the the study by Nataranjan et al. which stated that majority of the patients who suffer from anemia are female (71%) and are usually more than 15 years of age. This could be attributed to the low nutrition intake in the females and menstrual blood loss that occurs every month. [8]

We observed 219 (54.6%) pediatric patients were below 2 years of age, which concurrent with the study by A Zhao et al. in a South Asian country Burma where the result stated that the one of the predictors of anemia are young age (less than 5 years old) ($P < 0.001$) and that there is a high prevalence of anemia in children. [12] In adults, age was a risk factor for 128 (25.9%) patients. Although age above 60 years was not a highly distributed risk factor in adults, according to a study in 2019 by Duman T et al. etiology and causes of anemia should be carefully investigated in subjects with advanced age and it should be kept in mind that B12 deficiency and comorbidities were more common in elderly men. .[18]

Our study showed 19 (4.7%) pediatric females were of the child bearing age and 188 (38.1%) adults women were found to be of the child bearing age. Whereas in a study conducted by Ansari et al. it was found that out of 200 non-pregnant women 89 (44.5%) patients had IDA. [22]

It was found that 13 (2.6%) adult women were pregnant who had IDA. Many literatures stated that menstruating women, adolescents and pregnant women are the most risk of developing IDA [13] and apart from the importance of prophylaxis of IDA in pregnant women, oral and IV preparations are the best treatment option for IDA. [23]

Only 4 (0.8%) out of 493 adult patients had an occupation which is a risk factor to develop anemia because of worm infestation (farmer and fisherman). Hookworm infections remain a major cause of morbidity in the developing world. Prevalence is highest in agricultural areas, where use of waste water for irrigation and

poor hygiene increases infection rates among farmers. Infections present with gastrointestinal symptoms and chronic anaemia, and there are usually no signs of overt blood loss. [31]

We observed 109 (26.1%) pediatric patients were vegetarians and 34 (8.4%) were non vegetarians. In adult patients 71 (14.3%) were vegetarians and 180 (36.4%) were non vegetarians, also the data of diet habits of many of the patients was not available. So, we found that there is no significant difference in prevelance of IDA in vegetarians or non-vegetarians which is according to the study conducted by Craig W which concluded that the iron stores of vegetarians may be reduced but the incidence of iron-deficiency anemia in vegetarians is not significantly different from that in non-vegetarians [32]

Study found 348 (86.7%) pediatric patients were from a rural area and 423 (85.8%) adult patients were from a rural area. Many patients from the rural area were lower income group. Low socio economic group people have higher chances of developing anemia than that of the people in a better socio-economic group. [13]

Passive smoking is known to unfavourably affect pregnancy, childbirth and infants. It causes RBC metabolism causing anemia in children. [24] In our study we observed that only small group of population with smoker and alcoholics, that is 18 (3.6%) adult patients were smokers and 29 (5.8%) adult patients consumed alcohol. In a study by Ioannou GN et al. it was found that consumption of any form of alcohol was associated with 40% reduced risk of iron deficiency anemia. [25]

We observed only 2 (0.5%) pediatric patients had a history of GI bleeding, 10 (2%) adult patients had GI bleeding, 42 (8.5%) adult patients had a history of blood loss and 11 (2.2%) adult patients had hemorrhoids. Many literature proved that a major amount of Iron is lost through blood loss. [26] and Chronic gastrointestinal bleeding is the most common cause of iron deficiency anemia (IDA) in the general population. [28]

A lot of drugs are also associated with increased risk of anemia including Azathioprine, primidone, cytabine, vinblastin, tetracycline, etc. [13] whereas in our study we observed only 1 (0.2%) pediatric patients was reported with the usage of methotrexate and 5 (1%) adult patients were reported with the usage of Sulfasalazine, Methotrexate and Corticosteroids.

In this study pallor was present in majority of the population in adults (242-49.08%) and pediatrics (166-41.39%). In a study conducted by Stoltzfus R et al stated that pallor is a simple way to detect anemia, but more data are needed for its accuracy to assess severity. [30]

On evaluation of clinical manifestation we observed 12 (2.9%) pediatric patients felt fatigued, 9 (2.24%) patients were weak, 8 (1.9%) patients had shortness of breath, 4 (0.9%) patients were irritable, 3 (0.7%) patients were dizzy, 1 (0.2%) patient had palpitation, 1 (0.2%) patient had chest pain and 1 (0.2%) patient had tachycardia.

Whereas in adult patients 96 (19.47%) patients felt fatigued ,80 (16.2%) patients had shortness of breath, 52 (10.54%) patients were weak, 24 (4.86%) patient had chest pain, 10 (2.01%) patients had decreased exercise tolerance, 5 (1.01%) patient had palpitation, 5 (1.01%) patients had tingling, 4 (0.81%) patients were irritable, 3 (0.6%) patients were dizzy, 2 (0.4%) patients had vertigo and 1 (0.2%) patient had tachycardia

According to Dipiro J et al. the common clinical manifestations in anemia included chest pain, fatigue, dizziness, irritability, weakness, palpitations, vertigo, tingling, shortness of breath, decreased exercise tolerance, tachycardia and pallor. [13] It is not required that the patients show all the symptoms for the diagnosis of IDA, physicans diagnose and treat the anemia based on some of the symptoms and with the help of laboratory values.

In a retrospective observational study with a sample size of 100, conducted in the Medical Records Department, Pondicherry Institute of Medical Sciences (PIMS) the patients with IDA had severe IDA (58%), followed by moderate IDA (36%) [8] where as in our study we found in pediatrics the severity was moderate in [(269 (67.1%)], followed by mild in 19.2% and then severe in (7.7%) patients and in adults the severity was moderate in 49.3%, followed by severe (33.9%) and mild (12.4%).

Out of 401 pediatric patients 121 (30.1%) patients received treatment during hospital stay and out of 493 adult patients 199 (40.3%) patients received treatment. A varied array of interventions exist for the treatment of IDA involving dietary interventions, fortification of foods with iron and iron supplements can be used for the treatment of Iron Deficiency Anemia. Once or twice weekly dose of iron in school going children, non pregnant women and adolescents is recommended whereas for infants (6-24 months) of age require a much higher intake of iron as they are growing rapidly.[8]

For IDA, in a study by Ahmad et al. it is found that low ferritin levels are equally frequent among children with or without anemia.[15] And for treatment, a study by Okam et al. stated that oral iron replacement is an important line for therapy. But it is often poorly tolerated or ineffective. [16] There is a high physiological requirement of iron in pregnancy which is difficult to meet with most diets. Therefore, iron supplementation is given to pregnant women in all contexts. supplementation should also continue into the postpartum period to provide adequate iron stores to women. [14] In this study a regular dose of iron was provided to the patients with low iron, but iron treatment was not given to all patients. In this study the mean haemoglobin value for adults and pediatrics did not change drastically even after treatment was provided. Although the treatment is simple and effective, there is still a high prevalence of Iron Deficiency Anemia the reason maybe being non-compliance of the patients or due to ineffective or incomplete treatment by the physicians. [8]

IDA is more common is South Asian countries like India. Zlotkin et al. states that IDA is associated with impaired psychomotor development in childhood and there is a major need of new sustainable strategies to control IDA in children which include promotion of healthy food habits along with improving the nutritional value of these foods by using complementary supplements. [17]

LIMITATIONS

6. LIMITATIONS

- Since this is a retrospective study design, a lot of data was missing or not recorded.
- For a few patients CBC values were not recorded during follow up.

CONCLUSION

7. CONCLUSION

Though anemia is a treatable disease it is still highly prevalent around the world. An observational retrospective study was carried out in a tertiary care hospital with a sample size of 995 who were admitted in Kasturba Hospital, Manipal in the year 2017.

It was found that there were many more cases of IDA than Megaloblastic anemia and IDA was highly distributed in adults than in pediatrics. Young adults were the highly affected population in our study.

Among risk factors, female gender was the highly distributed risk factor in adults and age below 2 years was the highly distributed risk factor in pediatrics. Pallor was commonly observe clinical manifestation in both the age groups followed by fatigue.

On assessment of severity of anemia based on WHO scale, in pediatrics we found majority of them had mild followed by moderate and then severe form of anemia. In adults the moderate, severity followed by severe and then mild form of anemia

It was observed that after the treatment during stay and discharge the outcome of disease in both age groups did not improve drastically.

This study concluded that it helps in identifying the various risk factor and clinical manifestations of Iron Deficiency anemia which will in turn help in prevention of the disease by early assessment of the disease based on these factors. It also gives us an idea of the changes to be made in treatment pattern and//or to provide counselling to patients regarding adherence to medication and food rich in iron so that the outcome of the disease was improved.

FUTURE DIRECTIONS

8. FUTURE DIRECTIONS:

- A prospective study on comparison between different treatment regimens would yield better result.
- A similar study should be conducted regionally and nationally to yield results at a larger scale.

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APPENDICES

Appendix - I

KASTURBA HOSPITAL
MANIPAL
(An associate Hospital of MAHE, Manipal)

Kasturba Medical College and Kasturba Hospital
Institutional Ethics Committee
(Registration No. ECR/146/Inst/KA/2013/RR-16)

Communication of the decision of the Institutional Ethics Committee

Wednesday 15th August 2018 **IEC : 471/2018**

Project title	:	Assessment of pattern, risk factors and treatment of Iron Deficiency Anemia and Megaloblastic Anemia in Adult and Pediatric Population in a tertiary care hospital in South India.
Principal Investigator	:	Miss. Asthaa Malhotra
Guide/ Co Guide/ Co Investigators	:	Dr. Leelavathi D Acharya, Dr. Girish Thunga, Dr. Shrikiran A Hebbar, Dr Sneha, Naval Roshan, Upamayu Mondal, Asthaa Malhotra, Souptik Chatterjee
Name & Address of Institution	:	Department of Pharmacy Practise, MCOPS, Manipal, Department of Pediatrics, KMC, Manipal, Department of Medicine, KMC, Manipal, Department of Pharmacy Practise, MCOPS, Manipal.
Status of review	:	New
Date of review	:	14.08.2018
Decision of the IEC	:	Approved for the study period from 14.08.2018 to 13.08.2019 as mentioned in protocol.

- The PI and all members of the project shall ensure compliance to current regulatory provisions (as per Schedule Y of Drugs and Cosmetics Act and ICH-GCP), Ethical Guidelines for Biomedical Research on Human Participants by ICMR, and the SOP of IEC including timely submission of Interim Annual Report and Final Closure Report
- Participant Information Sheet and a copy of signed Informed Consent shall be given to every research participant
- Inform IEC in case of any proposed amendments (change in protocol / procedure, site / Investigator etc)
- Inform IEC immediately in case of any Adverse Events and Serious Adverse Events.
- Members of IEC have the right to monitor any project with prior intimation.

Dr. Stanley Mathew
MEMBER SECRETARY - IEC

ETHICS COMMITTEE APPROVED KASTURBA HOSPITAL, MANIPAL

IEC Secretariat, Room No. 22, Ground Floor, Faculty Room Complex, Kasturba Medical College Premises,
Kasturba Medical College, Manipal - 576104, Karnataka, India. Phone : +91 - 0820 - 2933522,Fax : +91 - 0820 - 2571927. Email : iec.kmc@manipal.edu

MR-798

(Yoga and Ayurveda services are excluded from the scope of NABH accreditation)

Appendix – II

AGE:	DOA:	PATIENT ID:	ADULT /PEDIATRIC
SEX:	DOD:	BMI:	

MEDICAL HISTORY :

MEDICATION HISTORY:

FAMILY HITORY :

SURGICAL HISTORY :

RISK FACTORS : AGE: GENDER:

OCCUPATION: CHILD BEARING AGE:

ALCOHOL: ☐ SMOKING: ☐

CHRONIC DISEASE: ☐ **LOW ABSORBTION IRON IN IDA:** ☐

PREGNANCY: ☐ GI BLEEDING: ☐

HISTORY OF BLOOD LOSS: ☐

HISTORY OF TAKING : ASPIRIN: ☐ NSAIDS: ☐

FOOD HABITS: VEG: ☐ NON VEG: ☐

PLACE : RURAL: ☐ URBAN: ☐

WORM INFESTATION : HOOK WORM: ☐ TAPE WORM: ☐

HEMORRHOIDS: ☐ NOSE BLEEDING: ☐ POST PARTUM HEMORRHAGE: ☐

DRUGS ASSOCIATED:

Corticosteroids: ☐	Iron : ☐	p-Aminosalicylates: ☐
Azathioprine : ☐	Primidone: ☐	Phenytoin: ☐
Chloramphenicol: ☐	Pyrimethamine : ☐	Colchicine: ☐
Cotrimoxazole : ☐	Sullfasalazine: ☐	Phenobarbital: ☐
Cyclophosphamide: ☐	Cytarbine: ☐	Vinblastin: ☐
Tetracycline: ☐	Hydroxyurea: ☐	Methotrexate: ☐
5-Flurodeoxyuridine: ☐	5-Flurouracil: ☐	6-mercaptopurine: ☐

CLINICAL MANIFESTATIONS:

CHEST PAIN:	☐	FATIGUE:	☐
DIZZINESS :	☐	IRRITABILITY:	☐
WEAKNESS :	☐	PALPITATIONS:	☐
VERTIGO:	☐	TINGLING:	☐
SHORTNESS OF BREATH:	☐	DECREASED EXERCISE TOLERANCE:	☐
TACHYCARDIA:	☐	PALLOR:	☐

INDICATION: MEGALOBLASTIC ANEMIA : ☐ IDA: ☐

LAB INVESTIGATIONS:

HB:	MCV:	MCHC:	MCH:
PCV:	TIBC:	RBC:	FERRITIN:
VIT B12:	FOLIC ACID:	RDW:	SERRUM IRON:
TRANSFERIN:	INTRINSIC FACTOR:	MMA:	HOMOCYSTEINE:

SEVERITY:

MILD: ☐ MODERATE: ☐ SEVERE: ☐

OUTCOME:

IMPROVED: ☐ NOT IMPROVED: ☐

LAB INVESTIGATIONS:

HB:	MCV:	MCHC:	MCH:
PCV:	TIBC:	RBC:	FERRITIN:
VIT B12:	FOLIC ACID:	RDW:	SERRUM IRON:
TRANSFERIN:	INTRINSIC FACTOR:	MMA:	HOMOCYSTEINE:

TREATMENT CHART:

GENERIC NAME	BRAND NAME	DOSE	FREQUENCY	DURATION

Assessment of pattern, risk factors and treatment of Megaloblastic Anemia in Adult and Pediatric population in a tertiary care hospital in South India

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LIST OF ABBREVIATIONS

1. Htn – Hypertension
2. DM– Diabetes mellitus
3. SPSS – Statistical Package for the Social Sciences
4. MA - Megaloblastic Anemia
5. IDA – Iron Deficiency Anemia
6. RBC- Red Blood Cell
7. DNA – Deoxy Ribonucleic Acid
8. MCG- Microgram
9. CRF – Case Record form
10. WHO - World Health Organization
11. GI- Gastric Intestinal
12. NSAID- Non Steroidal Anti Inflammatory Drug
13. SD- Standard deviation
14. Hb- Haemoglobin
15. MCV- Mean Cell Volume
16. MCHC- Mean corpuscular hemoglobin concentration
17. MCH- Mean cell hemoglobin
18. PCV- Packed cell volume
19. TIBC- Total iron binding capacity
20. RBC- Red blood cell
21. RDW- Red blood cell distribution width
22. MMA- methylmalonic acid

ABSTRACT

Introduction

Folic acid and cobalamin are B-group vitamins that play an essential role in many cellular processes. Deficiency in one or both of these vitamins causes megaloblastic anaemia, a disease characterized by the presence of megaloblasts**.** Treatment generally involves supplementation of VitB12 and folic acid. Generally a proper diet is very important along with supplementation.

Objectives

To assess the various the pattern, risk factors, and treatment of Megaloblastic anemia (MA) in paediatric and adult population in tertiary care hospital in South India,

Methodology

A retrospective observational study was conducted in tertiary care hospital after obtaining the approval of the ethical committee. Data of 184 MA patients who are admitted as MA in 2017 were collected from their files and recorded in the CRF which included demographic details, their diet and lifestyle, any medical or medication history, the type of anemia, it's severity, the treatment and outcome. SPSS version 20 was used to analyse the data.

Results

The sample size was taken as 184 patients which included 23(12.5%) paediartic and 161(87.5%) adult patient. Study shown that the number of male patients are more than female(1.55: 1). The highest risk factor in adult was gender as 63(39.13%) female patients. In-case of paediatric it was found to be age of less than 2 years(39.1%) .Pallor was found to be the most common clinical manifestation in both the population. Out of 23 paediatric patients 14(60.9%) patient patients had pallor and 109 (69%) adult patients had pallor. 62.1% of the adult population had severe MA,whereas it was 39.1% in paediatric. The most common cause for MA was found to be deficiency in VitB12.

Conclusion

Study concluded that the result will help us to understand the various preventable risk factor for MA, common clinical manifestions of disease, food habits which causes MA and the treatment pattern followed for improvement of the condition. Thus this epidemiological data will helpful for healthcare professionals.

INTRODUCTION

1. Introduction

Megaloblastic anemia is the condition in which there is presence of macrocytic red blood cells(RBCs) and there is distinct changes in morphology in the precursors RBC. The deficiency in Vit.B12 & folic acid, which plays an important role in many cellular process is the main reason for megaloblastic anemia. The presence of megaloblasts is a characteristic feature of megaloblastic anemia. When asynchronous mutation occurs between the nucleus and the cytoplasm it results in inhibition of DNA synthesis which results in the formation of megaloblast. Wide range of malabsorption i.e severe to mild of Vit.B12 can occur depending on the absorption of VitB12 in the gastric and ileal phase.

Vegetarian people are at a higher risk in case of nutritional deficiency of VitB12. Maternal deficiency of VitB12 is the reason of VitB12 deficiency in the infants as the content of B12 in the mother's milk is lower. Some disease condition such as Giardia infection can cause malabsorption of folate. *H.pylori* infection causes malabsorption of VitB12 in adults. Some drug therapies such as Trimethoprim, Methotrexate, pyrimethamine , metformin[13] which can lead to Megaloblastic anemia.[1]

Vit B12 deficiency affects around 6% in person aged less than 60 years and 20% of the people who are older than 60 years in the United States and in England. 40% of people in South American countries are affected. In Kenya 70% of the school children are affected. 80% of children and 70% adults are affected in India.[2]

To treat cobalamin deficiency oral cobalamin is initiated at 1-2 mg daily for one-two weeks, followed by 1mg daily. A common parental therapy 1000mcg daily for one week, then once a week for one month, and then monthly.

Oral folate 1mg daily for 4 months and 5mg in case of malabsorption is used to treat folic acid deficiency.[3]

NEED FOR THE STUDY

As seen in a study by Khandari U, et al. showed that out of total 120 patient's data 65% had cobalamin deficiency, 12% had both cobalamin and folate deficiency and 6% had folate deficiency. The female patients suffering from megaloblastic anemia was 71%. [4]

Alcohol can be a secondary reason for deficiency of VitB12 although a good nutrition can prevent deficiency of VitB12. Alcohol acts as a direct toxic on the bone marrow. A study done by Edward R.Eichner, et al showed in 65 alcoholic patient 40% of the patients developed megaloblastic erythropoiesis secondary to folic acid deficiency.[5] In a study done by Tungtrongchitr R, et al. in a military unit in Taiwan involving 123 male smokers and 63 nonsmokers it showed lower level of haemoglobin in smokers. 16.3% of the smokers were anemic and only 3% of the non-smoker were anemic. The folate levels were found to be lowered in the smokers.[6]

A cross sectional-study done by Hiren P Pandya and Asit Patil showed that out of 50 patients 10 patients were on mixed diet 40 patients were lacto vegetarian and 13 people were alcoholic i.e. 26% .[7]

A cross-sectional study done by Praphull Deepankar et.al , showed that out of 97 patients fatigueness was present in 92% of the patient , 59% showed exertional dyspnea, 19% showed palpitation and pallor was seen in 96% of the patient. [8]

This study is focused on the association of various risk factors associated with megaloblastic anemia like smoking ,alcoholism ,vegetarian diet. Also demographic details of the patient were assessed to obtain any link between them and megaloblastic anemia. Any underlying chronic disease were also checked for. The type ,treatment pattern and risk factors, severity both in adult and pediatric population were studied in south Indian population .

OBJECTIVES

2. RESEARCH AIMS AND OBJECTIVES :

AIM: To assess the pattern, risk factors and treatment of Megaloblastic anemia in adult and paediatric population in a tertiary care hospital in south India.

OBJECTIVE

- To assess the demographic and clinical characteristics of patients.
- To study the distribution pattern and various risk factors affecting anemia in adult and paediatric population.
- To study the treatment pattern and its outcome
- To find the severity of MA and the type of MA.
- To compare various study parameters in adult and paediatric population.

METHODOLOGY

3. METHODOLOGY

1. **Study site :**

This study was performed in the medicine and paediatric department in a tertiary care hospital.

2. **Study design :**

This was a Retrospective observational study.

3. **Study population :**

All patients who were admitted in the hospital due to Megaloblastic anemia during Jan 2017- Dec 2017, with the following inclusion and exclusion criteria were included in the study

- Inclusion criteria :

All in-patients with final diagnosis of megaloblastic anemia admitted in a tertiary care hospital, Manipal.

- Exclusion criteria:

Incomplete medical records and patients with other types of anemia.

4. **Sample size :**

The sample size was 181(107 MA+ 74 IDA+MA(mixed)) i.e. all the patients admitted during January 2017-Dec 2017.

5. **Ethical clearance :**

Ethical clearance has been obtained from KH Institutional Ethics Committee, Ref Number: 471/2018

6. **Sources of data collection :**

a. Patients record which includes
   - ❖ Reports of diagnostic and interventional procedures
   - ❖ Progress sheets
   - ❖ Laboratory investigation results
   - ❖ Discharge summary
   - ❖ Past history notes

b. Daily admission list kept at medical record department.

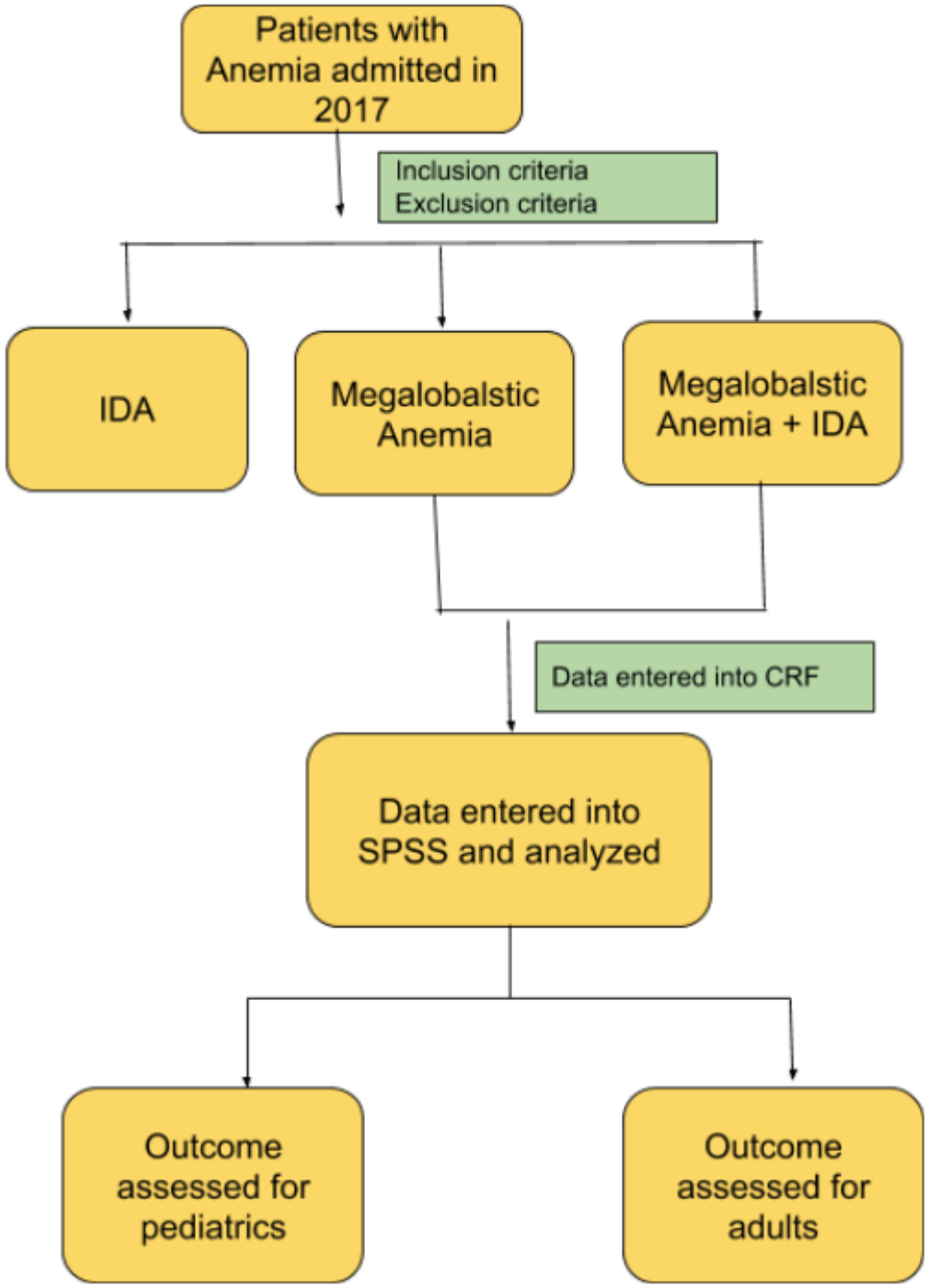
7. Materials used :

CASE REPORT FORM(CRF) (APPENDIX-2)

CRF includes hospital number, admission and discharge date, demography of the patients, duration of treatment, complaints on admission, medical and medication history, surgery history, risk factors such as smoking and alcoholism, the diet of the patient, any recent bleeding event, clinical manifestations if any present, the type of anemia and it's severity, the treatment pattern and it's outcome, discharge summary, lab data (appendix-2).

8. Operation Modality :

Study was done in the medicine and paediatric department of a tertiary care hospital in south India. The sample size was 181 and it included all the patients who were admitted between the time period of Jan 2017- Dec 2017. The data of the patient was recorded in the CRF which included the various risk factor the lab values, treatment pattern and it's outcome. The data was then analysed in SPSS version 20.



9. Collection of Data:

The medical records of all IDA patients were reviewed and the details of the patient were entered in a case record form. Demographic details like age, gender, occupation and social history were noted. Information regarding the presence of any Risk factors or chronic illness, pre-hospitalisation period and type of admission were retrieved from the files on a structured CRF.

10.Data Analysis :

The obtained data from the medical records of patients with MA were analysed for various parameters like demographic data, gender ratio, risk factor distribution, clinical manifestation, prescription pattern, discharge medications, laboratory values, outcomes and severity for pediatrics (age below 18 years) and adults (age above 18 years) etc using SPSS 20. The results of pediatrics and adults were compared and represented as descriptive statistics.

The various risk factors for MA were assessed as follows:

The various risk factors considered in this study were age, sex of the patient, previous disease and medication, any chronic disease if present. Any addiction to alcoholism and smoking were also taken as risk factors. History of blood loss, history of taking aspirin, diet of the patient, worm infestation, haemorrhoids, nose bleeding and post-partum haemorrhage if any present.[23]

The various clinical manifestations for MA were as follows:

Chest Pain, Pallor, Fatigue, Dizziness, Irritability, Weakness, Palpitations, vertigo, Tingling, Shortness of breath, Decreased exercise tolerance and tachycardia[23]

RESULTS

4. RESULTS

A total number of 995 patients' data were collected out of which 811 were diagnosed with IDA, 101 were diagnosed with Megaloblastic anemia and 83 were diagnosed as IDA and Megaloblastic anemia. In this study we are focusing on the patients diagnosed with MA.

1.Demographic characteristics of patients with MA

In the year 2017 total of 184 patients were admitted and diagnosed with MA. The distribution pattern of MA in Gender and various age category is shown in Table 2 respectively.

1.1 Gender wise distribution:

Out of 184 patients the number of paediatric patients were found to be 23(12.5%), in which 13(56.5%) paediatric patients were male and 10 were female. 161(87.5%) patients were adults. 98(60.9%) patients were male and 63(39.1%) patients were female.

Table 1; Distribution Pattern of MA according to gender:

CATEGORY		
Pediatric (N-23)	MALE	13 (56.5)
	FEMALE	10 (43.5)
Adult (N-161)	MALE	98 (60.9)
	FEMALE	63 (39.1)

1.2 Food Habit wise distribution :

Out of 23 paediatric patients 10 (43.5%) were vegetarians, 3 (13%) were non vegetarians and the data was not available for 10 (43.5%) patients. And out of 161 paediatric patients 33(20.5%) were vegetarians, 57 (35.4%) were non vegetarians and the data was not available for 71 (44.1%) patients.

Table 2; Food habits of paediatric and adult patients

Category	FOOD HABITS		
	NO OF VEG.PATIENTS(%)	NO. OF NON VEG PATIENTS(%)	NOT MENTIONED(%)
PEDIATRIC-N=23	10 (43.5)	3 (13)	10 (43.5)
ADULT- N=161	33 (20.5)	57(35.4)	71(44.1)

1.3 Geographical area-wise distribution:

Amongst the 23 pediatric patients 21 (91.3%) were from rural areas and 2(8.7%) were from urban areas. And out of 161 (85.6%) adult patients 143 (88.8%) were from rural areas and 18(11.2%) were from urban areas. In case of paediatric patient we saw that 2(8.69%) were from urban and 18(78.26%) were from rural area.

1.4 Age group-wise distribution

In infancy there were 6(26.08%) patients suffering from MA. In toddler there was two(8.69%) case of MA . Patient in the early childhood had one case of MA. 14(9.7%) patients in the age category of early adolescence had MA.

In adults there were 3 age groups; young adults, middle aged adults and geriatrics. In young adults 76 MA were present, in middle aged adults 60 MA patients were present, in geriatrics.25 MA patients were present

Table 3; Age groupwise distribution :

Age group	No. of Patients(%) N=184
Infancy (28 days to 12 months)	6 (26.08)
Toddler (13months-2 years)	2 (8.69)
Early Childhood (2-5years)	1 (4.34)
Middle childhood (6-11 years)	N/A
Early Adolescence (12-18 years)	14(9.7)
Young adult (19-30 years)	76(47.20)
Middle aged adults (31-59 years)	60(37.26)
Geriatrics (>60 years)	25(15.52)

2. Distribution of various risk factors in patient with MA

2.1 Distribution of Various Risk Factors in Paediatrics

Age below 2 years and above 60 years is a risk factor for anemia. The various risk factors for Anemia based on studies include, female gender, occupation, child bearing age, alcohol, smoking, chronic disease, low absorption in IDA, pregnancy, GI Bleeding, history of blood loss, history of taking aspirin or NSAID, food habits-veg, place-rural, worm infestation, haemorrhoids, nose bleeding, postpartum haemorrhage and various drug use. We assessed the various risk factor prevalence in our patients and found that out of 23 paediatric patients 10 (43.5) patients were female. 9(39.1%) paediatric patients were below 2 years of age. Amongst 10 females paediatric patients , 3 (13%) paediatric patients were of child bearing age. 1 (4.3%) patient had a family history. 1(4.3%) had a medical history of fever and gum bleeding. There was presence of TB in 1(4.3%) as a chronic disease. Valporate was found to be in the medication history of 1(4.3%) of the patient.

2.2 Distribution of Various Risk Factors in adults

In case of the 161 adults patients the risk factors were analysed. 63(39.2%) patients were female, 39(24.2%) amid the female adult patients were of child bearing age. 12(7.4%) had HTN 10(6,2%) had T2DM patients had chronic diseases which may or may not have been a direct risk factor for their anemia. Patients above 60 years of age have risk factor for developing megaloblastic anemia,30(18.6%) patients were above 60 years of age. Smoking and consumption of alcohol was found prevalent in 21(13%) and 23(14.3%) patients in the adults population. 9 patients were associated with history of blood loss.19 patients had medical history of disease which are associated with anemia,4(2.5%) patients had VitB12 def anemia, 2(1.2%) had anemia, HTN was present in 9(5.6%) of the patients and 4(2.5%) patients had T2DM 3(1.9%) patients were using aspirin and 1 patient(.6%) were on both aspirin and another NSAID and 2 patients had history of using Metformin. 3 patients(1.9%) had haemmorhoids and 1 patient had worm-infestation.

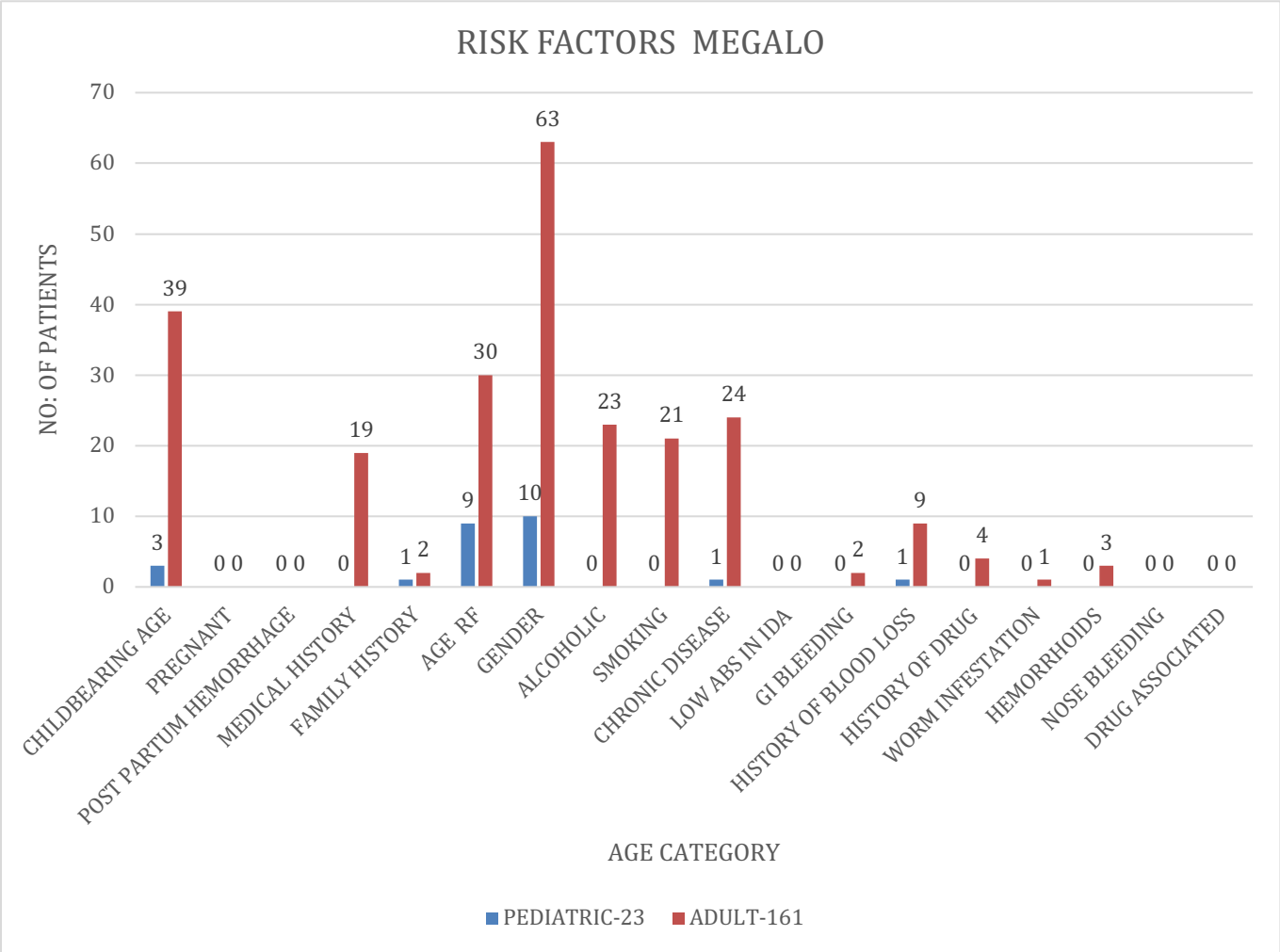


Fig 1; Distribution of various risk factors in Adults and Pediatrics

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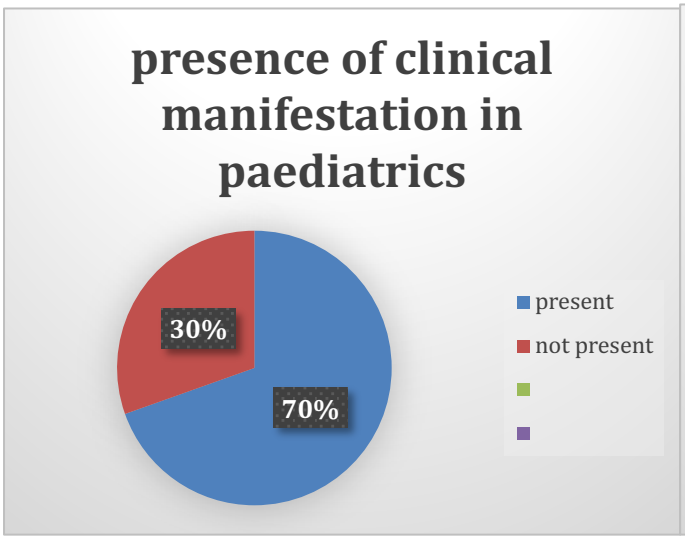
3. Presence of Clinical Manifestations

16(69.6%) paediatric patients out of 23 had clinical manifestations present. 7(30.4%) paediatric patients had no clinical manifestations.



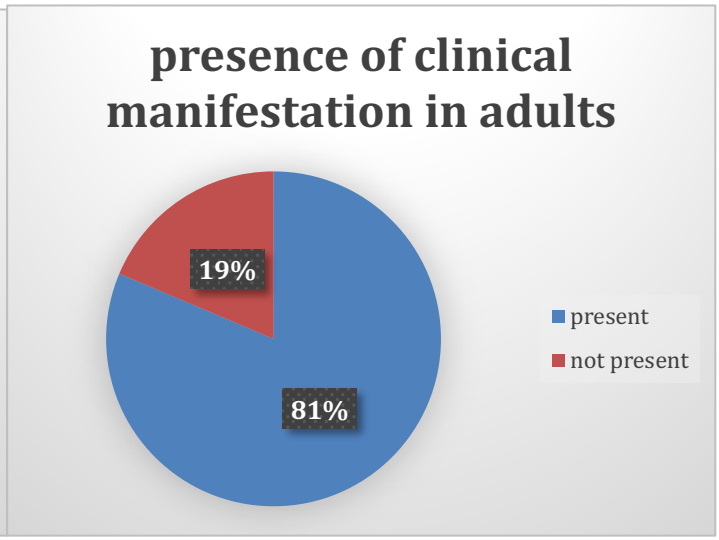


Fig 2; *Presence of clinical manifestations in pediatrics* *Fig 3; Presence of clinical manifestations in adults*

3. 1Distribution of Clinical Manifestations in Paediatric

The various clinical manifestations associated with anemia are chest pain, fatigue, dizziness, irritability, weakness, palpitations, vertigo, tingling, shortness of breath, decreased exercise tolerance, tachycardia and pallor. The clinical manifestations in the paediatric population was assessed. Out of 23 paediatric patients 14(60.9%) patient patients had pallor. Fatigue was found in 6(26.1%) patients. 3 (13%) patient had weakness. 2 (8.7%) patients felt dizzy. Palpitations and shortness of breath was found each in 1(4.3%) patient.

3.2 Distribution of Clinical Manifestations in Adults

The clinical manifestation of the adults were found to be the following. 109 (69%) patients had pallor. 73 (45.3%) patients were fatigued. Weakness was present in 24 (14.9%) patients. Dizziness was present in 8(5.0%) patients. 5 (3.1%) patients had a decreased exercise tolerance and tingling sensations each. 4 (2.5%) patients had shortness of breath.

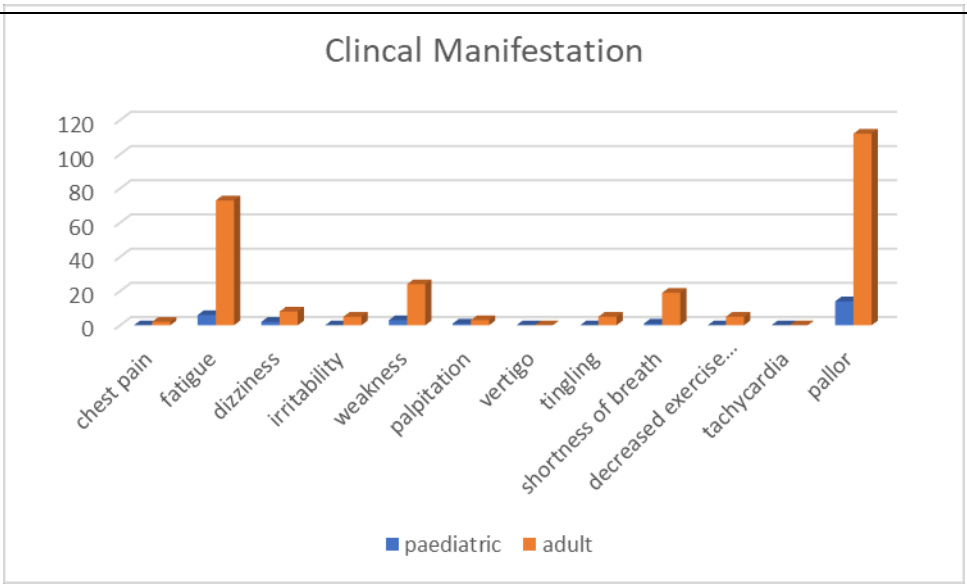


Figure 4; Distribution of clinical manifestations in pediatrics and adults

4. Severity in Paients with MA

4.1 Severity in Paediatric

Among the 23 the paediatric patients 5 patients(21.7%) were under mild category, 9 patients(39.1) were there in each moderate and severe category .

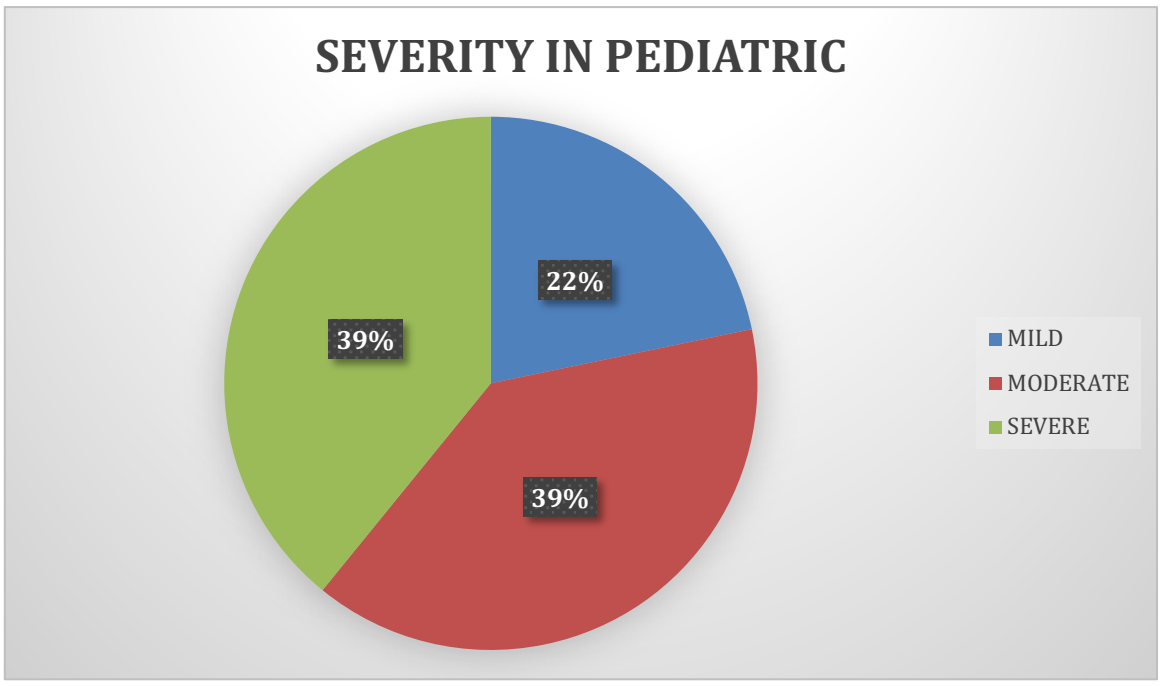


Fig 5;Severity in case of paediatric

4.2 Severity in Adults

Whereas in case of adult patients 7 patients(4.4%) were in mild category, 50(31.6%) were in moderate category and 97(61.4%) were in severe category.

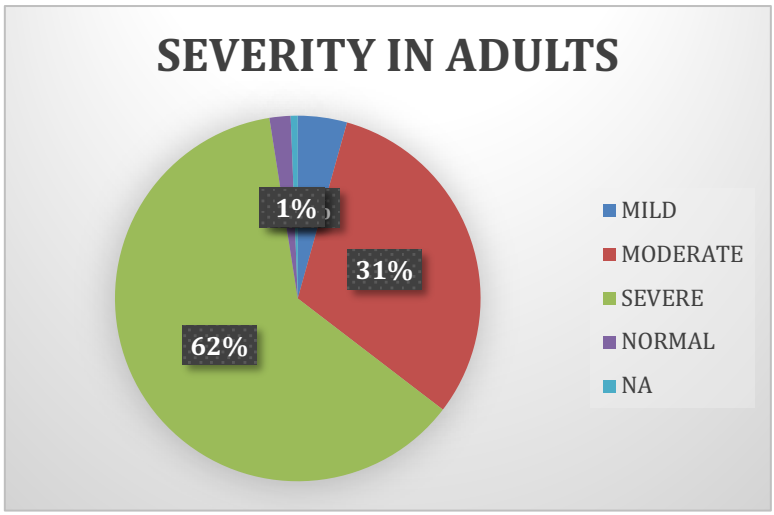


Fig 6;Severity in case of adult

5.Type : The most common deficiency found in both the population is that of VitB12. 12 patients from paediatric (52.2%) . Folate acid deficiency was found to be not present in any of the paediatric patient.

98 adult patients (60.9%) and only 7(4.3%) adults had folic acid deficiency. 5(3%) patients in adult population had deficiency in both vitB12 and folic acid.

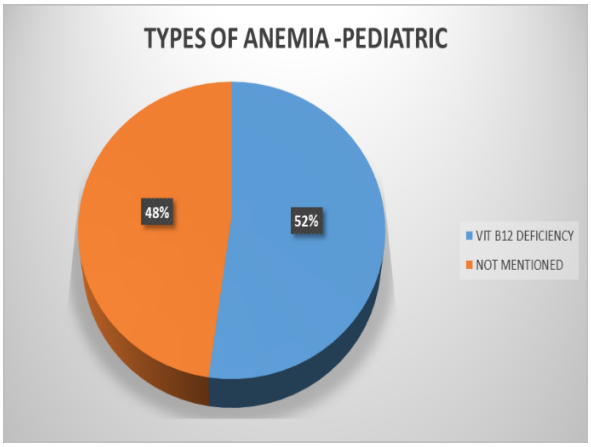


Fig 7; Types of anemia in paediatric

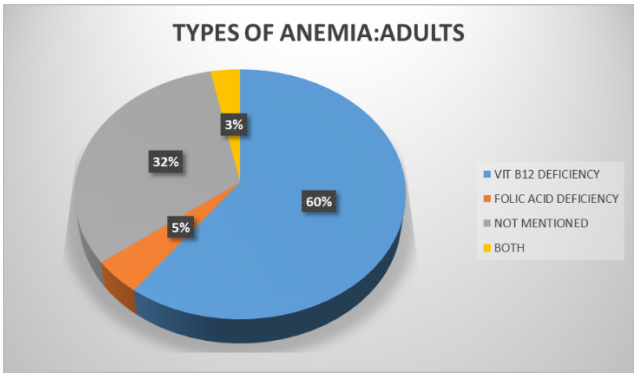


Fig 8; Types of anemia in adult

6. Assessment of Laboratory values

16 laboratory values were recorded on admission for all the patients pediatric and adults a total of and during follow up although the data was not available for all the patients. In table 5 and table 6 the values for pediatrics and adults are depicted during admission and follow up respectively.

Table 4; List of laboratory parameters with admission and discharge in paediatrics

	DURING STAY	DURING FOLLOW UP
	MEAN ± STANDARD DEVIATION	
HB (g/dl)	8.46±2.85	8.95±2.13
MCV (fl)	93.54±19.29	89.69±24.92mg/dL
MCHC(g/dl)	32.95±3.30	34.1±6.02
MCH(pg)	31.11±7.66	32.78±6.96
PCV (%)	25.24±8.92	26.51±7.66
TIBC(mcg/dl)	182.00±131.73	244.04±84.78
RBC(cells/µl)	2.54×10^6±1.28	2.73×10^6±1.26
FERRITIN	31.70±0	0
VITAMIN B12(pg/ml)	367.31±625.28	0
FOLIC ACID	39.12 ±48.99	0
RDW(%)	24.51 ±8.93	24.33±8.99
IRON(mcg/dl)	101.50±78.48	88±0
TRANSFERRIN	0	0
INTRINSIC FACTOR	0	0
MMA	0	0
HOMOCYSTEINE	0	0

Table 5; List of laboratory parameters with admission and discharge in adults

	DURING STAY	DURING FOLLOW UP
	MEAN ± STANDARD DEVIATION	
HB (g/dl)	6.99 ±2.55	9.33±6.50
MCV (fl)	89.89 ±27.25	87.74±21.96
MCHC (g/dl)	32.77 ±5.51	32.24±2.16
MCH (pg)	31.10 ±11.20	36.37±42.98
PCV (%)	22.12 ±10.30	27.12±8.42
TIBC (mcg/dl)	311.82 ±112.60	313.5±21.9
RBC(cells/µl)	2.80×10^6 ±2.76	$3.25\times10^6\pm1.25$
FERRITIN	283.70 ±429.19	47.05±30.05
VITAMIN B12(pg/ml)	290.04 ±507.10	814.80±890.31
FOLIC ACID	7.10 ±5.93	
RDW(%)	22.93 ±7.50	24.92±7.48
IRON(mcg/dl)	71.46±79.626	38±0

TRANSFERRIN	0	0
INTRINSIC FACTOR	0	0
MMA	0	0
HOMOCYSTEINE	0	0

7 Treatment pattern during hospital stay and discharge

The treatment pattern during hospital stay and discharge was recorded. Although not all the patients were given treatment during hospital stay and discharge, the overall frequency of drug use is given in Table 6 and Table 7 Table 8 Table 9. 18(78.26%) paediatric patients were given treatment during hospital stay ,and 5 patients (21.7%) did not receive any treatment.

In the adult population out of 161 patient ; 147(91.30%) patients received treatment and 15(9.31%). patients did not receive any treatment.

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Table 6; drug treatment pattern during hospital stay for paediatric patient

PEDIATRIC			
DRUG	DOSE	FREQUENCY	NO:OF PATIENTS(%)
T.FOLIC ACID	0.5 MG 5 MG	ONCE DAILY ONCE DAILY	3(13.04)
INJ VITB12 INJ VIT B12	0.3 ML	ONCE DAILY(1)	13(56.2)
	1000 mcg	ONCE DAILY(7)	
	16 mcg	ONCE DAILY(1)	
	166 mcg	ONCE DAILY(1)	
	2000 mcg	ONCE DAILY(2)	
	500 mcg	ONCE DAILY(1)	
SYP.VIT B12	1000 mcg	NA	1(4.3)
T.VIT B 12+FOLIC ACID	15 mcg+1mg	ONCE DAILY	1(4.3)
NA	NA	NA	5(21.7)

Table 7; drug treatment pattern during hospital stay for adult patient

ADULT			
DRUGS	DOSE	FREQUENCY	NO: PATIENTS(%)
VIT B12+FOLIC ACID	15 mcg+1mg	ONCE DAILY	5 (3.10)
VIT B COMPLEX	NA	ONCE DAILY	2(1.2)
	15mcg+1mcg	TWICE A DAY	
NA	NA	NA	15(9.31)
INJ VIT B12	NA	ONCE DAILY (2)	127(75.15)
	1000 mcg	ONCE DAILY(93) ONCE WEEKLY(1) NA(1)	
	12 ML	ONCE DAILY(1)	
	2000 mcg	NA (1)	
		ONCE DAILY(24)	
		THRICE A DAY(3)	
	4000 Mcg	NA(1)	
T.FOLIC ACID	5 MG	THRICE A DAY	12(7.45)
		ONCE DAILY	
		ONCE DAILY	

Table 8; paediatric discharge drug treatment pattern

		PEDIATRIC	
DISCHARGE MEDICATION	DOSE	FREQUENCY	NO:PATIENTS(%)
T.FOLIC ACID	5 MG	ONCE DAILY	4(17.39)
		ONCE DAILY	
		ONCE DAILY	

		ONCE WEEKLY	
VIT B12+ FOLIC ACID		ONCE DAILY	1(4.34)
NA	NA	NA	7(30.43)
	15 mcg + 1 mg	ONCE DAILY	11(47.82)
INJ VIT B12	1000 mcg	ONCE DAILY ONCE WEEKLY	
	330 mcg	ONCE MONTHLY	
	100 mcg	ONCE WEEKLY	
	500 mcg	ONCE WEEKLY	

Table 9; Adult discharge drug treatment pattern

ADULT			
DISCHARGE MEDICATION	FREQUENCY	DURATION	NO OF PATIENTS(%)
T.FOLIC ACID	5 MG	ONCE DAILY	19(11.80)
		ONCE DAILY ONCE WEEKLY	
	NA	ONCE DAILY	
VIT B12+ FOLIC ACID	NA	ONCE DAILY	10(6.21)
	15 mcg + 1 mg	NA	
		ONCE DAILY	
		ONCE DAILY	
		ONCE DAILY	
		ONCE DAILY	
INJ VIT B12	NA	NA ONCE DAILY	1O3(63.97%)
	1000mcg	NA(5) ONCE DAILY(18) ONCE WEEKLY(38) ONCE MONTHLY(1)	
	330mcg	NA(3)	
		ONCE DAILY(5)	
		ONCE WEEKLY(8)	
	2000 mcg	ONCE DAILY(6) ONCE WEEKLY(9) ONCE IN TWO DAYS(1)	
	2 ML	NA(1)	
	500 mcg	ONCE WEEKLY(2)	
	5ML	ONCE DAILY(1)	
	4000 mcg	ONCE DAILY(1) ONCE WEEKLY(1) ONCE MONTHLY(1)	

8. OUTCOME

The treatment outcome was assessed in both the population. Out of 23 pediatric patients, 11 (47.8%) patients' laboratory values and condition improved after treatment, and data was not available for 12 (52.2%) patients.

Out of 161 adult patients, 109 (67.7%) patients' laboratory values and condition improved after treatment, 11 (6.8%) patients' values did not improve and data was not available for 41 (25.5%) patients.

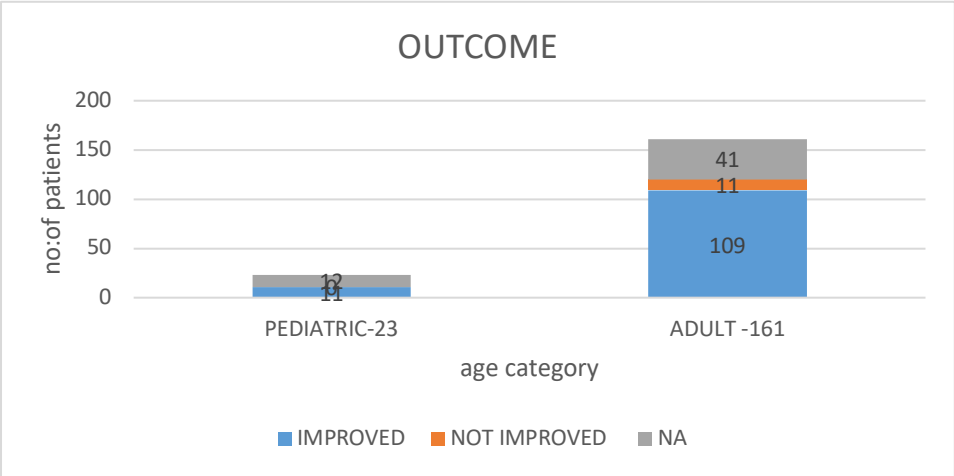

Figure 9; Outcome of treatment

DISCUSSION

7. DISCUSSION

The present study was conducted in the paediatric and medicine unit of a tertiary Health care hospital in south India and it was a retrospective observational study. Data from 181 MA patients' files were collected who were admitted in the year 2017. Out of which 161(87.97%) were adults and 23(12.56%) were paediatric

In the case of paediatric population 13 (56.5%) were males and 10 (43.5%) were female. In the adult population, the number of male patient was found to be 98((60.9%) and the number of females were 63(39.1%) Hence, the ratio of male:female is 1.55:1was found in adults. Similar results observed by Praphull Deepankar et.al, showed that the ratio of male to female is 2.6:1[8]i.e. men are affected by MA more than woman.

10 (43.5%) pediatric patients were vegetarian and 3 (13%) patients were non vegetarians and data of food habits was not available for 10(43.5%)patients. Amongst adult patients 33 (20.9%) patients were vegetarian and 55 were non-vegetarian (55%) and data was not available for 71 pateints (44.1%) where as in the study by Deepankar, et al. where63%of the population were non-vegetarian and 36 (37%) people were on vegetarian diet[8] and a cross sectional-study done by Hiren P Pandya and Asit Patil showed that out of 50 Megaloblastic Anaemic patients, 10 patients were on mixed diet and 40 patients were lacto vegetarian.[9] Incomplete data of not knowing how often a non-vegetarian diet is consumed by a non-vegetarian patient and missing data for a lot of patients megaloblastic anemia could not be positively correlated with the diet pattern in our study. A study done by Britt et.al showed that 96% of patients with VitB12 deficiency, 60% with mixed anemia and 100% with folic acid deficiency were vegetarians.[25] Chanarin et al. studied 138 Indian patients with MA in the year 1885 and their study all were vegetarians.[26]

21 (91.3%) pediatric patients were from rural areas and 2(8.7%) were from urban areas.And out of 161 (85.6%) adult patients 143 (88.8%) were from rural areas and 18 (11.2%) were from urban areas. It shows majority of MA patients are from rural are in our study.

63 patients in adults were female which was seen to be the highest risk factor .39(24.2%) female adult patients were of child bearing age, which was highest observed second highest risk factor in this study. In paediatrics it was seen that 10 female patient was present which is the highest risk factor in this study in the paediatric population..

It was observed that in the paediatric group a total of 8(34.70%)children who are below the age of two years were found to have Megaloblastic Anemia which correlates with the fact that children below the age of 2 years are under the risk of developing megaloblastic anemia[20]mainly in the tropical and subtropical countries. The main reason being that these children are breast-fed by mothers who are malnourished and have lower level of cobalamin and folate in their blood.[21]

Current study found 25 (15.52%) patients were diagnosed with Megaloblastic Anemia respectively in the geriatric population which was a risk factor. In UK and USA nearly 6% of the people under 60 years and 20% of the people above 60 years were affected with VitB12.[22].

We observed 60(37.26%) patients were detected with Megaloblastic Anemia in the middle aged adults. 76 (47.20%) patients with Megaloblastic Anemia were found in the young adults. This relates to the study done by Deepankar et al. where the highest incidence of MA was found in the age-group of 22- 40 years[8]

It was found that in adults, 11 (7%) patients had hypertension, 6 (3.8%) had Type2Diabetes Mellitus , 1(0.62%)patient also had history of Chronic liver disease. These diseases can cause damage to the kidney

which can lead to anemia.Deficiency of folic acid and/or VitB12 may be exacerbated in patients with chronic liver disease, who have a the lack of Vit B12 and/ folic acid in their diet.[10] .

Our study showed that 2 (1.3%) patients had history of taking metformin and 3 (1.9%) patients were using aspirin and 1(6%) patient were on both aspirin and NSAID. These drug interferes the synthesis of DNA like antimetabolites and alkylating agent can induce megaloblastic anemia. People who have dietary deficiency of folate are more prone to developing megaloblastic anemia in case they use drugs such as Trimethoprin. Drugs like aspirin, anticonvulsants (phenytoin), antibiotics like sulfasalazine all are associated with folic acid deficiency by reducing the transport of folate. Cobalamin deficiency can occur in persons with Type 2 Diabetes Mellitus and chronic use of metformin in large amounts. [13]Whereas Proton pump inhibitors can reduce cobalamin deficiency [11] [12]

Alcohol is said to be a secondary reason for deficiency of VitB12 although a good nutrition prevents deficiency of VitB12 in alcoholics. [23]Our study showed that 22 (13.9%) adults were alcoholics. Alcohol acts as a direct toxic on the bone marrow. A study done by Edward R.Eichner, et al showed among 65 alcoholic patient 40% of the patients developed megaloblastic erythropoiesis secondary to folic acid deficiency. [5]

It was found that 20 (12.7%) adults were smokers. A study done by Tungtrongchitr R, et al. in a military unit in Taiwan involving 123 male smokers and 63 non-smokers showed lower level of haemoglobin in smokers. 16.3 % of the smokers were anaemic and only 3% of the non-smoker were anaemic. The folate levels were found to be lowered in the smokers.[6][7]

The symptoms corresponding to anemia were fatigue, pallor which is the paleness of the skin, dizziness or light headedness an irregular heartbeat or tachycardia which are common in anemia, may develop it at some point.[24]

It was observed in our study that the highest clinical manifestation was pallor. Also 14 (60.9%) pediatric 73 (26.1%) adult patients complained of fatigue. Weakness and dizziness were present in 24 (14.9%) pediatric and 8 (5%) adult patients. 5 (3.1%) adult patients had a decreased exercise tolerance and/or tingling sensations. 4 (2.5%) adult patients had shortness of breath. In a study done by Deepankar etal. 92-96% dyspnea and palpitation were the presenting complaints in the patients.[8] It shows different patients shows different clinical manifestation of MA or anemia.

On evaluation of category of MA, the most common deficiency found in both the paediatric and adult was of VitB12. That is 12 (52.2%) paediatric and 95 (60.1%) adult patients had VitB12 deficiency. Only 7 (4.4%) adults had folic acid deficiency. 5(3.1%)patients in adult population had deficiency in both vitB12 and/or folic acid and data was not available for 51(31.7%) of the patient. Khandari U, et al. showed that out of total 120 patient's data 65% had cobalamin deficiency, 12% had both cobalamin and folate deficiency and 6% had folate deficiency.

On assessing the severity of anemia, we found 7 patients (4.4%) were in the mild category, 50 (31.6%) were in moderate category and 97 (61.4%) patients were in severe categoty in the adult population. Among the 23 the paediatric patients 5 patients (21.7%) were under mild category, 9 patients (39.1) were there in each moderate and severe category. A study done by Pandeya et al. showed that 94% of the adult patients were presented with moderate to severe anemia.[9]

Out of 23 pediatric patients, 11 (47.8%) patients' laboratory values and condition improved after treatment, and data was not available for 12 (52.2%) patients. In adult patients, 109 (67.7%) patients' laboratory values

and condition improved after treatment, 11 (6.8%) patients' values did not improve and data was not available for 41 (25.5%) patients.

18(78.26%) paediatric and 147 (91.30%) adult patients received treatment. Intramuscular injections containing crystalline VitB12 have been used since long to treat VitB12 deficiency. The duration of the treatment was for 8 weeks, and the dose was 1mg or 1000mcg. After that 1mg is given once monthly the whole life. [14][15] According to Cochrane review of 2005 oral dosage of VitB12 of 1-2 mg daily for 3-4 months showed better results of improvement of level of serum vitB12 compared to those who had received intramuscular injection of Vit B12.[16]Due to the lower cost and better results oral vitB12 remains a justified choice.

In megaloblastic anemia there was development of reticulocytes and the haematocrit normalized .[17]VitB12 is a water soluble vitamin so doses 1000 times the dietary allowances is considered safe [18]. The biologically active form of the vitamins and folic acid used as synthetic supplements or as fortified food and for treatment of folate . It is absorbed from the proximal small intestine and the rest half is found in the liver. According to a study by Mckillop et.al, the amount of natural folates in food is influenced by the cooking process as a variable degradation can take place. The bioavailability of food folate is lowered to half than folic acid.[19]

Since 1940 folic acid, a water soluble vitamin used to treat microcytic anemia with neurological disorder. The red blood cell folate level plus microcytosis and/or megaloblastic anemia was best way to diagnose folate deficiency. Folic acid not only helped to treat it's deficiency but also a daily dose of 400mcg helped in reducing the neural defects in women by 45%.According to British National Formulary Folate deficient megaloblastic anaemia (due to dietary insufficiency, pregnancy or antiepileptics): 5 mg of folic acid daily was taken for 4 months, except in pregnancy where it was continued until term, and up to 15 mg daily for 4 months was suggested in malabsorptive states. [20]

LIMITATIONS

8. LIMITATIONS

- Since this is a retrospective study design, a lot of data was missing or not recorded.
- For a few patients CBC values were not recorded during follow up.

CONCLUSION

9. CONCLUSION

Megaloblastic anemia is a disease mainly caused due to deficiency of Vit B12 and folic acid. It can be treated easily with a proper diet and nutritional supplements. . Male patients are having more megaloblastic anemia. Age less than 2 years and above 60 years were having anemia found in more numbers .Alcoholism and smoking were found to be present only in the adult population. 23(14.3%) people were found to be alcoholics and 21(13%) of the people were smoker. Pallor is the most common clinical manifestation in majority of the patients. The most common deficiency found in both the population is that of VitB12. Folic acid deficiency was not present in the paediatric patients. 98 adult patients (60.9%) had Vit B12 deficiency and only 7(4.3%) adults had folic acid deficiency. 5 patients in adult population had deficiency in both vitB12 and folic acid.

Majority of MA patients of both pediatric and adults received treatment according to standard therapy mentioned in the literature. Also majority patients imoroved after the treatment

Study concluded that the result will help us to understand the various preventable risk factor for MA, , common clinicalmanifestions of disease, food habits which causes MA and the treatment pattern followed for improvement of the condition. Thus this epidemiological data will helpful for healthcare professionals

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FUTURE DIRECTIONS

10. FUTURE DIRECTIONS:

- A prospective study on comparison between different treatment regimens would yield better result.
- A similar study should be conducted regionally and nationally to yield results at a larger scale.
- Taking a control group to find out the association of risk factor.

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APPENDICES

Appendix - I

Form to be filled by the Principal Investigator (PI) for submission to the Institutional Ethics Committee (IEC)
(for attachment to each copy of the research proposal - **Retrospective studies**)

IEC No : **Date of Receipt :**	**(Page1 must be typed)**

Project Title : Assessment of pattern, risk factors and treatment of Iron Deficiency Anemia and Megaloblastic Anemia in Adult and Pediatric population in a tertiary care hospital in South India

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Appendix – II

AGE:	DOA:	PATIENT ID:	ADULT /PEDIATRIC
SEX:	DOD:	BMI:	

MEDICAL HISTORY :

MEDICATION HISTORY:

FAMILY HITORY :

SURGICAL HISTORY :

RISK FACTORS : AGE: GENDER:

OCCUPATION: CHILD BEARING AGE:

ALCOHOL: ☐ SMOKING: ☐

CHRONIC DISEASE: ☐ **LOW ABSORBTION IRON IN IDA:** ☐

PREGNANCY: ☐ GI BLEEDING: ☐

HISTORY OF BLOOD LOSS: ☐

HISTORY OF TAKING : ASPIRIN: ☐ NSAIDS: ☐

FOOD HABITS: VEG: ☐ NON VEG: ☐

PLACE : RURAL: ☐ URBAN: ☐

WORM INFESTATION : HOOK WORM: ☐ TAPE WORM: ☐

HEMORRHOIDS: ☐ NOSE BLEEDING: ☐ POST PARTUM HEMORRHAGE: ☐

DRUGS ASSOCIATED:

Corticosteroids: ☐	Iron : ☐	p-Aminosalicylates: ☐
Azathioprine : ☐	Primidone: ☐	Phenytoin: ☐
Chloramphenicol: ☐	Pyrimethamine : ☐	Colchicine: ☐
Cotrimoxazole : ☐	Sullfasalazine: ☐	Phenobarbital: ☐
Cyclophosphamide: ☐	Cytarbine: ☐	Vinblastin: ☐
Tetracycline: ☐	Hydroxyurea: ☐	Methotrexate: ☐
5-Flurodeoxyuridine: ☐	5-Flurouracil: ☐	6-mercaptopurine: ☐

CLINICAL MANIFESTATIONS:

CHEST PAIN:	☐	FATIGUE:	☐
DIZZINESS :	☐	IRRITABILITY:	☐
WEAKNESS :	☐	PALPITATIONS:	☐
VERTIGO:	☐	TINGLING:	☐
SHORTNESS OF BREATH:	☐	DECREASED EXERCISE TOLERANCE:	☐
TACHYCARDIA:	☐	PALLOR:	☐

INDICATION: MEGALOBLASTIC ANEMIA : ☐ IDA: ☐

LAB INVESTIGATIONS:

HB:	MCV:	MCHC:	MCH:
PCV:	TIBC:	RBC:	FERRITIN:
VIT B12:	FOLIC ACID:	RDW:	SERRUM IRON:
TRANSFERIN:	INTRINSIC FACTOR:	MMA:	HOMOCYSTEINE:

SEVERITY:

MILD: ☐ MODERATE: ☐ SEVERE: ☐

Assessment of pattern, risk factors, and treatment of IDA and Megaloblastic Anemia in adult and Pediatric population in a tertiary care hospital in South India.

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