Socioeconomic determinants of severe anemia and assessment for iron and vitamin B\textsubscript{12} deficiency among anemic adolescents

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Abstract

Background: Adolescence is the period of most rapid growth due to which they face serious nutritional challenges and make them more vulnerable to anemia. Anemia in the adolescence has a negative effect on their growth & development. Objectives: To study demographic, socio-economic factors associated with severe anemia, to evaluate Iron and Vitamin B\textsubscript{12} deficiency as cause of anemia and to associate serum levels of ferritin and vitamin B\textsubscript{12} with severity of anemia in adolescents. Methods: Across sectional hospital based observational study done among 212 adolescents (10 – 18 years) with anemia. Complete history was taken. Serum levels of ferritin, vitamin B\textsubscript{12} were estimated. Statistical analysis was done by Chi-square test, “t” test and Mann Whitney U test. Results: 40.56% participant had mild, 48.58% had moderate and 10.84% had severe anemia. Statistically significant association was seen between severe anemia and educational status of mother (p = 0.0416); participant (p=0.0002) and vegetarianism (p=0.0084). Severely anemic participants had significantly low BMI (p=0.0097), delayed age of menarche (p=0.020) and high MCV values (p=0.000018) as compared to mild to moderately anemic participants. Among severe anemia 47.82% iron deficiency and 60.86% vitamin B\textsubscript{12} deficiency was seen. Severely anemic subjects were more likely to have combined iron and vitamin B\textsubscript{12} deficiency (39.12%, p=0.0027). Low vitamin B\textsubscript{12} level was significantly associated with severe anemia (p=0.008). Conclusion: Educational status and vegetarianism were significant determinant of severe anemia. Significant association of low vitamin B\textsubscript{12} level with severe anemia was seen.

Keywords: Adolescent, Nutritional anemia, Severe anemia, Socio-demographic factors, Iron deficiency, Vitamin B\textsubscript{12} deficiency

Introduction

Adolescents are a heterogeneous group of population existing in a variety of circumstances, having diverse needs. They are highly vulnerable to nutritional deficiencies including nutritional anemia owing to the great demand of nutritional requirement to meet their physical and physiological changes [1]. Nutritional anemia constitutes the most important cause of anemia in adolescents. It is mainly due to deficiency of Iron, Vitamin B\textsubscript{12} and Folate. Anemia has a negative effect on physical growth, cognitive performance and resistance to infection [1,2]. According to the NFHS 3 survey prevalence of anemia is 56% in females and 30% in males aged 15 – 19 yr. [3]. Various studies done in India showed the prevalence of anemia in adolescents ranging from 16.25% to 96.5%. [4-6]. Vast amount of work has been done in evaluating anemia in adolescent girls and pregnant women and young children. There are relatively few published studies done in evaluating association of factors related to severe anemia.

This study was planned to find demographic, socio economic factors associated with severity of anemia and to evaluate deficiencies of Iron and vitamin B\textsubscript{12} in adolescents having anemia.

Materials & Methods

Place & Type of Study: The present study was hospital based cross sectional observational study done in the pediatric department of SMIMER, Surat, India over a period of 18 months.
Ethical consideration: Written informed consent was taken from parent or guardian before enrollment. Ethical clearance was obtained from Institutional Ethical Committee.

Inclusion criteria: Study participants included were all adolescents (10 to 18 yr) admitted to the pediatric ward and having hemoglobin level below 12 g/dl.

Exclusion criteria: Patients having acute critical illness, chronic systemic disease, diagnosed cases of hemolytic anemia, blood transfusion history in past or reticulocyte count >2% were excluded from the study.

Data collection & sampling methods: A detailed history was taken and data like patient’s age, sex, literacy level, maternal literacy level, socioeconomic status (SES) based on modified Kuppuswami classification [7] and dietary history were recorded. Subjects consuming animal food like meat, fish at-least once per week were considered as non-vegetarians. Age group was divided as early adolescent (10–<13 year), mid adolescent (13 –<16 year) and late adolescent (16-18 year) [3]. Anthropometric measurements (weight, height) were noted. Body Mass Index (BMI) was categorized as under-nutrition (BMI <18.5 kg/m2), normal (BMI 18.5-24.9 kg/m2), overweight (BMI 25.0-29.9 kg/m2) and obese (BMI >30 kg/m2) [1]. CBC including hemoglobin, RBC count & RBC indices, WBC count, Platelet count was measured in venous blood by automated cell counter. Hemoglobin level between 10-11.9 gm % was taken as mild anaemia, between 7-9.9 mg% moderate and <7 gm% as severe anaemia [1,2]. Based on MCV value patients were categorized as having microcytic (<80fl), normocytic (between 80 fl-100 fl) and macrocytic anaemia (>100 fl). [1]

Serum Ferritin and Serum vitamin B₁₂ level estimation was done in venous blood using chemiluminescent enzyme immunoassay technique. Serum ferritin<30 ng/mL and vitamin B₁₂ level < 160 pg/mL were considered as deficient.

Statistical analysis: Data analysis was done using Openepi software. Estimated sample size was 212 based on anemia prevalence of 46% as per pilot study done at our institute. For statistical analysis of qualitative data Chi square tests were applied. Normality check for quantitative data was done by Shapiro-Wilk’s test. Independent “t” test was applied for data following normality and Mann Whitney U test was applied for data which didn’t follow normality.

Results

In our study out of 212 participants, 86 (40.56%) had mild anemia, 103 (48.58%) had moderate anemia and 23 (10.84%) had severe anemia.

Almost half, 98 (46.22%) of the participants belonged to mid adolescent age group and male to female ratio was 0.96:1. Among severely anemic patients, 52.17% belonged to mid adolescents, followed by 26.08% late and 21.37% to early adolescent age group. Among patients with severe anemia, 12 (52.17%) were male and 11 (47.82%) were female participants. Socioeconomic status was determined based on modified Kuppuswami scale. Among severely anemic subjects, 52.17% belonged to lower middle class, 30.43% to upper middle class and 17.40% to upper lower class. Upper class SES was seen in 3 (1.58%) of participants with mild to moderate degree anemia while none of the participants with severe anemia belonged to upper class. There were no participants in lower class category in both the groups. No statistically significant association was found between age, sex or SES and severity of anemia (Table 1 & 2).

| Variable | Mild to moderate n=189 | Severe n=23 | X², p value |
|----------|------------------------|-------------|-------------|
| **Age**  |                        |             |             |
| 10 – 13  | 53 (28.04%)            | 05 (21.37%) | 0.492       | 0.7803 |
| 13 – 16  | 86 (45.50%)            | 12 (52.17%) |             |       |
| 16 – 18  | 50 (26.45%)            | 06 (26.08%) |             |       |
| Mean age | 13.89 ± 2.14           | 14.65 ± 1.69| 1.91091     | 0.166862 |
| **Sex**  |                        |             |             |
| Male     | 92 (48.67%)            | 12 (52.17%) | 0.1003      | 0.7514 |
| Female   | 97 (51.32%)            | 11 (47.82%) |             |       |
Table-2: Socioeconomic Status.

| Socioeconomic status | Mild to moderate (n=189) | Severe (n=23) | $\chi^2$ | p value |
|----------------------|--------------------------|---------------|---------|---------|
| 2                    | 03 (1.58%)               | 00            | 0.8557  | 0.8361  |
| Upper Middle         | 70 (37.03%)              | 07 (30.43%)   |         |         |
| Lower Middle         | 85 (44.97%)              | 12 (52.71%)   |         |         |
| Upper Lower          | 31 (16.40%)              | 04 (17.40%)   |         |         |
| Lower                | 00                       | 00            |         |         |

Out of 23 participants with severe anemia, 30.43% mothers were illiterate, 43.47% had primary education and 26.08% had education till secondary level. None of the mother was graduate in both the groups. With regard to participant’s education level, 2(8.69%) were illiterate in severe anemic group whereas none were illiterate in mild to moderate anemia group. Overall proportion of number of participants having primary (52.91% Vs 47.82%), secondary (47.08% Vs 43.47%) education was more in patients having mild to moderate anemia as compared to patients having severe anemia. A statistically significant association was seen between mother’s education level (p value 0.04160) and patient’s education level (p = 0.00024) with severity of anemia among participants (Table 3).

Table-3: Educational Status and Degree of Anemia.

| Variable            | Mild to moderate (n=189) | Severe (n=23) | $\chi^2$, p value |
|---------------------|--------------------------|---------------|------------------|
| Mother’s Education  |                          |               |                  |
| No education        | 22 (11.64%)              | 07 (30.43%)   | 6.359, 0.04160   |
| Primary             | 115 (60.84%)             | 10 (43.47%)   |                  |
| Secondary           | 52 (27.51%)              | 06 (26.08%)   |                  |
| Above               | 00                       | 00            |                  |
| Patient’s education |                          |               |                  |
| No education        | 00                       | 02 (8.69%)    | 16.59, 0.0002494 |
| Primary             | 100 (52.91%)             | 11 (47.82%)   |                  |
| Secondary           | 89 (47.08%)              | 10 (43.47%)   |                  |
| Above               | 00                       | 00            |                  |

Table-4: Dietary Pattern

| Dietary pattern     | Mild to moderate (n=189) | Severe (n=23) | $\chi^2$, p value |
|---------------------|--------------------------|---------------|------------------|
| Vegetarian          | 93 (49.20%)              | 18 (78.26%)   | 6.939, 0.008433  |
| Nonvegetarian       | 96 (50.79%)              | 05 (21.73%)   |                  |

Severely anemic patients were mainly vegetarian. 78.26% of participants with severe anemia were vegetarian as compared to 49.20% in mild to moderate anemia group (p=0.008433) (Table 4).

Table-5: Nutritional Status.

| BMI | Mild to moderate (n=189) | Severe (n=23) | $\chi^2$, p value |
|-----|--------------------------|---------------|------------------|
| < 18.5 | 122 (64.55%) | 21 (91.30%) | 6.685, 0.009721  |
| 18.5 to 25 | 67 (34.92%) | 02 (8.69%) |                  |
| >25   | 00                       | 00            |                  |
| Mean BMI | 17.2719± 3.026 | 15.47 ± 2.29 |                  | - 0.000000001 |
Participant’s nutritional status was categorized according to BMI value. It was seen that 91.30% participants were undernourished (BMI <18.5) among severely anemic group as compared to 64.55% participants in mild to moderate anemic group (p=0.009721) (Table 5).

Table-6: Menarche Status of Female Participants

| Variable                             | Mild to moderate | Severe | X²,   | p value |
|--------------------------------------|------------------|--------|-------|---------|
| Number of females                    | 97               | 11     | 1.257 | 0.2632  |
| No of females with menarche attained | 76 (78.35%)      | 11(100%)|       |         |
| Mean age of menarche                 | 12.059 ±0.923    | 12.181± 0.60 |       | 0.02011 |

Out of 97 females in mild to moderate anemia group, 76 (78.35%) had attained menarche, while all 11 (100%) females in severe anemia group had attained menarche. However no statistical significance was found with regard to number of females with post-menarche status. When mean age of menarche was compared between two groups statistically significant association was seen. Mean age of menarche was higher in severe anemic group (Table 6).

Table-7: MCV Value.

| MCV       | Mild to moderate n=189 | Severe n=23 | X²,   | p value |
|-----------|-----------------------|-------------|-------|---------|
| <80       | 108 (57.41%)          | 11 (47.82%) | 11.51 | 0.003173|
| 80 – 100  | 70 (37.03%)           | 6 (26.08%)  |       |         |
| >100      | 11 (5.82%)            | 6 (26.08%)  |       |         |
| Mean MCV  | 77.248±13.173         | 77.65 ± 23.50 | -    | 0.00001850 |

Microcytic anemia was seen in 119 (56.13%), normocytic anemia in 76 (35.84%) and macrocytic anemia was seen in 17 (8.01%) of study participants. In severely anemic patients microcytic anemia was seen in 47.82% as compared to 57.41% in mild to moderate anemic group. Macrocytic anemia was more seen in severely anemic patients (26.08% Vs 5.82%). Statistical significance was also noted with regard to mean MCV values between two groups (Table 7).

Table-8: Comparison of Types of Anemia Based On Biochemical Parameters.

| Variable                             | Mild to moderate n=189 | Severe n=23 | X²,   | p value |
|--------------------------------------|-----------------------|-------------|-------|---------|
| Iron deficiency                       | 61 (32.27%)           | 11 (47.82%) | 2.211 | 0.1371  |
| Vitamin B12 deficiency                | 91 (48.14%)           | 14 (60.86%) | 1.327 | 0.2500  |
| Combined iron + B12 deficiency        | 27 (14.28%)           | 9 (39.13%)  | 8.978 | 0.002733|
| S. ferritin (ng/mL) Median(IQR)       | 68 (26,132)           | 32 (14,8,130) | -    | 0.125*  |
| S. Vitamin B12 (pg/mL) Median (IQR)   | 168 (110,228)         | 102 (55,5,175) | -    | 0.008*  |

*Mann Whitney U test applied

Overall iron deficiency was seen in 72 (33.96%) and vitamin B₁₂ deficiency was seen in 105(49.52%) of the participants. Among study participants 47.82% in severe anemia group while 32.27% in mild to moderate anemia group were found to have iron deficiency. Vitamin B₁₂ deficiency was seen in 30.64% of severely anemic and 48.14% of mild to moderately anemic participants. Combined iron and vitamin B₁₂ deficiency was seen in 39.13% of severely anemic participants as compared to 14.28% in mild to moderate anemia group. No statistical significance was noted with regard to number of patients having nutrient deficiency in isolation. While combined nutrient deficiency was significantly associated with severe anemia group. On comparing levels of S ferritin and S vitamin B₁₂ level between two groups, a statistical significance was noted with regard to low vitamin B₁₂ level with severity of anemia (Table 8).
Discussion

Anemia is a common health problem in India especially among adolescents reflecting nutritional deficiency in this age group [8]. The present study showed prevalence of 40.56% mild, 48.58% moderate and 10.84% severe anemia. According to NFHS 3 more than 39% adolescent girls are mildly anemic while 15 % and 2% have moderate and severe anemia respectively [3]. Similarly 2% to 4% prevalence of severe anemia was noted by other authors too [8-10]. Ours was a hospital based study which can be the reason of high prevalence of severe anemia. D Thomas et al also noted 20.5% prevalence of severe anemia in their study [2]. No association between age and sex of the participants with severity of anemia was seen in the present study. Very few studies were carried out among adolescent males and though not statistically significant our study observed equal distribution of different severity of anemia in both genders.

There was no association seen with regard to SES and severity of anemia in this study. However, literacy level of mother as well as participants was significantly associated with severity of anemia, which reflects better awareness regarding health and hygiene among them. Thomas et al didn’t find association of severe anemia with SES [2]. Upadhyay et al, P Bharti et al & Kulkarni M et al found statistically significant association of anemia with education status of parents or participants [9,11,12].

91.30% participants with severe anemia had BMI <18.5 M2 which was statistically significant. Also mean BMI was low in severely anemic subjects as compared to mild-moderate anemic group. This finding is in agreement with Upadhyay et al, Talpan et al & Hanan et al [9,13,14]. Low BMI in severe anemia suggests that anemia affects the overall growth of adolescents.

Attainment of menarche was not associated with severity of anemia, but mean age of menarche was significantly higher in severely anemic group. This may suggest that severe anemia is the cause of delayed menarche. Vegetarianism was significantly associated with severe anemia which is similar to the findings by Thomas et al [2] & Verma et al [15]. Vegetarian diet is poor source of iron due to poor bioavailability of non heme iron. Vitamin B12 is also derived from animal origin food. Microcytic hypochromic anemia was seen in 47.82% of severely anemic patients suggesting iron deficiency anemia. Low Serum ferritin value was seen in 47.82% of severely anemic subjects. Ours study didn’t show association of serum ferritin level with severity of anemia. Serum ferritin is a sensitive indicator of iron deficiency but being an acute phase reactant, its level is elevated in presence of acute infection or inflammation. Ours was a hospital-based study with participants having mild acute illness which may be the reason for no association seen between ferritin level with severity of anemia. 26.08% participants in severely anemic group showed macrocytosis suggesting megaloblastic anemia which could be due to vitamin B12 or folic acid deficiency. Severe anemia was significantly associated with low vitamin B12 level in our study. 60.86% of participants with severe anemia were having vitamin B12 deficiency. Thomas et al [2] found 43.9% and 68.2% prevalence of iron and vitamin B12 deficiency in their study. Patra et al [16] in their hospital-based study found 42.5% megaloblastic and 15% iron deficiency anemia. MCV value had significant association with severity of anemia where macrocytic anemia was found to be more associated with severe anemia.

Conclusion

Participant’s as well as their mother’s educational status and vegetarianism were significant determinant of severe anemia in our study. Among laboratory parameters severe anemia was significantly associated with high MCV, low vitamin B12 level and combined iron and vitamin B12 deficiency. It was found that mean BMI was significantly low in participants with severe anemia. There was significant delay in attainment of age of menarchae in severely anemic subjects.

Thus, anemia has significant effect on overall growth of adolescents. Adolescent males were found to be equally affected with severe anemia in our study. High prevalence of vitamin B12 deficiency was seen in our study. Improving the literacy level can be a good measure towards control of anemia. Supplementation of vitamin B12 in addition to IFA supplementation and inclusion of adolescent males as beneficiaries should be considered through national programs.

What is already known?
• Iron deficiency anemia is the most common nutritional anemia among adolescents.

What This Study Adds?
• Prevalence of vitamin B12 deficiency is highamong adolescents.
• Combined iron and vitamin B12 deficiency is common in adolescents with severe anemia.
Author contribution: AS: study concept, data analysis & manuscript preparation. CC & MS: data collection, laboratory work, data analysis. All authors contributed towards data analysis, data interpretation, drafting and critically revising the manuscript.

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