

Effect of Vitamin A Supplements with Iron Therapy among Adolescent Girls

Patel SK¹, Chaturvedi A², Bhardwaj A³, Chandra S⁴, Naik G⁵, Sharma HB⁶

¹Assistant Professor, Department of Physiology, Raipur Institute of Medical Science, Raipur, Chhattisgarh,

²Associate Professor, Department of Physiology, Govt Medical College, Badaun, U.P., ³Associate Professor, ⁴Lecturer, Department of Physiology, Sarojini Naidu Medical College, Agra, U.P., ⁵Senior Resident, Department of Community and Family Medicine, All India Institute of Medical Sciences, Raipur, ⁶Senior Resident, Department of Physiology, All India Institute of Medical Sciences, New Delhi

Abstract

Background: Despite of extensive management programmes for iron deficiency anaemia, it remains a challenge for healthcare professionals. So, there is a requirement of supplementing the conventional therapy with some micronutrients which have a possible role in combating the problems of anaemia. Vitamin A is one of those possible micronutrients.

Material and Method: Adolescent girl students from a school who were diagnosed as anaemia were categorised randomly into two interventional groups. Those who were not diagnosed as anaemia formed the third group. In group A, Vitamin A supplementation (2, 00,000 IU single dose) along with Iron in the form of FeSO₄ was given for 100 days. Group B students received only Iron supplementation for the same period. Only placebo was given to the students of group C.

Results: In group A the mean value for blood haemoglobin improved from 10.128±0.196 gm/dL to 12.216±0.215 gm/dL. The improvement was extremely significant (p<0.0001). In group B mean value for blood haemoglobin improved from 10.141±0.210 gm/dL to 11.766±0.218 gm/dL and was very significant (p<0.0001). In group C, the mean value for blood haemoglobin was 12.809±0.099, which significantly improved to 13.018±0.119 gm/dL. (p=0.008). The %age change over baseline was more in group A (20.39%) than group B (12.38%) as compared to group C (2.77%).

Conclusion: This study concluded that vitamin A supplementation helps to restore the blood haemoglobin level along with iron therapy and helps to improve the status of anaemia. Further studies involving large population are required to establish the definitive role of vitamin A supplementation in anaemia and to recommend it as a standard additive therapeutic agent.

Keywords: Iron deficiency anaemia, Vitamin A, Haemoglobin, Adolescence

Introduction

Anaemia is most common form of malnutrition globally and is the eighth leading cause of disease in girls and pregnant women in developing countries,¹ where the

prevalence ranges from 40-60% as per WHO.² Half of those are supposed to be suffering from iron deficiency anaemia.^{3,4} The risk factors for iron deficiency anaemia includes low intake, malabsorption of iron from diets and periods of life when iron requirements are especially high (growth and pregnancy).^{5,6} Anaemia retards physiological growth in adolescent girls.^{7,8} There are micronutrients other than Iron, such as vitamin A, play important role in prevention and treatment of anaemia. Vitamin A and iron (Fe) deficiencies are two challenging public health problems in adolescent girls also due to

Corresponding Author:

Dr Arun Chaturvedi,

Associate Professor, Govt Medical College, Badaun, U.P. Email id: dr.arunchat@gmail.com
Mobile No.: +919412516515

nutritional imbalance despite of increasing dietary requirement and additional blood loss via menstruation.⁹ Vitamin A can affect several stages of Fe metabolism, which include erythropoiesis and the release of Fe from ferritin stores.¹⁰ Since the study of Findlay and Mackenzie¹¹ in 1922, several studies have suggested the interrelation between vitamin A and iron metabolism.^{12,13} These studies demonstrated a reduction of hematopoietic cells in the bone marrow and also hemosiderosis in the liver and spleen in vitamin A-deficient subjects.¹⁴ Many epidemiological studies indicated that vitamin A deficiency and anaemia often coexist and that there are significant associations between serum retinol and biochemical indicators of the Fe status.^{15,16}

Strong correlations between vitamin A status and haemoglobin levels have been demonstrated.¹⁷ Prolonged vitamin A deficiency in animals negatively affects haematopoiesis, with a gradual replacement of the bone marrow by fibrous tissue.¹⁸ A depression of iron uptake by the bone marrow was postulated to be one of the mechanisms in these studies.^{19,20} Some recent studies have shown that vitamin A deficiency leads to ineffective erythropoiesis by the down-regulation of renal erythropoietin expression in the kidney, resulting in erythrocyte malformation and the consequent accumulation of the heme group in the spleen.²¹ Vitamin A deficiency indirectly modulates systemic iron homeostasis by enhancing erythrophagocytosis of undifferentiated erythrocytes.²²

In India, despite intensive efforts, several studies showed that anaemia and vitamin A deficiency are highly prevalent, particularly among adolescent girls.²³ That's why the aim of the present study was to investigate the effects of vitamin A supplementation on iron therapy in anaemic adolescent girls in an Indian city.

Material and Method

It was a Prospective study conducted in a school in urban Agra within a period of 1 year. The study population were school going young girls of age 13-16 years. Using the average prevalence rate of anaemia in young adolescent girls as 53.9 % according to NFHS -3 the sample size was calculated as 86 and then rounded to 100. One intermediate college was chosen which admitted lower & middle class students. The students of classes 8th, 9th and 10th, aged from 13 to 16 years, were included in the study.

Inclusion criteria: Students who were willing to participate in the study voluntarily after being informed in details about the study procedure and providing consent were included in the study.

Exclusion criteria: Students having following clinical features were excluded from the study. 1. Irregular menstrual bleeding. 2. Severe malnourishment. 3. Known haemolytic disease like sickle cell anaemia, thalassemia. 4. Haematuria. 5. Any other bleeding disorders. 6. Any chronic disease. 7. Features of vitamin A deficiency.

Written consent of the parents was taken before the study. De-worming of all the girl students was done. After obtaining relevant clinical history, blood samples of the participants were collected, for determining haemoglobin level. The level of haemoglobin was estimated by using Cyan-meth-haemoglobin method using Drabkin's solution. Universal precautions were followed for the collection of sample and for discarding the biomedical waste.

Students who were diagnosed as Anaemia on the basis of investigation were categorised randomly into two interventional groups. Students diagnosed non-anaemic formed the third group. Vitamin A supplementation (2,00,000 IU single dose) along with Iron in the form of FeSO₄ was given for 100 days to the students of group A. Only Iron supplementation was given twice a week for a period of same 100 days to group B. Group C students were given only placebo in the form of white coloured candies. Vitamin A was given in the form of red coloured oil-based gelatinous capsule, obtained from medical college OPD. Both iron and Vitamin A supplementation were given to the participants under direct observation.

Haemoglobin level of each participant was measured twice during the study: Before the initiation of the intervention and on the completion of the intervention i.e. 100 days. The cut-off level for haemoglobin concentration to be diagnosed as anaemia is 12 gm/dL for this concerned age group of 13 to 16 years in adolescent girls and were categorized as mild (11-11.9 gm/dL), moderate (8-10.9 gm/dL) and severe (<8gm/dL) according to WHO criteria (2001).

Results

Out of 100 girls screened for anaemia who were willing to participate in the study, 66 girls (66%)

were diagnosed as anaemic and 34 girls (34%) were diagnosed non-anaemic. Out of 66 girls those were diagnosed as anaemic, 21 were mild anaemic(21%), 43 were moderately anaemic(43%) and 2 girls(2%) were diagnosed as severely anaemic (Fig. 1). Severely anaemic students were excluded from the study and referred to medicine and gynaecology OPD for active therapy. Prevalence of anaemia before the study was 66 % and after the study, it was 37.76 %. Before the study, prevalence of moderate anaemia was 43 % and that of mild anaemia was 21%. After the study prevalence of moderate anaemia was 16.33 % and that of mild anaemia, it was 21.43 % (Fig. 2)(Table 1).

In group A, average age of students was 14.313 ± 0.198 years, which was comparable to group B (14.688 ± 0.188 years) and group C (14.5 ± 0.180 years). In group A out of 32 girls, 11 were mild and 21 were moderate anaemic. In group B out of 32 girls, 10 were mild and 22 were moderate anaemic. Group C contains 34 girl students, all of whom were non anaemic. In group A the mean baseline value for blood haemoglobin was 10.128 ± 0.196 gm/dL and after intervention value was 12.216 ± 0.215 gm/dL. The difference between before and after intervention was extremely significant

($p < 0.0001$) (Fig. 3). In group B mean baseline value for blood haemoglobin was 10.141 ± 0.210 gm/dL and after intervention value was 11.766 ± 0.218 gm/dL (Fig. 4). This difference was very significant. In group C, the mean baseline value for blood haemoglobin was 12.809 ± 0.099 gm/dL and after the study duration it was 13.018 ± 0.119 gm/dL. This difference was significant (Table 2). Out of total 98 girl students included in the study 61 were diagnosed as non-anaemic after the intervention, whereas 37 were still having anaemia. Out of 37 anaemic girls 21 were mildly anaemic and 16 were diagnosed as moderately anaemic.

Statistical Analysis

The data was analyzed using SPSS version 20. Normality of the scalar data was tested using *Shapiro-Wilk test*. Distribution of grading of anaemia was compared using Chi-Square test. The comparison of the distribution of grading of anaemia in various groups before and after intervention was done using McNemar-Bowker test. Comparison of pre and post intervention haemoglobin parameters among different groups was studied using Wilcoxon Signed Ranks Test. Significant level was set at p-value of < 0.05 .

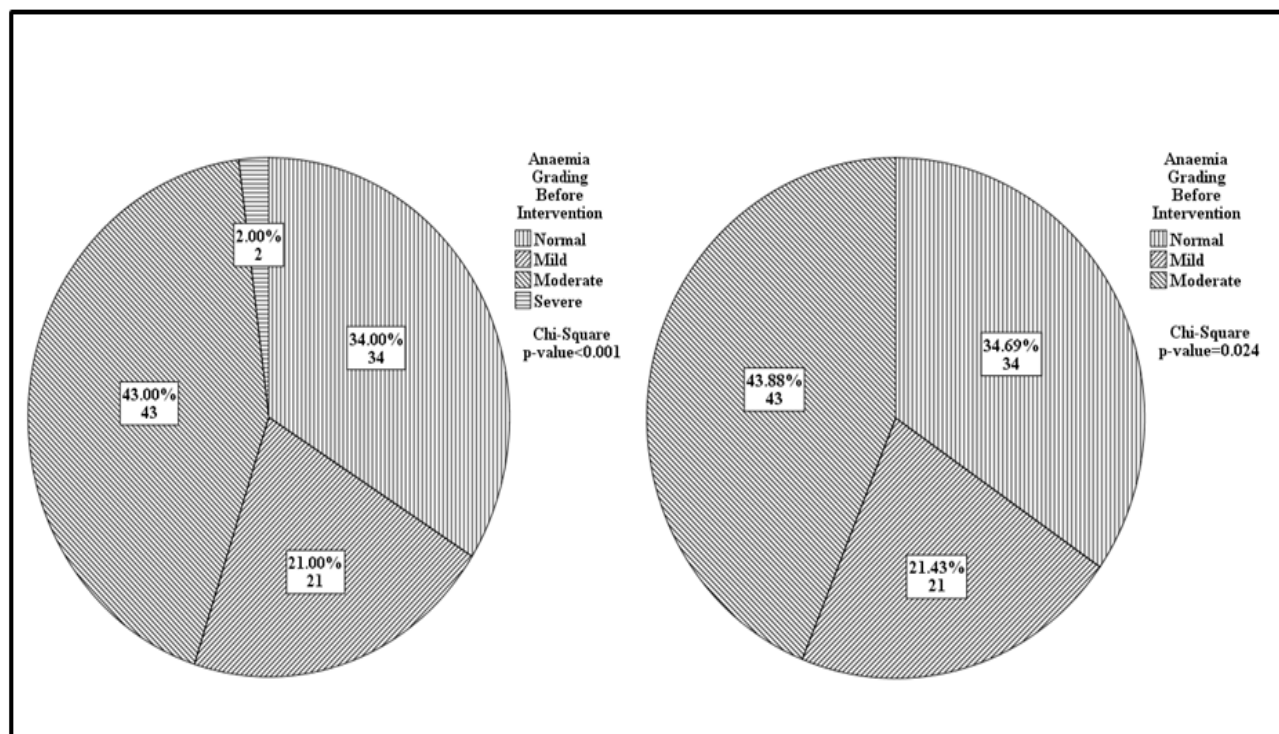


Fig.1. Distribution of grading of anaemia before the intervention (before and after removing those with severe anaemia).

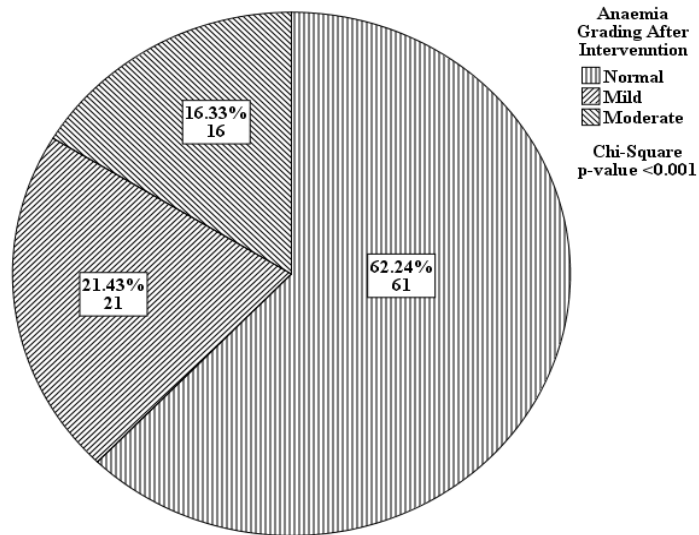


Fig.2. Distribution of grading of anaemia after the intervention

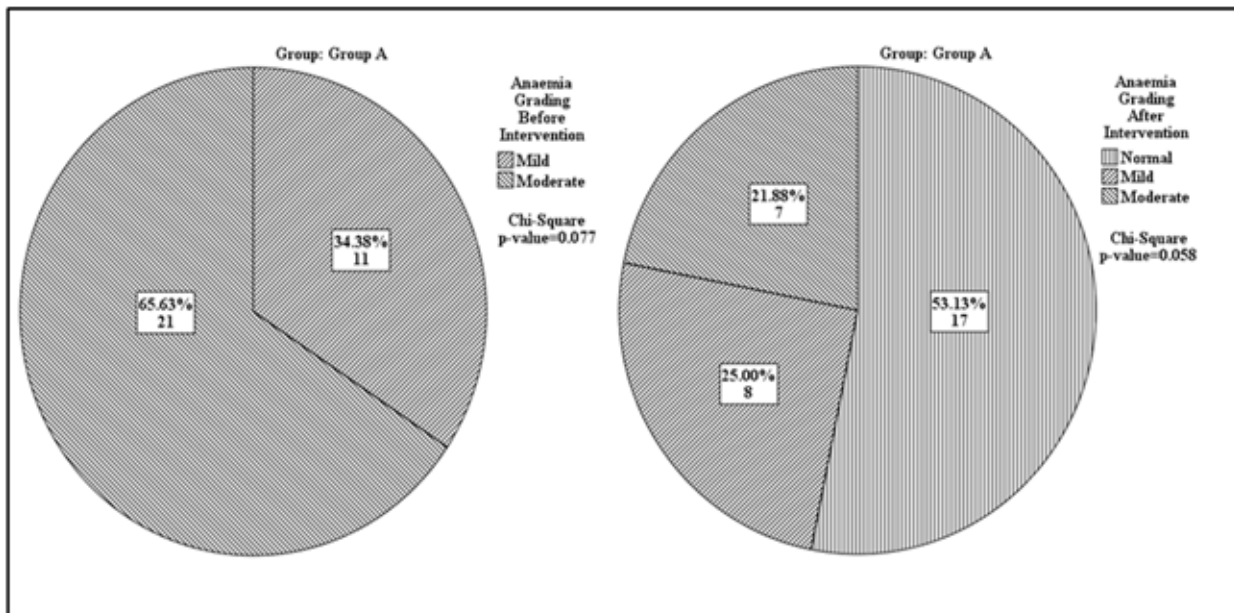


Fig.3. Distribution of grading of anaemia in group A before and after the intervention

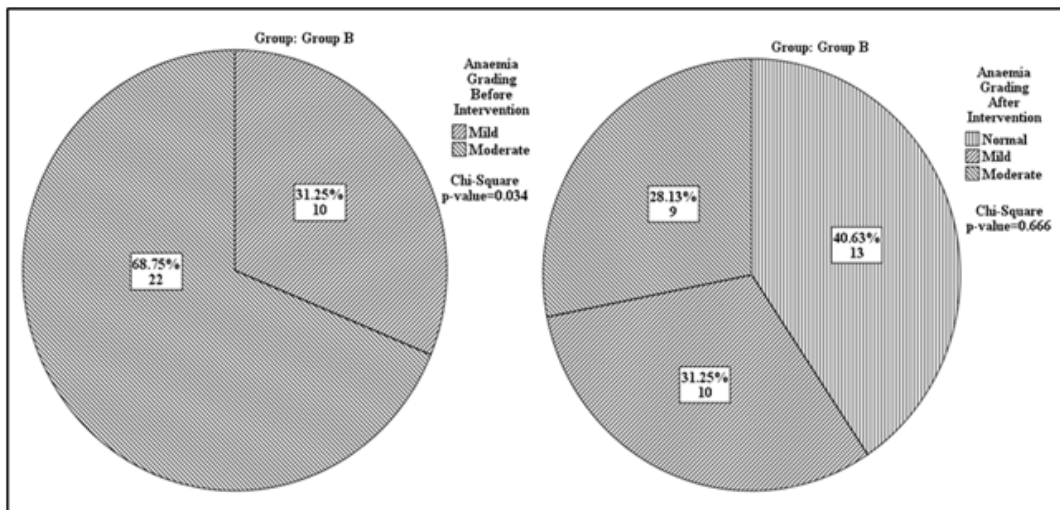


Fig.4. Distribution of grading of anaemia in group B before and after the intervention

Table 1. Comparison of the distribution of grading of anaemia in various groups before and after intervention.

Anaemia Grading Normal Mild			Before			Total	p-value
			Moderate				
After	Normal	Count	31 (50.8%, 91.2%)	19 (31.1%, 90.5%)	11 (18.0%, 25.6%)	61 (100.0%, 62.2%)	<0.001
		% of Total	31.6%	19.4%	11.2%	62.2%	
	Mild	Count	3 (14.3%, 8.8%)	2 (9.5%, 9.5%)	16 (76.2%, 37.2%)	21 (100.0%, 21.4%)	
		% of Total	3.1%	2.0%	16.3%	21.4%	
	Moderate	Count	0 (0.0%, 0.0%)	0 (0.0%, 0.0%)	16 (100.0%, 37.2%)	16 (100.0%, 16.3%)	
		% of Total	0.0%	0.0%	16.3%	16.3%	
Total % of Total		Count	34 (34.7%, 100.0%)	21 (21.4%, 100.0%)	43 (43.9%, 100.0%)	98 (100.0%, 100.0%)	
		34.7%	21.4%	43.9%	100.0%		

McNemar-Bowker test

Table 2. Comparison of the Haemoglobin level in various groups before and after intervention

Group	Intervention	Haemoglobin concentration (g/dl)		Median (Mean) Δ %	p-value
		Median (Mean)	QD (SD)		
Group A (n=32)	Before	10.300 (10.128)	1.000 (1.109)	20.388 (20.616)	<0.001
	After	12.400 (12.216)	0.950 (1.213)		
Group B (n=32)	Before	10.500 (10.141)	1.100 (1.187)	12.381 (16.024)	<0.001
	After	11.800 (11.766)	1.075 (1.235)		
Group C (n=34)	Before	12.650 (12.809)	0.400 (.576)	2.767 (1.632)	0.008
	After	13.000 (13.018)	0.400 (.695)		

Wilcoxon Signed Ranks Test. QD=Quartile deviation, SD=Standard deviation, Δ % = percentage of difference (post-pre) relatively to pre.

Discussion

According to WHO (2001), up to 88% of pregnant and 74% of non-pregnant women are anaemic in India. Anand K et al²⁴ in 1998 found the prevalence of anaemia

was 51 % among school going adolescent girl students. Sheshadri S (1997) studied¹ 1,500 rural girls (10-19 yrs), and the prevalence of anemia was reported to be 60%. Out of 66% prevalence of anaemia in our study, severe

anaemia, mild anemia and moderate anemia were 2%, 21% and 43% respectively. In a study of Deshpande et al (2013)³, among 1000 adolescent girls, 60 percent found to be anaemic, 18.4 percent as mild, 41.3 percent as moderate, and 0.4 percent as severe anaemia.

Effect of vitamin A supplementation on haemoglobin levels

In this study, in Group A, the difference between mean haemoglobin before and after intervention was 2.088 gm/dL and it was extremely significant ($p < 0.0001$). In Group B, the difference in mean was 1.625 gm/dL and it was very significant ($p < 0.0001$). In Group C, the difference in mean was 0.209 gm/dL and it was significant ($p = 0.0063$).

Mwanri Lillium et al (2000) found similar results²⁰ in a randomized controlled trial of the effects of dietary supplements on anemia in anemic school children. The supplements were vitamin A alone, iron and vitamin A, iron alone or placebo in four sample groups respectively, administered in a double-blinded design for 3 months. Vitamin A supplementation increased the mean hemoglobin concentration by 13.5 g/L compared with 3.5 g/L for placebo ($P < 0.0001$). However, the group of children who received combined vitamin A and iron supplementation had the greatest improvements as compared with placebo (18.5 g/L, $P < 0.0001$).

The influence of vitamin A and iron supplementation was studied by Suharno D et al (1993) in anaemic pregnant women.¹⁵ Maximum haemoglobin was achieved with both vitamin A and iron supplementation, with one-third of the response attributable to vitamin A and two-thirds to iron. They concluded that improvement in vitamin A status may contribute to the control of anaemic pregnant women.

Conclusions

Present study was conducted to evaluate whether vitamin A supplementation helps to restore the blood haemoglobin level along with iron therapy and helps to improve the status of anaemia. A major limitation of our study was relatively small sample size with anaemia in the concerned age and sex group. So, further studies involving large population need to be done to establish the definitive role of vitamin A supplementation in anaemia and to recommend it as a standard additive therapeutic agent.

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Conflict of Interest: None declared

Informed Consent: Informed consents were obtained from all the participants and their parents.

Human and Animal Rights: Procedures followed were in accordance with the ethical standards of institutional and national committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

Ethical Approval: The study was approved by the Institutional Ethics Committee

References

1. Sheshadri S. Nutritional Anemia in South Asia. *In: Malnutrition in South Asia: A Regional Profile* Ed. Gillespie S. Katmandu, UNICEF Regional Office for South Asia 1997; pp 75-124.
2. De Maeyer EM et al. *Preventing and controlling iron deficiency anaemia through primary health care*. Geneva, World Health Organization, 1989.
3. Deshpande NS, Karva D, Agarkhedkar S, Deshpande S. Prevalence of anemia in adolescent girls and its co-relation with demographic factors. *International Journal of Medicine and Public Health*, Oct-Dec 2013, Vol 3, Issue 4; 235-239.
4. WHO, UNICEF, UNU. *Iron deficiency anaemia: assessment, prevention and control, a guide for programme managers*. Geneva, World Health Organization, 2001
5. Wright.D. Anemia in pregnancy. <http://www.articlesbase.com/womens-health-articles/anemia-in-pregnancy-1541442.html>. dec 4, 2009; Accessed on 2/11/2012.
6. Toteja TS, et al Prevalence of anemia among pregnant women and adolescent girls in 16 districts of India. *Food and Nutrition Bulletin*, vol. 27, no. 4 © 2006, The United Nations University; 311-315.
7. Kapoor G, Aneja S. Nutritional disorders in adolescent girls. *Indian Pediatr* 1992; 29: 969-973.
8. Kaur S, Deshmukh PR, Garg BS. Epidemiological Correlates of Nutritional Anemia in Adolescent Girls

- of Rural Wardha . Indian Journal of Community Medicine Vol. 31, No. 4, October-December, 2006 ; 255-258.
9. Vasanthi G, Pawashe AB, H Susie, T Sujatha, Raman L. Iron nutritional status of adolescent girls from rural area and urban slum. Indian Pediatr 1994; 31: 127-132
 10. Thurnham, D.I. "Vitamin A, Iron, and haemopoiesis" commentary. Lancet 342:1312-1313(1993).
 11. Findlay GM, Mackenzie R. Oponins and Diets deficient in Vitamins. Biochemical Journal. 1922;16(5):574-577.
 12. Bloem MW, Wedel M, EggerRJ, Speek AJ, Schrijver J, Saowakontha S and Schreurs WHP. Iron metabolism and vitamin A deficiency in children in Northeast Thailand. Am J Clin Nutr 1989;50:332-8.
 13. Karyadi, D; Bloem, M.W. "The Role of Vitamin A in Iron Deficiency Anemia and Implications for Interventions." Biomedical and Environmental Sciences 9:316-324 (1996).
 14. Bloem MW, Wedel M, van Agtmaal EJ, Speek AJ, Saowakontha S, and Schreurs WHP. Vitamin A intervention: short-term effects of a single, oral, massive dose on iron metabolism. Am J Clin Nutr 1990;51:76-9.
 15. Suharno, D.; West, C.E.; Muhilal; Karyadi, D.; Hautvast, J.G.A.J. "Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia." Lancet 342:1325-1327 (1993).
 16. Roodenburg, A.J.C.; West, C.E.; Hovenier, R.; Beynen, A.C. "Supplemental vitamin A enhances the recovery from iron deficiency in rats with chronic vitamin A deficiency." British Journal of Nutrition 75:623-636 (1996).
 17. Majia LA, M.A., Hodges RE, M.D., Arroyave G, Ph.D., Viteri F, M.D. and Torun B, M.D. Vitamin A deficiency and Anaemia in central American children. Am. J. Clin. Nutr. 30 : 1175-1184, 1977
 18. Kolsteren P, Rahman SR, Hilderbrand K, Diniz A. Treatment of Iron deficiency anaemia with a combined supplementation of iron, vitamin A and zinc in women of Dinajpur, Bangladesh. European Journal of clinical nutrition (1999)53, 102-107
 19. Mejia, L.A.; Chew, F. "Hematological effect of supplementing anemic children with vitamin A alone and in combination with iron." American Journal of Clinical Nutrition 48:595-600 (1988)
 20. Mwanri L, Worsley A, Ryan P and Masika J. Supplemental Vitamin A Improves Anemia and Growth in Anemic School Children in Tanzania. J. Nutr. 130: 2691-2696, 2000
 21. Gamble MV, Palafox NA, Dancheck B, Ricks MO, Briand K, Semba RD. Relationship of vitamin A deficiency, iron deficiency, and inflammation to anemia among preschool children in the Republic of the Marshall Islands. Eur J Clin Nutr. 2004 Oct;58(10):1396-401
 22. Garcia-Casal MN, Layrisse M, Solano L, Baron MA, Arguello F, Llovera D, Ramirez J, Leets I and Tropper E. Vitamin A and -Carotene Can Improve Nonheme Iron Absorption from Rice, Wheat and Corn by Humans. J. Nutr. 128: 646-650, 1998
 23. Garg A, Abrol P, Tewari AD, Sen R and Lal H. Effect of vitamin A supplementation on haematopoiesis in children with anaemia. Indian Journal of Clinical Biochemistry, 2005, 20(1) 85-86
 24. Anand K, Kant S, Kapoor SK. Nutritional status of adolescent school children in rural north India. Indian Pediatr. 1999 Aug;36(8):810-5