Review of Literature

Chapter II

REVIEW OF LITERATURE

Adolescents are tomorrow's adults, and 85% of them live in developing countries (United Nations 1997). During this period, known as *adolescence*, individuals move toward physical and psychological maturity and economic independence, and acquire their adult identity.

As adolescents have a low prevalence of infection compared with under-five children, and of chronic disease compared with ageing people, they have generally been given little health and nutrition attention (Senderowitz 1995), except for reproductive health concerns. Traditionally, preschool-age children and women of reproductive age have been targeted as nutritionally vulnerable groups in developing countries, whereas in industrialized countries, the focus tends to be on nutrition related chronic diseases of the ageing population. Adolescents are an in-between group, with some nutrition problem commonalties with children, and with adults. However, there may be adolescent-specific priority issues, calling for specific strategies and approaches, which have received inadequate attention.

Adolescence is characterized by growth spurt, increased nutritional needs because of the metabolic demands of growth and energy expenditure. Increased nutritional requirements along with inadequate and inappropriate dietary intake make adolescents vulnerable to nutritional disorders and micronutrient deficiency (Beard 2000). The most widely prevalent micronutrient deficiency in the world is iron deficiency anemia and it is the eighth leading cause of disease in preadolescent and adolescent girls and women in developing countries (World Bank 1993).

In addition to causing anemia, iron deficiency (ID) may have other functional consequences, such as poor physical capacity, impaired growth, behavioral changes and decrease in cognition test scores. The effects of anemia and iron supplements on overall growth, cognition and physical work capacity have not been investigated adequately, especially in early and late adolescence which is a rapid period of development.

In view of the focus of the study, on adolescent anemia, especially among the young girls entering puberty, the present chapter reviews the available literature under the following heads:

- Adolescence – the vulnerable age group
- Iron Deficiency Anemia (IDA)
- Perceptions of adolescent girls regarding anemia and its control
- Iron folic acid supplementation in adolescent girls: Impact on anemia, growth and food intake, cognition and physical work capacity of girls.
- Need for addressing anemia at a younger age: in primary school children

Adolescence – The Vulnerable Age-group

Adolescent girls are particularly vulnerable to malnutrition because they are growing faster than at any time after their first year of life. They need protein, iron, and other micronutrients to support the adolescent growth spurt and meet the body's increased demand for iron during menstruation. Adolescents who become pregnant are at greater risk of various complications since they may not yet have finished growing. There is evidence that the bodies of the still-growing adolescent mothers and their babies may compete for the same nutrients.

Meeting Millennium Development Goals (MDG)

Children lie at the heart of international commitments to social justice. The Indian government has pledged at international forums to provide health and nutrition for all children and their mothers, and to guarantee essential education as a human right as well as a key to equitable growth and sustainable development. Thus, adolescent girls are stated as important beneficiary groups in nutritional policy at national and state level (National Nutrition Policy 1993, Gujarat State Nutrition Policy 1998).

Table 2.1: Better Nutrition Helps Achieve Millennium Development Goals

Millennium Development Goal	How Improving Women and Adolescent Girls' Nutrition Helps
Goal #1: Eradicate extreme poverty and hunger.	
Halve, between 1990 and 2015, the proportion of people who suffer from hunger.	• Well-nourished adolescents later become well-nourished women who are better able to provide for themselves, their children, and their families. • Well-nourished women when pregnant are more likely to have infants with healthy birth weights, and such children are less likely to ever suffer from malnutrition.
Goal #4: Reduce child mortality.	
Reduce, by two-thirds, between 1990 and 2015, the under-5 mortality rate.	• Well-nourished adolescents and mothers are less likely to bear low birth-weight babies. • Well-nourished mothers are more likely to have healthy babies who can survive childhood illnesses.
Goal #5: Improve maternal health.	
Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio.	• Adolescents with adequate stores of iron and other micronutrients, when pregnant, are less likely to suffer fatal infections and are more likely to survive bleeding during and after childbirth. • *Well-nourished adolescent mothers are less likely to experience obstructed labor than their undernourished peers.
Source: Ransom and Elder 2003.	
*Note: However, in the interest of the girl herself, and the future generation, adolescent pregnancy should be discouraged and delaying age of first delivery should be promoted.	

Investing in adolescents will help meet the MDGs (**Table 2.1**). Three of the seven MDG to be achieved by 2015 relate directly to children and adolescents: 100% primary school enrolment rate, elimination of gender disparities in primary and secondary education and reduction in maternal, infant and child mortality by two thirds. Further, IDA reduction will enhance educability and labor productivity, will lead to intergenerational benefits, as we recognize even more the need to intervene in adolescence (Hunt 2002).

Importance of Adolescent Nutrition, especially in Early Adolescence

Adolescence is an anabolic period and during this period of rapid growth, children are at risk of developing both macro and micronutrient deficiencies. Clearly, adolescence is a pivotal stage of the life cycle, and in turn, provides a unique opportunity to foster a healthy transition from childhood to adulthood. For ensuring that the nutritional needs of adolescents are met, essential for this transition, and primary issues relating to undernutrition are addressed, programs and research activities need to be undertaken among these age group. Thus, adolescence may represent a window of opportunity to prepare nutritionally for a healthy adult life. Some nutritional problems originating earlier in life can potentially be corrected, in addition to addressing current ones. It may also be a timely period to shape and consolidate healthy eating and lifestyle behaviours, thereby preventing or postponing the onset of nutrition-related chronic diseases in adulthood.

Accelerated growth during adolescence makes it a period during which earlier growth deficiencies might be at least partially compensated (Kurz and Gupta 1991). Therefore adolescence is an opportune time for interventions to address anemia and improve their nutritional status, thus reducing reproductive risk and increasing productive capacity (Keller et al 1996, Kurz 1997).

The period of early adolescence is especially important as over 80% of adolescent growth (attained weight and height) is completed in early adolescence (10-15 years), with a marked deceleration in weight and height velocity in the post pubertal phase (Srikantia 1989). In girls, the year preceding menarche marks the period of peak height velocity and maximum yearly height gain. In a longitudinal study in Vadodara which followed up 524 girls for over two years, it was observed that the age at PHV take off was 11.5 years and a majority attained menarche at age 13 years (Agarwal and Kanani 1998).

Unfortunately, undernutrition is high in adolescents. A high prevalence of stunting and thinness (BMI <5th percentile Must et al 1991) among adolescents has emerged from studies in India. Both the ICRW studies and the Indian data have indicated that about one-third or more of the adolescents are stunted; and about one half (50-55%) are undernourished or thin (Kotecha et al 2002, Kurz and Welch 1994). Undernutrition (BMI deficits) and stunting has been found to be relatively high in younger adolescent girls (who are in pubertal phase of growth) compared to the elder once (Kanani and Poojara 2000).

Pregnant adolescents who are underweight or stunted are especially likely to experience obstructed labor and other obstetric complications.

Iron Deficiency Anemia (IDA)

Among the "hidden hunger" issues that developing countries face today, none is more compelling than the pervasive problem of iron deficiency (ID) and its clinical form, iron deficiency anemia (IDA). Unfortunately, many of the effects of iron deficiency are not noticeable until after they have taken their toll. Its effects are subtle and insidious, less striking and therefore more difficult for policymakers to grasp and act upon.

Anemia is a condition of low circulating hemoglobin with serious and even life-threatening consequences (Gillespie 1998). Iron deficiency can be defined as that moment in time when body stores in iron have become depleted of iron and a restriction of supply of iron to various tissues become apparent. (Bothwell et al 1979) Growing adolescents need large amounts of iron for growth and are therefore vulnerable to iron deficiency, particularly those whose diets are marginal in iron content and who experience heavy iron losses due to parasitic infestations (Lawless et al 1994). Anemia is of critical health concern in adolescent girls because of its adverse consequences on growth and development and future reproductive health.

Prevalence of Anemia in School Children and Adolescence

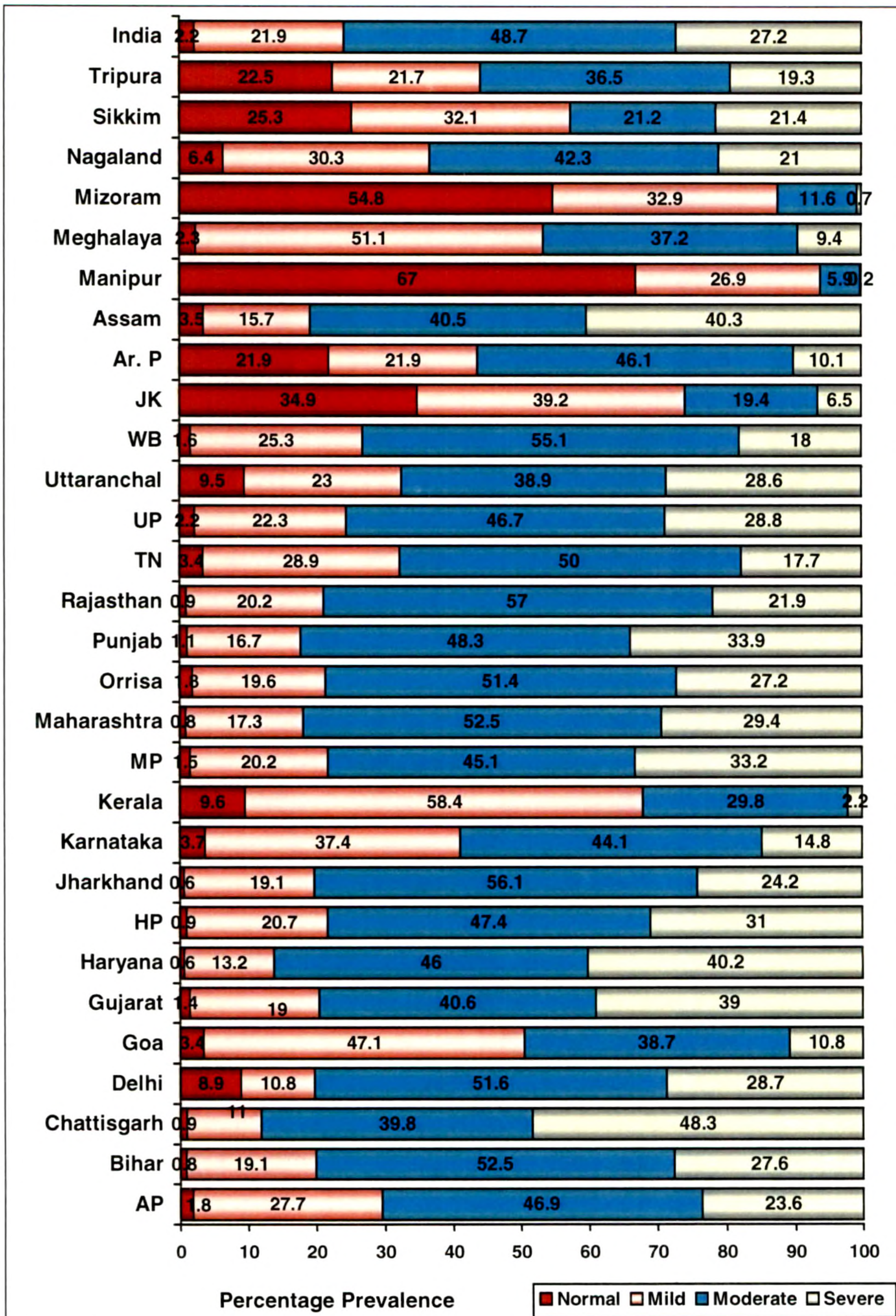
Recent estimates of the world wide prevalence of iron deficiency and anemia indicate that 46% of the world's 5 to 14 year-old children are anemic, with the overwhelming majority of this anemia occurring in individuals from the developing countries (Beard 2000). WHO (1998) estimates that about 63% children in the age groups of 5 to 14 years are anemic in Southeast Asia.

In an 11 country study >40% of adolescents were anemic (hemoglobin <11.5 g/dl) in the Asian countries including Nepal and India (Kruz 1996). In a large-scale study in 18 states of India, the prevalence of anemia (Hb<11g/dl) among unmarried adolescent girls was as high as 90.1% (ICMR 2001). Further, the prevalence rates in eight states falls in the severe category (>40% prevalence, WHO 2001) of public health significance, reinforcing that anemia urgently needs to be addressed among adolescent girls in India (NNMB-MND 2003).

Figure 2.1 illustrates the severity of anemia among adolescent girls in India and gives the state level variation in the prevalence of anemia among adolescent girls (IIPS 2006). The state of Himachal Pradesh and Chattisgarh had the highest prevalence of anemia (above 99%) among adolescent girls. The lowest percent of anemic girls were in Jammu and Kashmir, Manipur and Kerala. Overall, the prevalence of anemia was very high in most of the states in India. Gujarat unfortunately also is among the states with a high prevalence (98%). Various studies done over the years in different cities of India showed a similar trend (**Table 2.2**). The prevalence varies among tribal, rural and urban areas. The percentage prevalence ranges from 22% to 96.5%.

A pilot survey conducted in Vadodara district on secondary school girls in rural, tribal and urban areas under Gujarat Government's Adolescent Anemia Control Program (UNICEF supported) also reported 75% girls to be anemic (Hb <12 g/dl) (Kotecha et al 2000).

Figure 2.1: Prevalence of in India among Adolescent Girls by State



Source: International Institute for Population Sciences (IIPS) 2006 (DLHS 2002-04)

Table 2.2: Prevalence of IDA in Adolescent Girls of India

State	Author, Year and Place	Age	N	% Anemic
Orissa	Balgir, Murmu and Dash 1999, Ashram school (Tribal)	6-15 years	865	73.8 %[1]
MP	Gawarikar, Gawarikar and Tripathi 2002, Ujjain	10 – 18 years	459	96.5%[1]
Andhra Pradesh	Raman 1990, Hyderabad	Adolescent girls	239	73 %[1]
	IIHFW 2002-2003, Hyderabad (urban)	School going adolescents	767	82.9 %[1]
Delhi	Sharma et al 2000, Delhi (urban)	11-18 years	520	61.9 %[1]
Chandigarh	Swami, Thakur and Bhatia 1998, Chandigarh (rural)	6-14 years	122	13.1 %[1]
Maharashtra	Mehta, 1998, Mumbai (urban)	Adolescent girls	1748	63.8 %[1]
	Jondhale, Reddy and Nalwade 2001, Prabhani	School girls 13 to 15 years	300	20%[1]
Tamil Nadu	Rajaratnam et al 2000, Vellore (rural)	13-19 years	289	44.8 %[2]
	Yegammi and Gandhimathy 1993, Combatore (urban)	13-15 years	180	22 %[1]
	Leela and Priya 2002, Coimbatore	5 – 10 years	120	80 %[1]
Haryana	Anand et al 1999, Faridabad (rural)	12-18 years	534	48 %[1]
Rajasthan	Sharma et al 2000, Bharatpur (rural)	11-18 years	185	85.4 %[1]
Punjab	Verma et al 1998, Ludhiana (urban)	5-15 years	-	51.5 %[2]
Gujarat	Seshadri et al 1998, Bharuch (rural)	10-15 years	-	61 %[2]
	Gopaldas 1996, Vadodara (urban)	6-19 years	724	79 %[1]
	Kotecha et al, 2000 Vadodara (urban & rural)	12-19 years	2860	74.4 %[1]
	Verma, Rawal, Kedia et al 2004, Ahmedabad	6-18 years	1295	81.8 %[1]

[1]Hb < 12 g/dl, [2]Hb <11 g/dl

A compilation of 14 studies conducted at the Department of Foods and Nutrition, M. S. University of Vadodara during 1985 – 1997 shows a high prevalence of anemia (Hb <12 g/dl) in adolescent girls in urban Vadodara, in the range of 65% – 88% and 51% – 75% for poor and affluent groups respectively (Kanani and Ghanekar 1997). Recent research in the Department of Foods and Nutrition on urban school children also confirms that over 70% are anemic (hemoglobin <12 g/dl) (**Table 2.3**).

Table 2.3: Prevalence in Vadodara among Urban Poor Adolescent Girls

Kanani and Coworkers	Age in years	N	% Anemic		Mean Hb g/dl
			<12 g/dl	<11 g/dl	
2002	10-18	96	94	-	10.2
2001	11-16	130	62	33	11.3
1998	8-13	473	90	75	9.9
1998	10-15	259	77	53	10.7

Thus, the prevalence of iron deficiency anemia remains high, despite substantial efforts to alleviate this nutritional disease.

Role of Iron in the Body

Iron is an essential component of the hemoglobin molecule; without iron the marrow is unable to produce hemoglobin. The red cell number falls and those which do reach the circulation are smaller than normal (microcytic) and lack hemoglobin, hence they are pale and under colored (hypochromic). The deficiency in iron may be absolute, that is, there is no iron available for the production of hemoglobin. This is true iron deficiency anemia. The deficiency may be relative, that is, the iron is present in storage in the marrow but is unavailable for hemoglobin production, and this is anemia of chronic disease (Rice 2001).

Iron Balance and Occurrence of Iron Deficiency Anemia

Iron balance is the difference between iron retention and iron requirements (Beard et al 1996). The retention of iron often called the absorbed iron, is the product of iron intake and the bioavailability of dietary, supplementary or contaminant iron. The excess iron that accumulates beyond that necessary for the daily requirement is stored within the core of the ferritin molecule. This stored ferritin iron is then available for cellular iron needs should dietary intake fall below the organ needs. When this negative iron balance persists for a period of time, the iron stores are depleted and the iron supply to the essential iron pools of the body is diminished. Functional consequences then result from insufficient iron-dependent functioning for oxygen transport, oxidative metabolism, nuclear metabolism and gene transcription.

Clinical sequel to this poor iron status include anemia, poor immune function and decreased work performance.

The progression of iron deficiency occurs in three steps related to depletion of iron stores prior to depletion of functional iron:

1. **Iron depletion** with decrease in iron stores and reduction in ferritin levels with no evidence of any functional consequences or low hemoglobin,
2. **Iron deficient erythropoiesis** i.e. diminished erythropoiesis due to a negative balance leading to anemia and decreased activity of iron-dependent enzymes (Beard, Dawson and Pinero 1996). This stage develops when storage iron is depleted and iron absorption is insufficient to counteract the amount lost from the body and hemoglobin synthesis becomes impaired,
3. **Iron deficiency anemia** with significantly reduced hemoglobin production resulting in distortion of red blood cells, with microcytosis and hypochromia (Gillespie 1998).

The major diagnostic criteria for Iron Deficiency are as follows (**Table 2.4**)

1. Normal
2. Depletion of iron stores, decreased ferritin levels, no anemia
3. Decreased transferrin levels, fall in serum iron, no anemia
4. Development of anemia, fall in hemoglobin levels

Table 2.4: Diagnostic Criteria for Iron Deficiency

For adolescents and adults	Normal	Iron Depletion	Iron Deficient Erythropoiesis	Iron Deficient Anemia
Iron Stores (bone marrow, liver, spleen)	Adequate	Very low	0	0
Plasma Ferritin (μg/dl)	100 ± 60	20	10	< 10
Transferrin saturation (%)	30 ± 15	30	< 15	< 15
TIBC (μg/dl)	300 ± 30	360	390	410
RBC Protoporphyrin (μg/dl)	30	30	100	200
Plasm iron (μg/dl)	115 ± 15	115	< 60	< 40
Hemoglobin (g/dl)	12	12	12	<12

Source: Beard, Dawson and Pinero 1996

Iron Deficiency and Increased Requirements for Growth

Iron requirements depend on body needs for tissue growth and tissue maintenance, which vary with the life cycle and certain environmental factors (Beard, Dawson and Pinero 1996). Total iron requirements for adolescent are computed from the increased iron requirements for the expansion of the total blood volume (0.18 mg/d in boys and 0.14 mg/d in girls on an average) and the increase in the total body essential pool with the increase in the lean body mass (0.55 mg/d in boys and 0.33 mg/d in girls median additional requirements). The increase in the iron requirements for the red cell mass includes both the increase in total blood volume as well as the increase in the mean hemoglobin concentration from the early adolescent years through the adolescent growth spurt. The additional iron requirements for adolescent girls include the additional amount of iron lost in menses beyond the growth requirements (Hallberg 1996). The mean menstrual blood loss of 84mL/period (Hallberg 1996), assuming a mean hemoglobin of 133 g/L, provides an estimate of 0.56 mg of additional iron per day.

Fairweather-Tait (1996) estimates the iron requirement for adolescent girls before menses to be between 1.22 and 1.46 mg/d, and after menses to be between 1.39 and 2.45mg/day. Further, adolescent iron requirements are even higher in developing countries due to infectious diseases and parasitic infestations that cause iron loss, and because of low bioavailability of iron from diets limited in heme iron. Low iron status among adolescents may limit their growth spurt (Brabin and Brabin 1992).

Iron Deficiency and Cognition

There are many pathways through which iron deficiency can affect cognition. Briefly it is proposed that even at the very early stages of iron deficiency, a decrease in iron dependent dopamine D_2 receptors in the cortex alters dopamine neurotransmission, which, in turn, impairs cognitive function (Leibel et al 1979, Youdim 1990). The alternative hypothesis is less explicit and refers to more advanced stages of iron deficiency when hemoglobin concentration is compromised. It postulates that in the presence of anemia there may be systemic effects that interfere with cognition (Leibel et al 1979).

In iron deficiency, changes in brain iron content and distribution, and in neurotransmitter function may affect cognition. Attentional processing of environmental information is highly dependent on appropriate rates of dopamine. Alteration in dopamine is associated with altered perception, memory and motivation (Beard 2001). Therefore, iron deficiency impairs cognitive function thus compromising learning abilities (Kurz and Johnson-Welch 1994). Anemia may produce scholastic under-achievement and behavioral disturbances in school children (Pollitt and Liebel 1976). Studies show that iron deficient children perform less well on psychomotor tests than do non-anemics (Bhatia and Seshadri 1993). However, little is known as regards impact on children entering adolescence and those undergoing the pubertal growth spurt.

There is consistent evidence showing how level and quality of dietary intake influences both the development and function of the central nervous system. Early IDA may have relatively permanent effects on brain myelination, thus restricting the level of gains that can result from early iron supplementation (Lozoff 1998). Alternatively, IDA may also act to reduce the number of D_2 dopamine receptors, and thus disrupt function mediated by the dopamine neurotransmitter system.

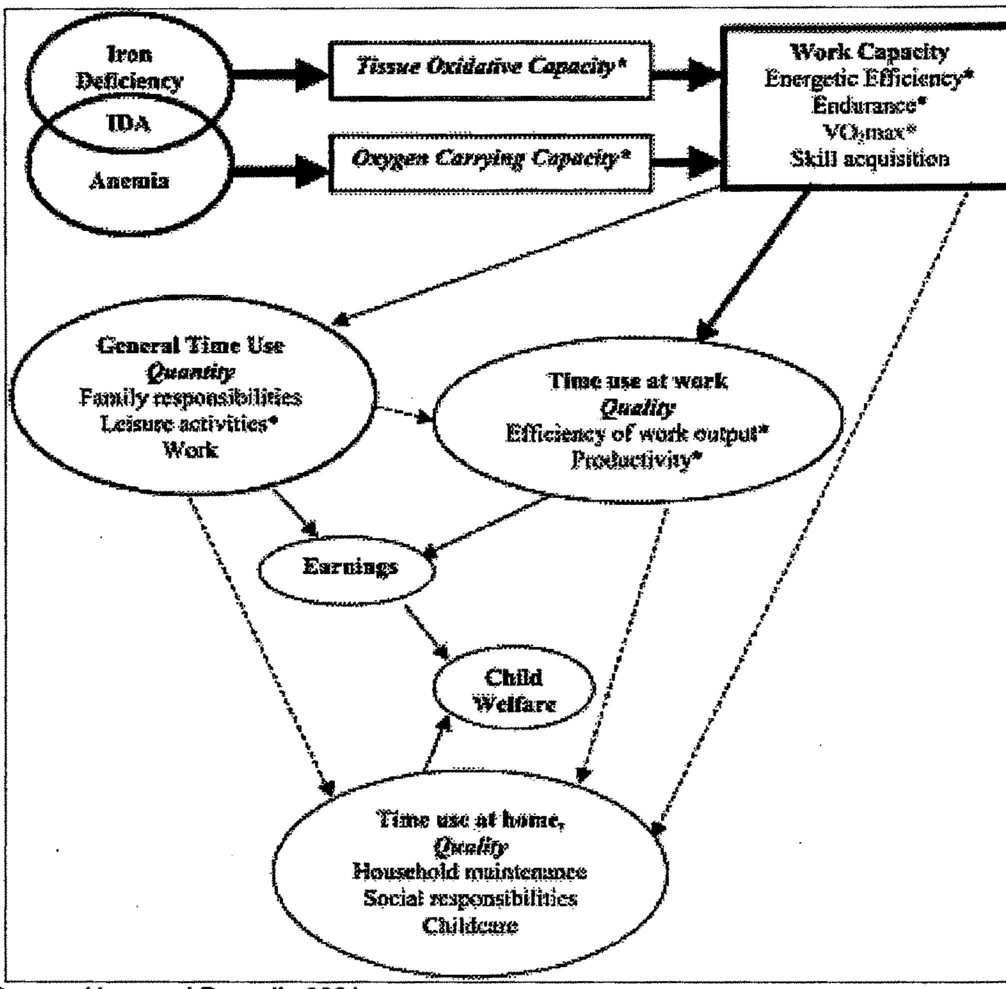
Iron Deficiency and Physical Work Capacity

Iron has a key function in oxygen transport, either as part of hemoglobin, or as myoglobin. In IDA the decrease in hemoglobin reduces the availability of oxygen to the tissues, which in turn affects the cardiac output (Beaton, Corey and Steel 1989). The movement of oxygen from the environment to terminal oxidases is one of the key functions of iron. Dioxygen binds to porphyrin ring iron containing molecules either as part of the prosthetic group of Hb within the red blood cells or as the facilitator of oxygen diffusion in tissue myoglobin (Beard, Dawson and Pinero 1996). The very significant decrease in myoglobin and other iron containing proteins in the skeleton muscle seen in iron deficiency anemia contributes significantly to the decline in the muscle aerobic capacity (Dallman 1986). Pyruvate and malate oxidase were decreased to 35% of normal in iron deficient muscle and improved to 85% of normal in 10 days of treatment (Beard, Dawson and Pinero 1996). Iron is essential for the oxygen carrying capacity of hemoglobin and myoglobin as well, being a component of many enzymes, which are required for the adequate functioning of brain cells, muscle cells, and the cells of immune system (Vir 1998).

The different mechanisms through which iron deficiency and anemia affect work capacity are reduced tissue oxidative capacity and reduced oxygen-carrying capacity. Tissue oxidative capacity is affected across all levels of iron deficiency, whereas the oxygen-carrying capacity is affected only at the most severe stages of deficiency when Hb concentration is reduced. In turn, these two impairments affect different aspects of physical performance. Reductions in oxygen-carrying capacity impair aerobic capacity, whereas reductions in tissue oxidative capacity impair endurance and energetic efficiency (Davies et al 1984). Various work capacity outcomes have been shown to be affected by iron deficiency and anemia.

The **Figure 2.2** depicts the potential relationships between iron deficiency and societal outcomes such as the quantity and quality of time allocated to various activities related to work, leisure and family responsibilities. Iron status alters the ratio of energy expended at work to energy expended outside of work. In other words, in absence of anemia, as the amount of physiological energy required to complete the work-related tasks decreases (because of increased physical fitness and energetic efficiency), individuals are less fatigued and therefore more likely to engage to a greater extent in non work-related activities. Consequently, the amount of time and the quality of such non-work related activities should increase. The framework also recognizes that iron deficiency may affect cognitive ability and skill acquisition at work, which may affect productivity as well.

Figure 2.2: Effect Of Iron Deficiency On Biological And Socioeconomic Aspects Of Work



Source: Haas and Brownlie 2001

The evidence is the strongest for IDA causing reductions in aerobic work capacity. Animal and human studies have consistently found that aerobic capacity is significantly reduced with severe IDA and moderate IDA. The evidence clearly suggests that severe and moderate form of IDA also impair endurance capacity, but this is based almost exclusively on studies of experimental animals. The evidence from both animal and human studies suggests that a strong causal relationship exists between all levels of iron deficiency (with or without anemia) and voluntary physical activity.

Iron thus appears to play a vital role in growth, physical work capacity (PWC) and cognitive development of growing children and adolescents.

Causes and Consequences of Iron Deficiency Anemia In Adolescence

Iron deficiency results from any condition of iron imbalance in the body. This occurs mainly when dietary iron intake or absorption fails to meet physiologic needs (Leibel et al 1979). The main causes of iron deficiency anemia are as follows.

1. Deficient Dietary Intake of Iron

The iron nutrition status of an individual is largely a function of the amount of dietary iron, the bioavailibility of that iron, and the extent of iron losses. Basal obligatory losses in humans are approximately 1 mg/day and must be replaced by an equivalent amount of iron derived from the diet (Beard, Dawson and Pinero 1996). Deficient intake of iron in our diet and/or low absorption and availability of iron from foods consumed are the principal causes of anemia (Vir 1998).

Poor bioavailability from Indian diets: Many foods that are potentially good sources of iron are limited by the bioavailability of iron. Bioavailability of iron is a function of its chemical form and the presence of food items that promote or inhibit absorption. The non heme iron present in vegetables has a poor bioavailability of 1-5% as against 15-20% for heme iron present in meat and flesh foods (Swaminathan 1985). Although most habitually consumed diets in different regions of India contain adequate amounts of iron, absorption of iron from such diets is only 1-5% (Gillespie 1998).

One key enhancer of non-heme iron absorption in a vegetarian diet is ascorbic acid which reduces ferric iron to ferrous iron (the form in which iron is absorbed from the intestine). The dietary constituents which are important inhibitors of non-heme iron absorption are phytates from cereals and tannins in tea and coffee. Calcium inhibits the absorption of not only non heme iron, but also heme iron.

Poor dietary intake: The available data on iron intakes in adolescents suggests that adolescent girls are unlikely to acquire substantial iron stores during this time period because intakes may average as little as 10-11 mg Fe/day (Beard 2000). Kanani et al (1998) in Vadodara, among adolescent girls, reported low dietary iron intake of only about 10% to 15% of RDA. Further, the calorie and protein intakes were two-third of the RDAs.

2. Increased Requirements of Iron Due To Growth

The onset of adolescence triggers a growth rate greater than in any other stage of human life (Sederowitz 1995). Iron requirements increased during adolescence, reaching a maximum at peak growth (Kanani and Poojara 2000, Barbin and Barbin 1992). The peak need for iron has been showed to be more closely related to maximal growth spurt and maturation than to age (Sjolin 1981).

The iron requirements increase dramatically as a result of the expansion of total blood volume, increase in lean body mass and rapid skeletal muscle development. Rao (1985) reported that blood volume increases from 2.5 to 3.5 liters in girls during adolescence. There is rapid increase in the length and thickness of the muscles. Girls on marginal or deficient iron intakes are likely to develop anemia due to urgent need for iron during the growth period.

3. Blood Loss/ Menstruation in Girls

The onset of menarche is a visible event in a sequence of changes which occur during adolescence. Adolescent girls have an additional demand created by the onset of menses (Fairweather-Tait 1996, Beard 2000). This increased demand due to the physiological status aggravates the deficiency of iron.

4. Infections / Infestations

Worm infestation can contribute to malnutrition through anorexia, malabsorption, and anemia through loss of blood (Drake et al 2002). Malaria in particular is a very widespread and highly significant contributing factor to severe anemia. Adolescent iron requirements are even higher in developing countries because of infectious diseases and parasitic infestation that cause iron loss (Kanani and Poojara 2000). Virtually all children in the Keniyan study were reported infected with hookworm and Trichures and had a high prevalence of anemia (75.6%) (Lawless et al 1994).

Consequences Of IDA

Literature reports several adverse consequences of anemia in children and young adolescents.

1. Delayed Growth and Development

IDA tends to delay growth and development in terms of weight and height gain in children (Lokeshwer et al 1990), possibly because the adolescent on marginal iron intake cannot meet iron demands for growth, as explained earlier. A study conducted by Kanani and Poojara (2000) on 10 to 18 years old adolescent girls living in slums of Vadodara indicated that about 42% of the girls had BMI below normal (<80% NCHS standard) and growth retardation was more evident in subjects who were anemic.

2. Decreased Appetite and Anorexia

One symptom associated with iron deficiency is loss of appetite, also referred to as anorexia (Judisch et al 1966, Pollitt and Leibel 1976, Theuer 1974). IDA is reported to suppress appetite in anemic adolescent, leading to poor food intake, which again may adversely influence adolescent growth (Kanani and Poojara 2000). Some studies have speculated that the improved growth observed in children provided with iron supplements might be attributed to a correction of anorexia (Auckett et al 1986, Chwang et al 1988, Latham et al 1990).

3. Lowered Cognitive and Mental Development

Most studies show that IDA is associated with poor performance in infant development, IQ and learning tasks in preschool children, and educational achievement among school-age children (Pollitt 1993). Learning disabilities represent either a general development lag or include several specific cognitive dysfunctions that, when combined, interfere with school performance in most or all areas of learning (Pollitt 1999).

Independent of age, the subjects with IDA perform, on average, less well than those whose iron stores are replete, in various mental tests (Pollitt 1999). In India, Pondicherry, anemic young adolescent girls (10 – 12 years) had significantly lower grades measured using Raven's Progressive Matrics Intelligence scale and had impaired learning and school achievements (Many and Rajini 2006). In Jamaica, anemia in adolescent girls (13-14 years) (n=452) was associated with poor school performance, which remained after controlling for social background and attendance (Walker et al 1996).

IDA among school children (≥6 years old) has been associated with poor performance on intelligence tests such as the WISC; on tests of specific cognitive processes such as short-term memory and attention (Seshadri and Gopaldas 1989, Soemantri 1989) as well as low scores in school achievements (Pollitt et al 1989).

Hutchinson et al (1997) in a study in Jamaica, concluded that even mild levels of anemia, undernutrition and infections were significantly associated with poor achievement levels even after taking into account the social background differences among primary school children (9-13 years) (n=383).

4. Decreased Physical Work Capacity (PWC)

Work output, endurance and maximal work capacity are impaired in iron deficient state (Basta et al 1979, Viteri et al 1974). People with mild or moderate anemia generally feel normal at rest and note fatigue only with exertion (Eichner 2001). Iron deficiency anemia affects the physical capacity by reducing the availability of oxygen to the tissues and interfering with work efficiency (Vijayalakshmi and Selvasundari 1983). In adults as well as adolescent children, iron deficiency results in impaired work performance and productivity.

In Indonesia, Scholz et al (1997) reported a significantly positive correlation between height, weight and total body hemoglobin levels was found among anemic female jute mill workers (n=92). Although factory work was not physically strenuous, it was very demanding in terms of attention and alertness. Therefore, not only physically strenuous work, anemia also adversely affects physically less demanding work.

Among Indian adolescent children (9-16 years) moderate to severe forms of undernutrition adversely affected the physical work performance (Chiplonkar et al 1992). Vijayalakshmi, Sharada and Venkatramana (2000) reported that anemic adolescent girls (n=65) had significantly lower work output compared to non-anemic counterparts.

5. Impaired Immune Function

Chwang et al (1988) found myeloperoxidase activity to be reduced and morbidity to be increased in anemic children compared to normal. They found a significant reduction in the level of morbidity in rural Indonesian children (8.2 to 13.5 years) receiving iron supplements as compared to children receiving the placebo.

All the above functional deficits due to anemia have adverse implications for school performance, subsequent adolescent growth and development and also future reproductive health. If these young women become pregnant, they are exposed to additional risks. (Bothwell et al 1979, Scholz et al 1997).

Perceptions of Adolescent Girls Regarding Anemia

Knowledge of adolescent girls has been found to be inadequate regarding anemia. Some of the studies conducted over the years to understand the knowledge, attitude and practices of the adolescent girls have reported that a majority of the girls believed that they did not suffer from 'paleness of blood' though most had low Hb levels. Regarding problems faced due to anemia about half were not aware about the adverse consequences (Kanani et al 1998).

Under the Adolescent Anemia Reduction Program (AARP), formative qualitative research was conducted among secondary school girls of Vadodara district (Kanani 2000). Most of the school going adolescent girls were not aware of the term 'anemia' or 'pale blood' (*phiku lohi*). Few girls mentioned terms such as jaundice or malaria to describe anemia, perhaps associating yellow pallor of jaundice with 'pale blood'. They described symptoms such as "*tene ashakti laage, thak laag*'" (she feels weak an tired) and "*kaam na thaye, dodiye to thaki jaaye*" (cannot work, if she runs she gets tired). More than half could not state the causes of anemia. A few mentioned 'inadequate' or 'inappropriate' food intake as the main cause. Several girls mentioned that consuming milk, raddish leaves, shepu leaves, beet root make the blood red.

Both the teachers and the girls had very generalized and non-specific information regarding causes of anemia; dietary measures and IFA supplementation to combat anemia. Most important, there was no realization among adolescent girls about the grave consequences of anemia and need to give due attention to this pervasive problem. Under the program the girls received once weekly IFA for one year. IEC material on anemia were developed and distributed among the girls and put up in the school. After supplementation the prevalence reduced by 50% with some improvement in the knowledge of the girls and teachers regarding the causes, ill effects and preventive measures of anemia.

Therefore, not only are adolescent girls vulnerable to anemia, they are often not aware of the causes and possible adverse consequences on their health.

Strategies for Prevention and Control of Anemia

IDA control measures aim at improving iron status by focusing on creating positive iron balance that will yield significant benefits to health (Vir 1998). A varied array of interventions exists that are designed to prevent and correct iron deficiency anemia, including

- Food based approaches such as diet diversification and food fortification

- Non-food based approaches such as supplementation with medicinal iron, nutrition health education and parasitic disease control

The section below presents available literature on iron-folate supplementation as an intervention strategy for adolescent girls keeping in view the focus of the present study.

Iron Folic Acid Supplementation

Medicinal iron has an advantage of producing rapid improvement in iron status and can be targeted to specific population groups. According to Gillespie (1998), IFA supplementation is one of the most important nutritional interventions for adolescents. Nationally, as well as in Gujarat, rather than daily iron folate supplementation, once weekly IFA has been recommended for adolescent girls and is an accepted strategy in many states.

Daily vs. Intermittent (Once Weekly or Twice Weekly) Iron Folic Acid Supplementation

The desirability of intermittent iron supplementation compared with daily supplementation is increasingly being recognized. The theory behind intermittent oral supplementation is based on the concept of a "mucosal block" of iron absorption which states that mucosal enterocytes down-regulate iron absorption in response to daily exposure to a high intake of iron (Brown et al 1958).

Absorption of iron is highly regulated process. There is reduced iron absorption when the intestine is exposed continuously to high doses of iron. Recent clinical studies have shown that intermittent supplementation of iron is as beneficial as daily supplementation (Haas and Brownlie 2001). On providing supplementary iron at a similar timing as gastrointestinal cell renewal, the blocking effect of previous iron bolous can be avoided. True absorption and retention would be more efficient. It is suggested that large does of iron may be supplemented every 5^{th} day, which is the turnover cycle of the intestinal absorptive cells.

As regards impact, weekly IFA supplementation has been shown to be as effective as daily supplementation, on hemoglobin levels and growth, this is evident from studies shown in next section. The sections presented below take a glance at the available review with regard to impact on hemoglobin levels, growth, food and nutrient intake, cognition and physical work capacity.

Impact of IFA Supplementation on Anemia

Table 2.5 summarizes the results of research studies among adolescent girls and provides convincing evidence for policy makers that iron supplementation is a highly appropriate strategy to combat iron deficiency anemia in this age group. Further, these studies have highlighted the beneficial impact of IFA on hemoglobin status even with intermittent supplementation, with additional benefits like fewer side effects, less cost and greater feasibility in program situations.

While more research is needed on the comparative efficacy, program effectiveness and cost of iron supplementation given daily or intermittently, literature indicates that iron folic acid supplementation has beneficial impact on Hb levels of school going adolescent girls. Further, those with lower initial Hb levels seem to benefit more compared to their non-anemic counterparts. IFA program reviews conclude that in controlled situations such as in school settings where direct supervision is possible, intermittent IFA supplementation can effectively reduce prevalence of anemia. The review also shows that compliance with IFA may play a very important role with regard to impact of intermittent supplementation.

Schultnik (2006) reviewed the status, characteristics and impact of adolescent anemia programs initiated in 13 states of India which was a collaborative effort of the Department of Education, the Department of Women-Child Development and the Ministry of Health-Family Welfare with support from Unicef-India. Interventions

Table 2.5: Impact of Iron Folic Acid Supplementation on Hemoglobin levels

Authors / Place	Age Group	Intervention	Impact Hemoglobin change g/dl
Daily IFA Supplementation			
Kanani and Poojara 2000, India	Adolescent girls (n=203)	60mg elem Fe + 0.5mg folic acid for daily 3 months	Experimental group + 1.73 vs. - 0.08 g/dl control Increase in Hb was higher in anemic girls
Bruner et al 1996, Baltimore	Adolescent girls (n=73)	260 mg elem Fe daily or placebo for 8 weeks	Post intervention hematological measures significantly improved in E (serum ferritin 27.3 vs. 12.1 μg/L)
Lawless et al 1994, Kenya	6 – 11 yrs (n=87)	2 mg elem Fe/Kg/ Day or Placebo for 14 weeks	Hematinic status significantly improved in experimental group (Hb levels: 0.32 vs.-0.24 g/dl, Serum ferritin: 16.5 vs. 0.3 μg/L)
Pollitt et al 1989, Thailand	9 – 11 yrs (n=1358)	50 mg ferrous sulphate for 2 weeks and 100mg for 14 weeks	Hb gains were higher in anemics (E + 2.8, C + 1.4) than non-anemics (E + 0.2, C – 0.2).
Soemantri 1989, Indonesia	School children (n=130)	2 mg elem Fe/kg/day or placebo for 3 months	Significant improvement in anemic subjects hematinic status (anemics 3.29 vs. non-anemics 0.3 g/dl)
Seshadri and Gopaldas 1989, India	5 - 8 yrs (n=94)	20mg elem Fe + 0.1 FA for 60 days	Significant improvement in Hb 1.1 vs. 0.15
	8-15yrs (n=48)	60mg elem Fe for 60 days	Significant improvement in Hb 2.4 vs. 0.5 in control
Chwang et al 1988, Indonesia	8 – 13 yrs (n=119)	2 mg elem Fe / kg/ day for 12 weeks	Anemic children, Hb experimental group 3.5 g/dl vs. C -0.2 g/dl
Once Weekly IFA Supplementation			
Indian Institute of Health and Family Welfare 2002-2003, India	Adolescent girls (n=767)	Once weekly IFA for 52 weeks	Significant increment of 1 g/dl in Hb levels after intervention and reduction in prevalence of anemia. 53% consumed all tablets.
Kotecha et al 2002, Vadodara, India	Adolescent Girls (n=3000)	100 mg elem Fe + 0.5 mg Folic Acid after 1 year under	Prevalence reduced by 20% and mean Hb increased from 11.02 g/dl to 11.72 g/dl.
Roschnik and Maiga 2001, Mali	School children (n=1200)	65 mg IFA or placebo for 10 weeks	Prevalence of anemia reduced by 8% vs. increase of 10% in control. 90% compliance.
Ahmed et al 2001, Bangladesh	14 - 19 yrs (n=289)	120mg elem Fe + 3.5 mg FA or Fe + FA + VitA or placebo for 12 weeks	Hb increment E 0.91, C 0.12 g/dl Significant reduction in anemia: 92% in IFA + Vit A, followed by 85% in IFA group.

Continued…

Authors / Place	Age Group	Intervention	Impact Hemoglobin change g/dl
Tee et al 1999, Malaysian	12 – 17 yrs (n=611)	60mg (low dose)/120mg (high dose) elem Fe + 3.5 mg FA or only 5mg (control) FA for 22 weeks	Anemics low dose (2.14g/dl) vs. high dose (2.31g/dl), Borderline anemics low dose (1.14g/dl) vs. high dose (1.3g/dl), control 0.93g/dl. 96% took more than 90% tablets.
Kanani et al 1998, Vadodara, India	School girls (10 – 15 yrs) (n=729)	100mg Elem Fe + 0.5 mg Folic acid for 6 months	No significant impact on Hb levels after weekly supplementation (1.2 vs. 1.0 g/dl in control)
Katelhut et al 1996, Indonesia	Adolescent girls (n=85)	Either 60 mg Fe + 0.5 mg FA + 20,000 IU Vit A + 60 mg Vit C weekly or 60 mg Fe + 0.25 mg FA for 5 Weeks	Weekly supplementation effective in improved iron status in short period. In anemics improvement was in Hb, while in non-anemics it was serum ferritin which improved.
Daily / Twice weekly / Once weekly IFA Supplementation			
Ahmed et al 2005, Bangladesh	Adolescent school girls (14-18 years) (n=197)	Twice weekly IFA or multi micronutrients including IFA for 12 weeks to two groups	Both supplementation showed similar impact on the Hb status of the girls.
Siddiqui, Rehman and Jaleel 2004, Pakistan	School children (5 – 10 years) (n=60)	Either 200gm ferrous sulphate daily or once weekly for 2 months	There was significant rise in Hb (daily 2.4 vs. 2.02 g/dl weekly) and Hct in both groups
Jain et al 2001, India	Adolescent girls (n=243)	ICDS beneficiaries – 100mg Fe + 0.5 mg FA Daily	Negligible impact on Hb levels; poor compliance, monitoring and lack of motivation.
	School going girls 14-16 yrs (n=50)	For 8 weeks twice weekly 100mg Fe + 0.5 mg FA	Increase in Hb levels 1.42 vs. 1.19g/dl, Good compliance. Supervised supplementation
	Primary school girls 8-9 yrs (n=111)	20mg Fe + 1 mg FA with MDM program for 2 months	Increase in Hb levels (0.71 g/dl)as well as growth (weight +1.07kg) after two months. Supervised supplementation and compliance was good.
Kimiagar and Ghaffarpour 2001, Iran	Anemic adolescent girls (n=298)	50mg elem Fe for 3 months – Daily or once weekly or twice weekly	Increase in Hb: similar for all regimens and were higher than controls
Sharma, Prasad and Rao 2000, Delhi and Rajasthan India.	Adolescent girls (Delhi n=64 Rajasthan n=82)	For 6 months • daily 100 mg Fe + 0.5 mg FA or • once weekly 100 mg Fe + 0.5 mg FA, 25 mg VitC or placebo for 6 months In Rajasthan, the third group received	Daily IFA supplementation was more effective than once-weekly IFA; however with inclusion of Vit C in weekly supplementation the impact was as good as daily IFA supplementation. After 6 months overall the reduction in prevalence of anemia was similar.

continued...

Authors / Place	Age Group	Intervention	Impact Hemoglobin change g/dl
		once weekly 100 mg Fe + 0.5 mg FA, 25 mg VitC	
Tiwari and Seshadri 2000, Nepal	School going adolescent girls (10 – 18 years) (n=420)	Single dose 500 mg mebendazole + 60 mg elem iron given • deworming + daily for 3 months • deworming + weekly for 6 months • only deworming or only placebo.	Weekly IFA (0.33 g/dl) as effective as daily (0.3 g/dl) group with regard to Hb increments, however, there was no significant reduction in prevalence of anemia.
Unicef 1998, Mumbai, India	ICDS beneficiaries, Adolescent girls (10-18 years) (n=1500)	100mg elem Fe + 0.5 mg Folic Acid tablets • daily for 100 days • weekly for 25 weeks Placebo once weekly + nutrition and health education for 25 weeks.	Weekly supplementation was as effective as daily in terms of rise in Hb levels (1.54 vs. 1 g/dl). Anemics benefited more than non-anemics. However side effects were more in daily regimen.
Seshadri et al 1998, Bharuch, India.	Adolescent girls (10 – 19 years) (n=1513)	Unsupervised supplementation of 100mg elem Fe + 0.5 mg Folic Acid tablets • daily for 100 days • weekly for 6 months Placebo once weekly for 6 months + brochure on anemia.	Weekly supplementation was not as effective as daily in terms of rise in Hb levels. Weekly: 0.5 g/dl Daily: 0.3 g/dl
Angeles-Agdeppa et al 1997, Indonesia	Adolescent school girls (14 to 18 years) (n=273)	For 3 months, • Daily (60 mg Fe + 0.25 mg FA + 750 µg retinol + 60 mg VitC) • Once weekly (60 mg Fe + 0.5 mg FA + 6000 µg retinol + 60 mg VitC) • Once weekly (120 mg Fe + 0.5 mg FA + 6000 µg retinol + 60 mg VitC)	Daily and weekly groups had similar impact on Hb levels and serum ferritin (27 µg/L vs. 15µg/L) after 3 months.
Seshadri and Shankar 1996, Vadodara	Adolescent girls (10-19 years)	For 3 months 100mg elem Fe + 0.5 mg Folic Acid: daily or weekly, or placebo tablets	Among anemic girls the gains in Hb levels were similar in two intervend groups (D 1.5g/dl vs. W +1.9 g/dl).

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reviewed included school girls as well as out-of-school girls who were supplemented once weekly with 100 mg elemental Fe + 500 μg folic acid under supervision. The supplementation significantly reduced the anemia prevalence ranging from 5% in Jharkhand to 50% reduction in UP after one year. AP reported a reduction of 70% after 2 years of supplementation. Therefore, it was evident that once weekly supplementation of adolescent girls with IFA tablets led to marked decrease in prevalence of anemia. The small decrease seen in some cases may have been due to low compliance with tablet intake.

Further it is likely that a larger reduction in anemia prevalence from intermittent IFA may be achieved only after a supplementation of long duration which is required for improvement in iron status.

Impact of IFA Supplementation on Growth and Appetite

Functional benefits of iron supplementation such as impact on pubertal growth have not been adequately studied in the crucial stage of early adolescence especially weekly or twice weekly IFA. Available literature and reports are presented in **Table 2.6**.

Though iron supplementation regimens among adolescents have shown consistent impact on the iron status, there is conflicting evidence concerning the beneficial effect of iron supplementation on growth in adolescents. Some studies have shown that daily supplementation improves growth and appetite, while others have not found any beneficial growth response in this age group.

Bhandari, Bahl and Taneja (2001) reviewed studies on the effect of micronutrient supplementation (iron, vitamin A, zinc, copper and calcium) on linear growth of children and concluded that iron supplementation has significant impact on linear growth only in anemic children. The impact in non-anemic children was not very clear.

Table 2.6: Impact of Iron Folic Acid Supplementation on Growth And Appetite

Authors and Place	Age Group	Intervention	Impact on Growth
Daily IFA Supplementation			
Kanani and Poojara 2000, Vadodara	Urban Adolescent girls (n=203)	60mg elem Fe + 0.5mg folic acid for 3 months	Significant improvement in BMI in supplemented girls compared to controls (0.0 vs. -0.35 Kg/m^2)
Kanani and Singh 1999, Vadodara	9 – 12 yrs (n=296)	60 mg elem Fe + 0.5 mg Folic acid for 3 months	Significant improvement in weight (3.33 Kg vs. 1.56 Kg) and BMI as compared to controls
Chwang et al 1988, Indonesia	8 – 13 yrs (n=119)	2 mg elem Fe/Kg/day for 12 weeks	Anemic children had significantly better weight gain (0.41 Kg) than control (-1.21 Kg) after intervention.
Lawless et al 1994, Kenya	6 – 11 yrs (n=87)	2 mg elem Fe/Kg/Day or Placebo for 14 weeks	Mean change in height (1.4 vs. 1.1 cm) weight (1.6 vs. 0.7 Kg) and appetite was significantly better in iron treated group than controls.
Bhatia and Seshadri 1993, Vadodara	3 – 5 yrs (n=170)	40 mg elem Fe daily for 6 months or placebo	Anemic girls receiving iron had significantly better weight than controls (mean weight gain 1.0 vs. 0.6 Kg)
Weekly IFA Supplementation			
Kotecha et al 2002, Vadodara	Adolescent girls (n=3000)	100 mg elem Fe + 0.5 mg Folic Acid under Adolescent Girls' Anemia Reduction Program	Significant improvement in BMI after 1 year Before 17.23 After 17.74
Roschnik and Maiga 2001, Mali	School children (n=1200)	65 mg IFA of placebo for 10 weeks	There was no significant impact on growth.
Beasley et al 2000, Tanzania	Adolescent girls	400mg ferrous sulphate for 4 months or placebo	Children given iron had better weight gain (+2.4 Kg) than control (+1.4 Kg)
Kanani et al 1998, Vadodara	10 – 15 yrs (n=729)	100mg Elem Fe + 0.5 mg Folic acid for 6 months	No difference in BMI gain between supplemented (0.68 Kg/m^2) and control group (0.49 Kg/m^2) after the intervention.

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A randomized, double blind, placebo-controlled iron supplementation trial conducted in Kenya examined the effect of iron supplements given daily for three months on appetite and growth in 87 primary school children (6-11 years) receiving sustained-release ferrous sulfate (150 mg) or placebo tablets. Appetite was measured using a culturally appropriate food which the children consumed ad libitum as a snack during mid morning. Iron supplements resulted in improved growth and appetite as compared with children receiving placebo capsules (Lawless et al 1994). It is plausible that the provision of iron tablets to anemic children improved appetite, which in turn improved growth. Further research into the underlying physiology mechanisms may shed more light on the relationship between iron nutritional status and appetite.

A study done by Kanani and Poojara (2000) on adolescent unmarried girls of Vadodara revealed that daily iron folic acid supplementation (60 mg elemental iron and 0.5 mg folic acid) significantly improved hemoglobin levels, weight and appetite. However, Kanani et al (1998) did not find any consistent differences between those receiving weekly IFA doses (100 mg elemental iron and 0.5 mg folic acid) and placebo with regard to appetite scores and dietary intake.

Impact of Iron Supplementation on Cognition and Physical Work Capacity

Most studies have found associations between iron-deficiency anemia and poor cognitive, motor development and behavioral problems. Longitudinal studies consistently indicate that children anemic in infancy continue to have poorer cognition, school achievement, and more behavior problems into middle childhood.

As reported in preschool children and adults, in the adolescent period also, anemia may compromise cognition and PWC. In India, to combat the pervasive problem of anemia, initiation of iron supplementation early in the adolescent years has been recommended to benefit adolescents. However, research among adolescents has primarily focused on the impact of IFA supplements on hematinic status. **Table 2.7** gives a review of the literature with regard to impact of iron supplementation on cognition and PWC. As literature reporting impact of IFA on young school going adolescents is scanty, preschool children have also been included in the table.

A majority of the research studies on the impact of IFA on work capacity and cognition, have given a daily dose of IFA supplement for maximum of three months, irrespective of the age group studied. The table clearly shows that daily iron supplementation showed a significant improvement in terms of improved cognitive abilities and work capacity.

Among adult women, supplementation with iron daily showed a significant 5-7-fold improvement in cognitive performance with regard to improvement in short term memory and attention span. Improvement in physical work capacity was reported in terms of decreased heart rate and energy expenditure for a given task, improved productivity efficiency and increased earnings.

Among adolescent girls, iron supplementation given daily significantly improved cognition and work capacity. Girls reported improved attention, concentration and school achievement scores after iron supplementation. Very few studies have been done with regard to effect on PWC among adolescents and school children, and these reported benefits in terms of improved efficiency and work capacity.

In Vadodara, India, a positive impact of iron folate supplementation on physical work capacity and cognitive abilities of school children was seen in a pilot study (Kanani, Singh and Zutshi 1999). On supplementing girls (9 – 15 yrs) with 60 mg elemental Fe + 0.5 mg folic acid for 3 months, there was a significant increase in the number of skips done by the girls using a skipping rope; and also in selected cognitive tests, compared to the baseline values. Similarly cognition and motor development were significantly better among preschoolers who were supplemented with iron compared to the placebo groups (Bhatia and Seshadri 1993).

Table 2.7: Impact of Daily Iron Folic Acid Supplementation on Cognition And Physical Work Capacity

Authors and Place	Age Group	Intervention	Impact on PWC and Cognitive Abilities
Adult Women			
Murray-Kolb and Beard 2007	18-35 year old women (n=149)	60 mg elemental iron or placebo daily for 16 weeks	A significant improvement in serum ferritin was associated with a 5-7-fold improvement in cognitive performance
Groner et al 1986, Baltimore	14 – 24 yrs (≤ 16 weeks pregnant women (n=25)	For 1 month • 60 mg elem Fe + vitamins • only vitamins alone	A beneficial effect of iron was seen on short term memory and attention span. (Digit Symbol: experimental group +1.3 vs. control +0.3 points)
Li et al 1994, China	Iron deficient female workers (n=80)	For 12 weeks • 60mg ferrous sulphate/day • 120mg ferrous sulphate/day • placebo	Mean heart rate at work decreased from 95.5 to 91.1 beats/min and productivity efficiency increased in iron treated group.
Edgerton et al. (1979), Srilanka	20–60 years old female tea estate workers (n=199)	200 mg $FeSO_4$ for 1 month	Tea picked increased by 1.2% Voluntary activity higher in iron supplemented group than placebo group
Dodd, Sheela and Sharma 1992, Bombay, India	Women (non-pregnant and non-lactating) (n=250)	Elemental iron (25 mg or 35 mg or 50 mg or 55 mg (time release dose) or 115 mg for 14 weeks	Increase in the number of steps taken, decrease in post exercise pulse rate and recovery time in all the treated groups.
Das and Kalita 2003, Assam, India	Adult coal-mine workers	60mg or 120 mg ferrous sulphate for 6 months	Significant improvement in coal cutting performance and money earning capacity of the workers. The number of days worked improved from 18 days to 24 days in group 1 and from 20 days to 25 days in group 2.
School Children and Adolescent Girls			
Buzina-Suboticanec et al 1998, Croatia	School children (8-10 years) (n=60)	100 mg iron for 10 weeks or placebo tablets.	Iron supplementation improved scores in all the tests. Impact was more marked among initially anemics.
Bruner et al 1996, Baltimore	Adolescent girls (13 to 18 years) (n=716)	260 mg elem Fe daily or placebo for 8 weeks	Treatment group girls showed better improvement in concentration (25.8%) and memory (21.2%) than control

continued...

Authors and Place	Age Group	Intervention	Impact on PWC and Cognitive Abilities
Kanani and Singh 1999, Vadodara	9 – 12 yrs (n=296)	60 mg elem Fe + 0.5 mg Folic acid for 3 months	Increase in number of skips done by the girls receiving IFA and they performed better in cognition and memory test compared to control
Soemantri 1989, Indonesia	School children (n=130)	2 mg elem Fe/kg/day or placebo daily for 3 months	In anemics, improvement in learning achievement scores after supplementation (Math scores: before 56.3, after 65.7)
Pollitt et al 1989, Thailand	9 – 11 yrs (n=1358)	50 mg ferrous sulphate for 2 weeks and 100mg for 14 weeks	Maths scores higher in anemics receiving IFA (48% correct) than controls (44% correct)
Seshadri and Gopaldas 1989, Vadodara	5 - 8 yrs (n=94)	20mg elem Fe + 0.1 FA for 60 days	WISC test Scores, higher in IFA group (+11) than control (no change)
	8-15 yrs (n=48)	60mg elem Fe for 60 days	Mazes: higher in IFA group (+3.19) than control (+1.81)
Soemantri, Pollitt and Kim 1985, Indonesia	Anemic Primary school children (n=109)	10mg ferrous sulphate/kg or placebo for 3 months	Increase in concentration test (CT) and achievement test (AT) higher in iron group than control (CT: +20.5 vs. -38.6, AT: +3.64 vs. -0.67)
Pollitt et al 1985, Egypt	Primary school children (n=68)	50mg ferrous sulphate or placebo (2 mg elemental iron) for 4 months.	No significant effect on mean change after supplementation in Continuous Performance Test and Picture Vocabulary Test. However, efficiency score of iron treated anemic group became similar to that of non-anemics.
Agarwal et al 1987, Varanasi, India	School children (6-8 years	Ferrous gluconate 200 mg daily for one year	The mean scores for recovery period were better for the iron group than controls in AAPHER subtest. Cognitive function tests such as object assembly and digit span showed significant improvement in iron group
Preschool Children			
Soewonda, Husaini and Pollitt 1989, Indonesia	Preschool children (n=173)	50mg elem Fe in 10 ml syrup for 8 weeks or placebo.	Alterations produced by IDA related to visual attention and concept acquisition reversed by iron treatment
Aukett, Parks, Scott and Wharton 1986	17-19 months (n=97)	Iron and vitamin C or vitamin C only (control group) for two months	Higher percentage of children acquired more number of skills in treatment group with >2g/dl Hb gain than in non-treated group or those who gained less Hb.
Harahap et al 2000, Indonesia	12 – 18 months (n=36)	A high energy supplement + 12 mg iron or 104 KJ + 0 iron for 6 months	After intervention intervened anemics became more active and had better motor development and greater physical activity than controls.

Further, the reviewed literature also shows that there is a more marked benefit among the anemic children compared to non-anemic counterparts. This suggests that mental abilities like attention, memory, and concentration, may improve with iron supplementation, in turn improving scholastic performance of the children.

However, there is inadequate information on impact of intermittent IFA especially among young adolescents entering the pubertal growth spurt on cognition and physical work capacity.

Two studies with intermittent (once and twice weekly) iron supplementation given to women showed significant benefits in terms of increase in work capacity and improved cognitive test scores in India and Nepal. Gopaldas and Gujral (2003) supplemented 60 mg elemental iron (twice weekly) + 1600 IU vitamin A (once weekly) + use of iodized salt (30 ppm) for nine months to women tea pickers (n=339) of South India. Average tea picked per woman increased significantly. There was a decrease in the number of moderate pickers and an increase in good pickers. Income (daily wages) also increased.

In Nepal, school children received deworming pills (500 mg mebendazole) followed by 60 mg elemental iron or placebo once a week for 6 months (Tiwari and Seshadri 2000). Higher improvement in Maze test scores was observed in iron treated group vs. controls.

Summing up this section, overall the review on iron supplementation highlights the following points.

- Daily iron folic acid supplementation has shown positive impact on hematinic status, growth (BMI) as well as cognition and physical work capacity. However, daily supplementation has its limitations in terms of feasibility and cost as discussed earlier, pointing out to the need of assessing impact of intermittent IFA.

- Children and adults receiving intermittent iron supplementation in several studies reviewed achieved significant benefits with regard to hemoglobin and in some studies on growth, which was similar to benefit experienced by daily supplemented group.
- Anemic and non-anemic iron deficient girls both benefit from weekly supplements with anemics showing greater benefits.
- Intermittent doses reduce side effects and increase compliance. Weekly supplementation is also a cost effective strategy, as the cost reduces to one-seventh, and is also feasible to administer in field settings.

Close Supervision

Beaton and McCabe (1999) in their review supported by the Micronutrient Initiative, concluded that though both daily and weekly iron supplementation are efficacious for reducing anemia under favourable conditions, weekly supplementation should be introduced only when there is evidence that compliance will be high (e.g. under supervised administration) as in schools.

Other Benefits

Though weekly supplementation has shown impact on hemoglobin levels, a few studies did not show significant impact on the growth (BMI) variable. An impact evaluation of the Adolescent Girls' Anemia Control Program (Kotecha et al 2002) also reported that growth benefits were not as marked as hemoglobin changes after a year of weekly IFA supplementation.

The impact of intermittent supplementation with regard to cognition and physical work capacity needs to be further investigated.

It is worthwhile to explore if twice weekly supplementation over a longer period (at least one year) shows a significant impact on linear growth, BMI, physical work capacity and cognitive functions.

Need For Addressing Anemia at a Younger Age

The period of early adolescence corresponds with the adolescent growth spurt and the highest iron needs. In addition, younger adolescents are easier to reach than the older ones because of higher enrolment rates in primary schools. There has been a steady increase in the school enrolment rates of girls in India (Unicef 1993). Therefore, the school network offers an excellent opportunity to reach "captive" adolescent children. These girls could be motivated to take responsibility of reaching "non-school going" girls.

There are other factors favouring the initiation of IFA supplementation in primary school:

- Weekly supplements, while bringing down anemia in older adolescents, may not be adequate to cause a substantial decrease, in view of the high prevalence already existing in this group. Thus final prevalence may continue to remain unsatisfactory, according to a Micronutrient Initiative review by Beaton and McCabe (1999). Hence, if supplementation is started early in primary school years, then residual anemia, which remains in adolescents in secondary schools receiving weekly supplements, can be better addressed.
- Iron may enhance adolescent pubertal growth and thus can be a more feasible and less expensive proxy for food supplements. Eighty percent of the adolescent growth is completed by 15 years of age (Srikantia 1989). IFA supplementation in early adolescence will help prevent growth retardation, and also achievement of growth potential in the critical period of pubertal growth spurt, which occurs between 11-13 years in girls.
- IFA may improve school performance. IFA supplementation to school children in early adolescence would also improve school performance, physical work capacity and cognitive functions and thereby their quality of school life. According to Draper (1997), "iron supplementation has resulted in significant improvement in school measurements of verbal and other measurable skills among primary school children and adolescents". This will especially help reduce school dropouts among girls.

In brief, then, the justification of the present study can be stated as follows:

- Iron deficiency in adolescence has been primarily studied for its detrimental effect on hematinic status. However, anemia in early adolescence may compromise pubertal growth spurt, physical work capacity and cognitive function, about which little is known. This in turn may adversely affect learning and scholastic performance of the schoolgirls entering adolescence.
- Literature reports impact of once weekly IFA supplementation on hemoglobin levels and anemia reduction, but little is known of other functional benefits of weekly dosing on growth (especially pubertal growth in pre-menarcheal stage), cognition and physical work capacity.
- The relative impact of daily, once weekly and twice-weekly IFA supplementation on Hb levels, BMI and PWC/ cognition indicators needs to be studied. Given the fact that enrolment of girls is high in government primary schools compared to secondary schools, it is worthwhile to test the feasibility and compliance of intermittent IFA supplementation in a primary school setting.

The next chapter details the objectives and methodology of the present research.