REVIEW ARTICLE

PUBLIC HEALTH SIGNIFICANCE OF IRON DEFICIENCY ANAEMIA

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INTRODUCTION

Anaemia is a condition that results in a lowering of haemoglobin levels (Hb) below that is considered to be normal for specific demographic groups [1]. In clinical terms anaemia is an insufficient mass of red blood cells circulating in the blood; whereas in public health terms anaemia is defined as a low haemoglobin concentration in blood, or less often, as a low haematocrit, the percentage of blood volume that consists of red blood cells [2]. The limits which define anaemia (table-1 & 2) [3]. Nutritional anaemias are caused when there is an inadequate body store of a specific nutrient needed for Hb synthesis. The most common nutrient deficiency is iron [4]. Iron plays an important role in the production of haemoglobin. Deficiency of iron result due to deficient-diet, decreased absorption, increased requirement in pregnancy and lactation, blood loss due to blood donation, menstruation & gastrointestinal reason, haemoglobinurea and pulmonary haemosiderosios [5]. Iron deficiency is defined as a condition in which there are no mobilizable iron stores and in which signs of a compromised supply of iron to tissues, including the erythron, are noted (3). Iron deficiency is ranked at the top of three global "hidden hungers" (Iron, Iodine and Vit A: sub clinical deficiency without visible signs of deficiency) with about one fifth of the world's population is suffering from iron deficiency anaemia. [6]. Iron deficiency in its most severe form results in anaemia–IDA and since haemoglobin concentration is relatively easy to determine, the prevalence of anaemia has often been used as proxy of Iron Deficiency Anaemia (IDA) [7]. When individual haemoglobin levels are below two standard deviations (-2SD / 5th percentile) of the distribution mean for haemoglobin in an otherwise normal population of the same gender and age who are living at the same altitude, iron deficiency anaemia is considered to be present. In a normal population, 2.5% of the population would be expected to be below this threshold. Hence, iron deficiency anaemia would be considered a public health problem only when the prevalence of haemoglobin concentration exceeds 5.0% of the population. A consultation group of WHO / UNICEF / UNU on iron deficiency anaemia purposed additional epidemiological criteria for assessing the severity and magnitude of nutritional anaemia in the population (table-3) [3]. The WHO has also laid down the classification of countries with respect to the level of public health significance of anaemia: a prevalence of 15% is low, 15-40% is medium and >40% is high [4]. IDA prevalence studies are recommended to be based on a statistically selected random sample of the whole population but when this is not feasible the prevalence in high-risk groups provides a valid indication of the magnitude of the problem [8]. For every case of iron deficiency anaemia found in a population, there are thought to be at least two cases of iron deficiency [9].

Clinically the iron deficiency anaemia present with easy fatigability, tachycardia, palpitation and tachypnea on exertion. Severe deficiency causes skin and mucosal changes, including a smooth tongue, brittle nails, and cheiolsis. Many iron deficiency anaemia patients develop Pica, craving for specific

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foods (ice chips, lettuce, etc) often not rich in iron [5].

EPIDEMIOLOGY

Age:

Iron deficiency commonly develops after six months of age if complementary foods do not provide sufficient absorbable iron, even for exclusively breastfed infants [10]. Among infants from six months onwards, a high prevalence of anaemia is reported, with iron deficiency anaemia being the single most important cause [11,12]. Iron deficiency is most common in the preschool years and during puberty and in old age [3].

Gender:

Iron deficiencies occur in adults of both sexes. The high prevalence of anaemia among adolescents has been attributed to increase needs for iron due to rapid growth and menarche. The prevalence of anaemia, declined sharply in boys after the age of 16 years coinciding with the end of a growth spurt while the prevalence of anaemia among girls started to rise after the age of 18 years as they proceeded to marriage and child bearing (13,14). Women with anaemia are reported to have high fetal mortality [13] and deliver babies with lower birth weight, and low Hb and serum ferritin levels as compared to non-anaemic women in different gestational age groups [11,15]. Pregnant women are the highest risk group, as the gap between the requirement for iron and intake during pregnancy cannot be filled by diet alone [1,3].

Physiological State:

Normally in whole pregnancy there is an increased need of about 700-850 mg of body iron while lactation results in loss of iron via breast milk. However, lactation amenorrhea compensates for this [3].

Birth Order:

Among preschool children, the magnitude of anaemia is reported to be associated with birth order thereby indicating a gradual depletion of the iron stores of mothers after repeated pregnancies [16,17].

Pathological State:

Certain infections, like malaria, hookworm, trichuriasis, amoebiasis, and schistosomiasis (both vesical and intestinal forms), cause blood loss directly which contributes to iron deficiency. Certain genetic factors, e.g. thalassemia, sickle cell trait, and glucose-6-phosphate dehydrogenase deficiency (G6PD) also cause iron deficiency [3].

Dietary Pattern:

Iron is obtained in the form of non-haem iron from vegetable and as haem iron from meat. A small amount of haem iron in the diet can improve absorption of non–haem iron [18-20]. The best sources of dietary iron are meat, fish and poultry but their intakes remain low due to multiple reasons.

Family Size:

Prevalence of anaemia remains high in large families [21].

Literacy Level:

Literacy level particularly of mothers has got direct effect on the prevalence of anaemia in preschool children [16,17]..

Cultural and Religious Factors:

Iron rich diet is avoided for various cultural and religious reasons. With much of the world population eating a predominantly vegetarian diet, only slight increase in physiological iron requirements or pathological blood loss (e.g. related to hook worm infestation) may lead to a failure to maintain iron balance and the development of progressive iron depletion [22].

Socioeconomi Status:

Iron deficiency is most common among groups of low socioeconomic status [3,16,17]

Environmental Factors:

A given diet may be low in iron or may contain adequate amounts of iron, which are of low bioavailability. Other nutrients necessary for haematopoiesis may also be deficient. These include folic acid, vitamins A, B12 and C, protein, and copper and other

minerals (23). Trauma or childbirth can result in acute or chronic blood loss, with consequent iron deficiency and anaemia

Information on Bioavailability of Iron:

This has got direct effect on the prevalence of IDA. Bioavailability of food iron is strongly influenced by enhancer and inhibitors in the diet. Enhancer of iron absorption includes haem iron, present in meat, poultry, fish and seafood, ascorbic acid, some fermented or germinated food and condiments like sauerkraut and soy sauce. Inhibitors are phytates, present in cereal bran, cereal grains, high extraction flour, legumes, nuts and seeds, food with high inositol content, iron binding phenolic compounds (tannins) present in tea, coffee etc, calcium particularly from milk and milk products. The bio availability of non haem iron can be increased by taking food rich in Vit C. Avoiding of tea with meals will also increase the uptake of iron from the gut [24,25]. The effect of ascorbic acid on nonhaem iron absorption has been shown to be dose related but even as small an amount as 25 mg can bring about a two fold rise in non haem iron absorption [26].

AGE AND GENDER IRON REQUIREMENT

Iron is stored in the reticulo-endothelial system as ferritin and haemosiderin (20) At certain periods in life; iron requirements are particularly high, and therefore less likely to be met. Iron requirements are highest for pregnant women; 1.9 mg/1000Kcal of dietary energy in the second trimester and 2.7 in the third .The figures for other groups are; infants, 1.0; adolescent girls, 0.8; adolescent boys 0.6; non pregnant women, 0.6; preschool and school children, 0.4 and adult men, 0.3 [25].

The criteria for determining the presence of iron deficiency anaemia (table-4) [19].

Detection of Iron Deficiency Anaemia:

Worldwide, the most common method of screening individual or populations for iron deficiency involves the determining of the prevalence of anaemia by measuring blood Hb or Haematocrit. Anaemia is not a specific indication of iron deficiency. Other nutrient deficiency and most infectious diseases can also result in significant anaemia. Assessment can be made whether or not anaemia is due to the iron deficiency involves monitoring the response in Hb or Haematocrit level after 1 or 2 months of oral supplementation with iron. An increase of 10 g/l in Hb or 3 % in haematocrit is indicative of iron deficiency. [27]. In addition to Hb/Haematocrit estimation following specific lab tests are used to determine iron status [3].

a. **Serum Ferritin**:

   This is best indicator in the absence of infection but of limited usefulness during pregnancy because it diminishes late in pregnancy, even when bone marrow iron is present.

b. **Erythrocyte Protoporphyrin**:

   Levels of erythrocyte protoporphyrin, the precursor of haem, become elevated when the iron supply is inadequate for haem production, its elevated level correlates well with low serum ferritin, and can serve to screen for moderate iron deficiency without anaemia [28].

c. **Serum Iron, Transferrin, and Transferrin Saturation:**

   Iron deficiency results in a reduction in serum iron (SI) levels, an elevation in transferrin (total iron-binding capacity [TIBC] levels, and hence a net reduction in transferrin saturation (i.e. SI/TIBC).

d. **Serum Transferrin Receptors**:

   It is a new test but epidemiological studies have yielded limited information concerning its usefulness, however it is not significantly affected by infection or inflammatory processes, and it does not vary with age, gender, or pregnancy [29,30] but it may be elevated when there is increased red cell production,

turnover, or both, such as in the case of haemolytic anaemia [31].

e. Red Cell Indices:

Mean corpuscular volume (MCV) and Mean corpuscular haemoglobin (MCH) are the two most sensitive indices of iron deficiency.

f. Bone Marrow Iron Stain:

It is not useful in simple population-based surveys.

PROBLEM STATEMENT

Global Situation:

Anaemia is one of a wide spread public health problem in the world. WHO estimates the number of anaemia, people worldwide to be a staggering 3.5 billion in the developing countries [32] and that approximately 50% of all anaemia can be attributed to iron deficiency [33]. The global distribution of the disease burden of Iron deficiency anaemia is heavily concentrated in Africa and WHO regional Southeast Asia-D. These regions bear 71% of the global mortality burden and 65 % of the disability-adjusted life years lost [34]. Although estimates of the prevalence of anaemia vary. Widely and accurate data are often lacking, it can be assumed that significant proportions of younger children and women of the child bearing age are anaemic [35,36]. It is the only nutrient deficiency that is also significantly prevalent in the industrialized countries. Perusal of WHO global database on Anaemia depicts that the most affected groups are pregnant women (48%) and 5-14 year old children (46%). Preschool children (39%) are also a high- risk group. Predictably, the prevalence of anaemia in developing countries is three to four times higher than in industrialized countries. The most highly affected population groups in developing countries are pregnant women (56%), school age children (53%), non-pregnant women (44%), and preschool children (42%). But another group demands attention as well: older children, half of whom are anaemic (51%). In industrialized countries, the most affected groups are pregnant women (18%) and preschool children (17%), followed by nonpregnant women and older adults, both at 12%. The prevalence is low for adult males (5%). Prevalence of anaemia by age group in industrialized and developing countries (fig. 1). WHO regional picture for anaemia prevalence in preschool children and pregnant women (fig. 2 & 3) respectively [36]. Asia has the highest prevalence of anaemia in

Table-1: Haemoglobin& haematocrit, the levels below which anaemia is present in a population.

Age or gender Group	Haemoglobin g/l	Haematocrit Mmol/l
Children 6 months to 59 months	110	6.83
Children 5 Years to 11 Years	115	7.13
Children 12 Years to 14 Years	120	7.45
Non Pregnant Women above 15 years of age	120	7.45
Pregnant Women	110	6.83
Man (Above 15 years of age)	130	8.07

Source [3]

Table-2: Normal increases of haemoglobin and haematocrit values related to long-term altitude exposure.

Altitude (metres)	Increase in Haemoglobin (g/l)	Increase in Haematocrit (l/l)
<1000	0	0
1000	+ 2	+0.005
1500	+ 5	+0.015
2000	+ 8	+0.025
2500	+13	+0.040
3000	+19	+0.060
3500	+27	+0.085
4000	+35	+0.110
4500	+45	+ 0.140

Source [3]

Table-3: Classification of public health significance of anaemia.

Category of public health significance	Prevalence of anaemia (%)
Severe	> or = 40
Moderate	20.0 – 39.9
Mild	5.0 – 19.9
Normal	< Or = 4.9

Source [3] (Based on cut-off levels of haemoglobin and Haematocrit given in Table-1)

the world. About half of all anaemic women live in the Indian subcontinent where 88% of them develop anaemia during pregnancy. Vast number of infants and children are also affected. [3, 4].

Pakistan:

Pakistan is placed in mortality stratum group –D of the EMRO WHO with high child and adult mortality [37]. The population comprised the most vulnerable, the poorest and the least educated group of people who are disproportionately affected by iron deficiency. Iron deficiency is most prevalent among older adolescent girls, lower socio-economic groups and pregnant teenagers [24]. Recent statistics shows a prevalence of around 45% of Iron deficiency anaemia in Pakistan realizing failure of public health measures to control it [38]. The prevalence rate of anaemia in different age group as compiled by the nutrition unit of EMRO WHO (table-5) [39]. It has been found that overall ,more than one fifth of women in Pakistan suffer from anaemia (40).At state level there is general awareness regarding this persisting health problem in the country as evident by several regional surveys. In the early 1980s the planning commission of Pakistan reported the incidence of anaemia (Hb < 10 mg%) to be 39% in adolescent girls and 20 % in the adolescent boys; of these 80-85% was iron deficiency anaemia [24]. To assess the national nutritional situation in the country and to assess macro and micro nutritional status; surveys are conducted at national level. Perusal of the record from 1965 to 2002 in Pakistan (fig. 4) shows a downward trend in anaemia in pregnant and lactating women (Hb <11 gm/dl) and an upward trend in prevalence of moderate and severe anaemia among < 5 years (fig. 5) [41]. Karim at al [42] found 32.7% prevalence of anaemia in pregnant women (Hb < 10 g /dl). Prevalence of anaemia in preschool children in Pakistan as reported by national nutritional survey 1988 [43] was 65% (Hb <11 g /dl), Hamdani and Hashmi 1987 [44] found 47% (Hb <11.5 g / dl) and Jhaver and Baig 1994 [45] found 78% (Hb <11g/dl). Two different

Table-4: Iron status in iron deficiency anaemia.

Specific Tests	Normal	Iron Deficiency Anaemia
Serum Ferritin µg/l	15-3000	< 10
Serum TIBC (µ mol/l)	45-70	>75
Serum Iron (µ mol/l)	10-30	< 7
Saturation of TIBC (%)	16-60	< 10
Serum Transferin receptor (mg/l)	2.8-8.5	>8.5
Marrow Sideroblasts (%)	30-50	< 10
Red Cell Protoporphyrin (µ mol/l)/mol Hb	< 80	> 80
Hb (g/dl)	>13 Male >12 Female	<13 Male <12 Female
Mean Red Cell Volume (MCV) (F1)	80-92	<80
Mean Red Cell Hb, MCH (PG)	27-32	<27
Morphology Red Cell	Normal	Microcytic/ Hypochromic

Source [2]

Table-5: Estimated percentages of anaemia prevalence (1990-95) Based on blood haemoglobin concentration.

Percentage of total affected population in:		
	Industrialized Countries	Non-industrialized Countries
Children (0-4 yrs)	20.1	39.0
Children (5-14 yrs)	5.9	48.1
Pregnant women	22.7	52.0
All women (15-59 yrs)	10.3	42.3
Men (15-59 yrs)	4.3	30.0
Elderly (+60 yrs)	12.0	45.2

prevalence studies, in semi urban areas of Peshawar [46] found 69% prevalence (Hb <11 g/dl) of anaemia in children under two years, and in urban slums of Karachi [47] detected 61 %(Hb <11 g/dl) of anaemia in children aged 6- 60 months .A recent study [48] at Abbottabad detected 68 % anaemia prevalence. Females were more affected and age group 21-60 years with two peaks, one in 21-30 years and other in 41-50 years were involved.

Consequences of Anaemia: Cognitive Development:

Iron deficiency anaemia delays the psychomotor development and impair

cognitive performance of infants in various countries like India and USA [49-51]. Various studies revealed that children having moderate anaemia shows low IQ and other cognitive performance upon entry in school [52-54].

Resistance to Infection:

Morbidity from infectious disease is increased in iron deficient population [55-59] because of the adverse effects of iron deficiency on the immune system [60-63].

Work Capacity & Productivity:

A linear relationship has been reported between iron deficiency and work capacity for agricultural workers in Colombia [64] and other countries.

Pregnancy:

Iron deficiency in childbearing women increases maternal mortality. [65], prenatal and perinatal infant loss, and prematurity [66,67].

Growth:

Supplementary Iron improves the growth in iron deficient children [68].

Endocrine and Neurotransmitters:

Iron deficiency causes impaired temperature response to a cold environment. In both experimental animals and human subjects, those with iron deficiency anaemia more readily become hypothermic and have a depressed thyroid function [69-73].

Heavy Metal Absorption:

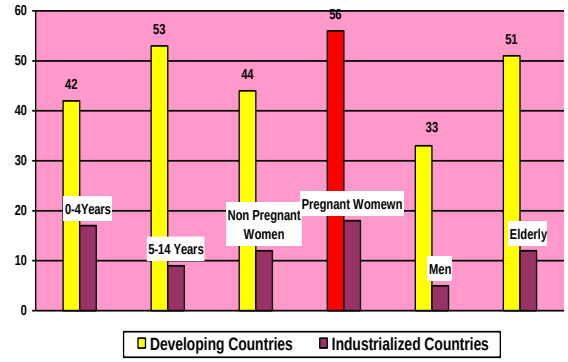
An important consequence of iron deficiency is an apparent increased risk of heavy metal poisoning in children. Iron-deficient individuals have an increased absorption capacity that is not specific to iron. Absorption of other divalent heavy metals, including toxic metals such as lead and cadmium, is also increased [74].

Post Operative Surgical Patients:

High prevalence of anaemia in surgical patients may increase the risk of postoperative morbidity and mortality [75].

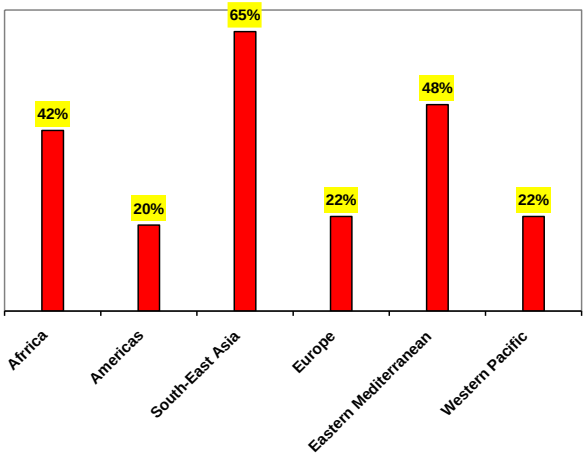
Table-6: Dosage schedules for iron supplementation to prevent iron deficiency anaemia

Specific Indication (Anaemia Prevalence >40%)
Children (6-59 months) Iron: 2mg/Kg body weight/day up to 30 mg for 3 months
School age Children (Above 60 months) Iron: 30mg/day Folic Acid 250µg/day for 3 months
Women of Child bearing age Iron: 60mg/day Folic Acid 400µg/day for 3 months
Lactating mothers Iron: 30mg/day Folic Acid 400µg/day for 3 months
Universal Supplementation
Low Birth Weight Infants (2-23 months) : Iron :2mg/Kg body weight/day
Pregnant Women: Iron: 60mg/day Folic Acid: 400µg/day



Source [32]

Fig. 1: Prevalence of anaemia by age group in industrialized & developing countries, 1998.



Source: [32]

Fig. 2: Prevalence of anaemia in children 0-5 years by who region 1998.

Economic Implications of Iron Deficiency:

Micronutrients deficiencies, rob many countries of about 5% of their GDP through

death and disability. Yet, micronutrient malnutrition could be effectively addressed for as little as 0.3% of the GDP [76]. The World Bank, WHO and Harvard University have described iron deficiency as having a higher overall cost than any other disease except tuberculosis [28].

Prevention Strategies:

Broadly the approaches for the control of anaemia are of two types.

(1) To increase the intake of absorbable iron:

a. Food Fortification:

It refers to the addition of iron to foods over and above what is naturally present in them. It is a long-term cost effective and sustainable means of improving the iron status of the population. The food vehicles commonly used are cereal flour, infant cereal, infant milk formulas, instant noodles, fish sauce, curry powder, cookies, sugar and salt [77-79] while iron fortificants used are ferrous sulphate, chiefly for fortifying bread and bakery products stored for short time [80], ferric orthophosphate with sodium acid sulphate for fortifying salt [79] and iron EDTA for sugar, fish sauce and curry powder [81,82]. A promising recent innovation is the development of and introductory use of a variety of "in –home fortificants". These range from small packets of microencapsulated micronutrients that can be sprinkled on any complementary food to crushable multimicronutrient tablets and spreads containing micronutrients [83]. Among these, the sprinkles developed at sick kids hospital in Toronto Canada is now being used in several countries for infants and young children, and as part of the emergency relief effort in Indonesia following the December 2004 tsunami [84].

b. Increasing the bioavailability of iron in the diet:

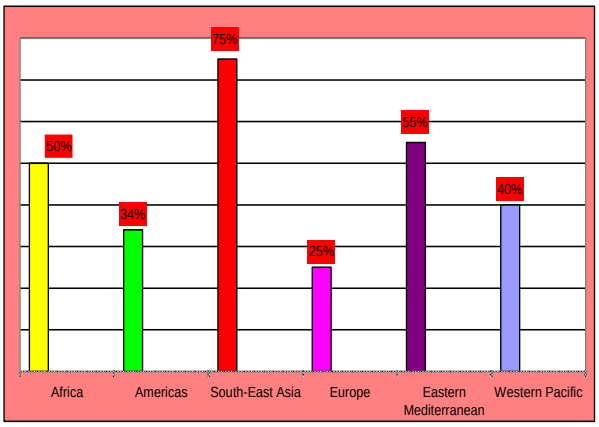


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Fig. 3: Prevalence of anaemia in pregnant women by who region 1998.

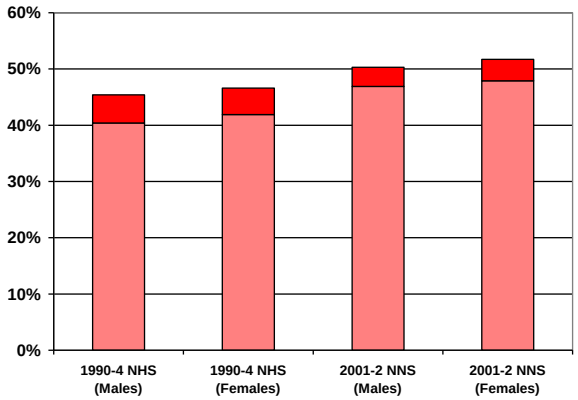

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Fig. 4: Prevalence of Moderate & Severe Anaemia in Pakistan.

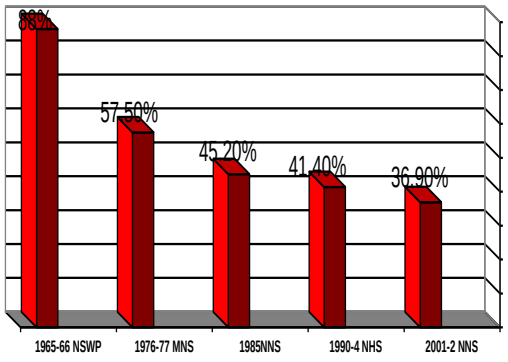

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Fig. 5: Prevalence of anaemia in pregnant & lactating women (Hb <11 Gm/Dl) in Pakistan.

Promoting enhancer of iron absorption and restricting inhibitors in the diet can achieve this aim.

c. Iron Supplementation:

It refers to providing iron through medical supplementation. It is

targeted to the high-risk groups of population namely pregnant women, infants and women of reproductive age. The highest risk group most in need of supplementation is pregnant women. [3] Dosage and schedule for different risk groups (table-6) [3] It carries with its serious logistic, cost, and compliance problems and recently, concern about its safety for iron-replete children in areas where malaria is endemic [84].

(2) For this approach various public health measures are used. Although they have an impact on iron deficiency, but they alone cannot control iron deficiency and thus give incremental benefits in combination with other intervention measures. They are:-

a. **Promotion of Breast-feeding:**

Iron in breast milk is highly bio-available and even in low quantity protects the child from infection.

b. **Deworming Programmes:**

These programme have significant impact on haemoglobin levels, with extensive reduction of blood loss but it should be combined with supplementation or fortification and be performed two or three times per year using a low cost anti parasitic agent.

c. **Family Planning Programmes:**

These include child spacing and improvement of the nutritional status of women.

d. **Others:**

Various other public health measures that decrease the frequency of infections. e.g. sanitation, immunization, controls of diarrhoeal diseases, are also important [85].

CONCLUSION

Iron deficiency anaemia affects a quarter of the world's population and is wide spread in most developing countries population where invisible yet ubiquitous, the true toll of iron deficiency and anaemia lies hidden in the statistics of overall death rates, maternal hemorrhage, reduced school performance and lowered productivity. It has serious effects on immunity, morbidity from infectious, physical work capacity, and cognition. The development potential of individuals, societies and national economies. This need not be so. We not only know the causes; we also have solutions that are both inexpensive and effective. Iron deficiency and anaemia have close links therefore there is a need to tackle these simultaneously using a multifactorial and multisectorial approach. It should also be tailored to local conditions and take into account anaemias specific etiology and the population groups affected.

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