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Iron Supplementation Protocols for Iron Deficiency Anemia: A Comparative Review of Iron Regimens in Three Countries of India, Iran and England

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ABSTRACT

Background & aim: Iron deficiency anemia is the most common micronutrient deficiency in the world today. It affects the lives of millions of women and children through contributing to poor cognitive development, increased maternal mortality and decreased work capacity. Because of the important role of Iron in the physical and cognitive health, and for the universal consideration of eradication of this problem, this review aimed to compare iron supplementary programs in three countries if India, Iran and England.
Methods The design was a comparative review of iron supplementary programs in three countries of India, Iran and England. These countries were selected for review, as they represent the spread of iron deficiency anemia in three different level of low, medium and high. Relevant data were retrieved from databases including PubMed as well as WHO, World Bank Ranking and BMJ Center reports and then were included in comparative tables to provide the basis for detecting similarities and differences.
Results: The included countries in this review were different in terms of preventive and treatment strategies to overcome iron deficiency. The reason for this difference was due to health conditions, and availability of healthy drinking water, and also prevalence of various diseases like anemia, parasitic diseases, and malaria. In Iran and India the preventive programs are confined to all groups at risk, however, in England it just encompasses the immigrants and the people who are supported by the government.
Conclusion: This review showed that in low income countries, the most economic and cost-effective practice is enriching the nutritionals. Additionally, the treatment and preventive programs and policies for anemia in different countries are related to health conditions and health indicators of that country

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Introduction

Iron deficiency is the most prevalent micronutrient insufficiency in the world today (1). This disorder is one of the most important factors leading to higher mortality rates in developing countries. Due to its high prevalence, iron deficiency anemia is one of the problems threatening the health of the people (2, 3). Anemia is the second cause of mortality and morbidity and leads to the death of one million people a year.

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Three quarters of deaths in Africa and South Asia, and 2.4% of disability-adjusted life years (DALY) have been associated with anemia (3).

According to WHO and World Bank categorization, anemia is considered the third cause of DALY in women aged 15-44 years. Treatment of anemia in developing countries costs 4.4% of the Gross Domestic Product (GDP) (3, 4).

In 2005, WHO announced the spread of iron deficiency anemia 9% and 43% in developed and developing countries, respectively. One billion and 620 million people in the world suffer from anemia. About 293 million of them are preschool children, and 56 million and 468 million are pregnant and non-pregnant women, respectively; approximately, 85% are from Africa and Asia. Of all countries, the incidence of anemia is the highest in India (3).

Pregnant women have the highest demand for iron among all. This requirement starts from 1.9 ml/1000 kcal in the daily diet of the second trimester, and gets to 2.7 ml/1000 kcal in each day of the third trimester of pregnancy. The required amount of iron is 1 ml for infants who are breastfed, 0.8 ml for teenage girls, 0.6 ml for teenage boys and non-pregnant women, 0.4 ml for the pre-school and school children, and 0.3 ml for adult men (3).

Iron plays an important role in the developpment of nervous system, especially during growth years. Iron deficiency leads to various health conditions such as physical, behavioral and cognitive disorders in pre-school and school children (4). Different studies in developing countries have shown that almost all pregnant women in the second half of their pregnancies, and 40% of school children suffer from iron deficiency anemia (4). In some of these countries, parasitic infections, malaria, AIDS, and tuberculosis are worsening the situation.

Due to the significant impact of iron on physical functional capacity, iron deficiency anemia reduces the capacity of the whole population and interferes with social development (4). Controlling anemia leads to a 20% increase of national production in developing countries. However, since this disease is being controlled in industrialized countries, the situation is different in these countries. The disease is mostly controlled by the improvement of public health and health indicators, decreasing malnutrition, and controlling parasitic diseases and malaria (4).

WHO has categorized different countries, based on the prevalence of anemia. According to this categorization, countries are divided into 3 groups with low (under 20%), medium (20%-39%), and high prevalence (more than 40%) of anemia. Among developing countries, India has the highest prevalence of iron deficiency anemia. Fifty eight percent of pregnant women, 50% of non-pregnant women (and the women who do not breastfeed), 56% of teenage girls, 30% of male adults, and 80% of children under two years of age suffer from iron deficiency in India. Twenty percent of direct maternal deaths and 20% of indirect maternal mortality in India are due to iron deficiency anemia. Seven out of 10 children in India present with iron deficiency; 3% and 40% have high and moderate anemia, respectively (3).

Iran, as one of the developing countries, is considered to be at the medium level (20% - 39%) of anemia prevalence. A study conducted in 2009 in Iran, showed that the prevalence of anemia in school girls aged between 7 and 12 years is about 15%; its prevalence in rural areas is more than the urban regions (5). The overall estimate of anemia prevalence was %13.6 and nearly 29.1% in Iranian pregnant women and children, respectively (5-7).

In 2012, The Ministry of Health in UK reported that almost 3% of men and 8% of women have iron deficiency anemia in England. The data show that 11% of non-pregnant women (aged 16 to 49 years old) have iron deficiency, and that 3%-5% of the whole population suffer from iron deficiency anemia (8).

The protocols in these three countries are designed based on the general health condition of that particular country. For instance, in India, the focus is on preventive measures to control anemia together with enriching the nutrition, increasing the sanitation of drinking water and controlling malaria. The protocol regarding India includes the highest number of instructtions, and greatest costs and cooperation between ministries and different sections. This protocol was issued in 1995, and 14 ministries and governmental organizations were involved to execute the instructions. Moreover, anemia-controlling program in India is reviewed every

12 years to decrease anemia prevalence up to 50% in young girls.

In Iran, this protocol was issued in 2002, and two ministries were involved to execute the instructions. Therefore, a committee was formed in each province and followed the program once a month; afterwards, the number of meetings gradually decreased. The priority of the program was female boarding schools, and the committee presented the report of the process. The program was executed step-by-step and started from November 2002 until May 2002.

In England, anemia prevalence is at the minimum level, therefore, implementing preventive measures to control this disease from childhood till the time of delivery a baby in adulthood has not been recommended. Due to the significant role of iron efficiency in physical and cognitive functions, and the universal importance of eradicating iron deficiency, this comparative review was performed regarding the situation of anemia and various iron supplementary programs in India, Iran, and England. This study also aimed to gain an insight into the approaches of different countries towards iron supplementation protocols.

Materials and Methods

The present study is a comparative review to examine and compare the existing protocols of iron supplementations in three countries of India, Iran and England. In order to identify the frameworks adopted in these countries, WHO/ World Bank categorization was utilized. According to this classification, countries are divided into four groups, based on the prevalence of anemia:

1. Normal countries in which the prevalence of iron deficiency anemia is less than 5% such as Canada and Italy, and some industrialized countries including Germany and France,
2. Low-prevalence countries (with 5%-19.9% iron deficiency anemia) e.g. England, United States, New Zealand, Japan, and Australia,
3. Medium-prevalence countries (with 20%-39.5% iron deficiency anemia) such as Iran, Pakistan, and countries in North Africa and parts of Central America,
4. High-prevalence countries (with more than 40% iron deficiency anemia) such as India, Central Africa, and some countries in South America.

The reviewed countries in this study were India, Iran, and England. The main reason for selecting these three countries was to study iron deficiency anemia with three different levels of prevalence (low, medium and high). According to the latest categorization of WHO in 2008, India has the highest level of iron deficiency anemia with more than 49%, Iran is at the medium level with 20%-39%, and England with 5% - 19% has a low prevalence of iron deficiency anemia (3).

In order to collect the data, PubMed, WHO/ World Bank ranking, BMJ Center reports, and data distributed by health ministries were used. The countries were compared with respect to anemia prevalence, preventive protocols, and treatment strategies for the newborns, children between 1-4 years of age, teenagers, and pregnant women. Comparative tables were provided as the basis for detecting similarities and differences between the three countries.

Results

All the mentioned countries have set long-term targets to monitor the prevalence, treatment and preventive protocols related to anemia. The implementation of the programs has being regularly examined in all these countries; for instance, examining the protocols in India is carried out every 12 years, in Iran every year, and in England every five years.

The underlying reasons for anemia in the aforementioned countries are different. In India, lack of iron-rich diets (e.g. no consumption of red meat due to religious beliefs), epidemics of parasitic diseases like malaria, and poor health indices such as unavailability of safe drinking water and low levels of hygiene (3) are the most significant risk factors for anemia in children.

In India, the reasons for iron deficiency anemia in women are: not consuming iron-rich foods; using food products containing non-heme iron-like vegetables; drinking tea and coffee; consuming calcium-rich products which prevent the absorption of iron; not using iron supplements during menstruation; decrease of iron storage due to frequent pregnancies, deliveries, postpartum bleedings, and teenage pregnancy; losing iron because of malaria; poor health conditions; and finally unavailability of safe drinking water (3).

Since Iran is a large country, measuring the prevalence of anemia in its different regions is a difficult task. A comprehensive study in Iran showed that the highest prevalence of anemia is observed in children studying in the third grade of elementary school. The elementary school students who lived in Tehran in 2010 had the highest prevalence of anemia among 31 provinces of Iran (10, 11). A study conducted in 2008 showed that anemia prevalence in female school students within the age range of 7-12 years was about 15%.

The level of iron deficiency in pregnant women was different in various regions of Iran; it was between 13% and 40% in different provinces with different socio-economic status. Pregnant women, 6-month to 2–year-old children, teenage girls aged 11-19 years, and pre-term newborns were the target groups of iron deficiency preventive program in Iran (10). Table 1 shows the prevalence of iron deficiency anemia in high-risk groups of the reviewed countries.

Table 1. Estimation of anemia prevalence in high-risk groups in India, Iran and England

Country	Group	Prevalence of IDA
India	Children (6–35 months)	79%
	All women (15–49 years)	53%
	Adolescent girls (15–19 years)	55.8%
	Pregnant women (15–49 years)	58.7%
	Lactating women (15–49 years)	63.2%
Iran	Children (6–35 months)	Moderate group according to WHO classification
	All women (15–49 years)	33%
	Adolescent girls (15–19 years)	
	Pregnant women (15–49 years)	39.9%
	Lactating women (15–49 years)	-----
England	Children (6–35 months)	8%
	All women (15–49 years)	8.8%
	Pregnant women (15–49 years)	15.2%

In England, anemia is mostly observed in cities where the immigrant children from developing countries reside (8, 9). Anemia is generally seen in the immigrant children from Africa and South Asia who live in Birmingham. The medium prevalence of anemia was 27% in 1985, and decreased to 19% after 10 years. In England, anemia is observed in 6-month to 2-year-old children whose main source of nutriation is cow's milk (4, 8). The average spread of anemia in England is estimated as 12%.

Different measures have been taken in England which have great impacts on decreasing anemia. These measures include: improving the absorption of nutrients; decreasing the consumption of cereals which hinder iron absorption; increasing nutrients which help with iron absorption such as animal-derived foods; increasing the consumption of processed iron-rich foods, especially for children; and taking supplements with high-iron absorption.

Late marriage, having the first pregnancy after the age of 25 years, taking contraceptive pills for long periods of time, and decrease in the number of pregnancies and deliveries are the effective factors in lowering the prevalence of anemia in developed countries such as England (2, 4, 8-9).

Table 2 compares the preventive and treatment protocols of anemia prevalence in high-risk groups in the studied countries; these groups include children, 10-19-year-old adolescents, pregnant and lactating women, and women in their reproductive age.

There are some differences between the programs implemented in India and Iran; for instance, folic acid is less recommended for children in Iran in comparison with India (50 mcg vs. 100 mcg). Moreover, the duration of anemia preventive program for Iranian children is limited to two years; after this period, three-month examinations (in a year) are performed for six years. However, in India, it includes the whole childhood period.

It seems that in England, infant-formula feeding is more common than breastfeeding, since eating cereal which is enriched by iron is recommended for two years. In comparison with Iran, iron supplementation program for adolescents in India, not only recommends higher doses of iron and folic acid, but is also mandatorily implemented for boys and girls. However, in Iran, iron supplementary program is optional for boys, and the family can provide them with the necessary iron. Also, the dosage of iron and folic acid is lower than the Indian program; England has no particular program designed for this population.

Using Iron supplements for pregnant women in these three countries is completely different both in terms of dosage and anemia screening program. India and Iran have no program for

Table 2. Strategies and policies regarding iron supplementation in three countries of India, Iran and England

Country	Group					
	Children		10–19-year-old adolescents		Pregnant and lactating women	Women in their reproductive age
	0-5 Years old	6-10 Years old				
India	20 mg elemental iron and 100 (mcg) folic acid per ml of liquid formulation and age appropriate de-worming for 100 days (Biweekly throughout the period of 6–60 months of age and de-worming for 12-month-old children and older.	30 mg elemental iron and 250 mcg folic acid per child per day for 100 days in a year. Weekly throughout the period of 5–10 years of age and biannual de-worming	Weekly dose of 100 mg elemental iron and 500 mcg folic acid with biannual de-worming		100 mg of elemental iron and 500 mcg of folic acid daily for 100 days during pregnancy, followed by the same dose for 100 days in the post-partum period	100 mg elemental iron and 500 mcg of folic acid. Weekly throughout the reproductive period
Iran	2 mg/kg iron elemental + 50 microgram folic acid up to 24 months and 30 mg elemental Iron from 2 up to 5 years, 3 months a year	30-60 mg elemental iron 3 months in a year	Boys 60 mg elemental Iron+400 microgram folic acid, 3 months in a year during the puberty period	Girls 60 mg elemental Iron + 400 microgram folic acid, 3 months in a year during puberty period	60 mg elemental Iron + 400 microgram folic acid from 16th week of pregnancy to 3 months after delivery	60 mg elemental Iron + 400 microgram folic acid, 3 months in a year
England	The free use of cereals rich in Iron for children till 24th month of age in Birmingham and Prescribing free Iron for families who receive financial support from the government. Using Iron rich formula for the children over 2 years in families supported by the government	Using the formula containing Iron	--------	----------	Using iron supplementary assistance for pregnant women with homoglobinopathy history if their serum ferritin is less than 30. Prescribing 100ml-200ml of Iron for women with evident anemia and with ferritin lower than 30. Prescribing the daily 100mg-200mg of Iron for the women whose hemoglobin is less than 10, until 3 months after the delivery	

screening pregnant women, whereas in England, prescription of iron is limited to women who have a history of hemoglobinopathy, and those with ferritin lower than 30(mg/L). Unlike England, the programs of India and Iran include routine iron supplementation during pregnancy and lactating period. There is also a plan for preventing anemia in women during their reproductive age in India and Iran, while England has no plan in this regard.

Discussion

Anemia is a widespread public health problem with major consequences for human health as well as social and economic development. It is the world's second leading cause of disability and is responsible for about 1 million deaths in a year, of which three-quarters occur in Africa and Southeast Asia. Physical and cognitive losses due to iron deficiency anemia cost developing countries up to 4.05% loss in GDP per year, thereby delaying social and economic developments (10, 12). In young children, iron deficiency is a result of increased iron requirement due to rapid growth, which is almost 10 times higher (per kilogram of body weight) than that of an adult male.

Children who suffer from anemia have delayed psychomotor development and impaired performance. In addition, they experience impaired coordination of language and motor skills, equivalent to a 5–10 point deficit in intelligence quotient (IQ) (3, 4, 8). The consequences of anemia in women are devastating as the condition adversely affects both their productive and reproductive capabilities. It is estimated that about 20% of maternal mortality is caused by anemia worldwide. Furthermore, anemia contributes partly to 50% of all maternal deaths (3, 4).

The present study reviewed different strategies implemented for the prevention and treatment of anemia in high-risk groups, and studies different preventive principles. By comparing the protocols, one can see the differences between high-risk groups in these three countries.

The differences in the rate and risk factors of pregnant women mortality in three countries show the variations in preventive measures to control anemia. For instance, 20%- 40% of direct deaths of Indian pregnant mothers and about 20% of Iranian maternal deaths are due to anemia. Therefore, there are no filtering programs in these two countries in order to identify the anemia of pregnant women, and all mothers should benefit from iron supplementary programs during pregnancy, according to the recommended regimens (11, 12).

India is experiencing more iron deficiency anemia due to various reasons such as not eating red meat, consuming significant amounts of milk and dairy products, and increased risk of parasitic diseases and malaria. Therefore, taking albendazole is recommended as an important anti-parasitic drug in India; this medication is used along with preventive programs in India, though it has not been recommended in Iran and England (8, 12).

According to WHO instructions, if the prevalence of parasitic diseases is higher than 30% in a country, people who are more likely to get iron deficiency anemia should benefit not only from iron supplementary but also anti-parasitic programs (3). In England, high-risk groups are not those at the age of puberty, but are children under two years of age, who are mostly the children of immigrants, low-income families, and those subsidized by the government.

Having reviewed the operational instructtions for controlling anemia in different countries, we can conclude that:

1. Preventive programs and policies are affected by health indicators and conditions of each country e.g. safe drinking water.
2. The main purpose of these programs is to reduce the incidence of anemia, and the related consequences in risky groups.
3. In all countries especially the developed ones, the program of iron supplementation is carried out for free for the low-income people. In Iran and India, the supplementary programs have been provided for pre-school children by The Ministry of Health and Family Welfare. After the age of six, the program is provided by the schools during the academic year. In Iran this protocol is regularly executed during the first 16 weeks of the academic year. If the time of program implementation coincides with the fasting month of Ramadan, students will be educated to follow the instructions, as soon as they break their fast. In England, this program is provided for free only for the low-income families, however, in Iran and India, it is cost-free for all high-risk groups.
4. The success of iron supplementary program is not only dependent on the performance of one single program, but the cooperation of all sections is also required. The collaborative attempts of the ministries of Education and Health & Family Welfare of India, and Ministry of Health and Medical Education of Iran are good examples.
5. In low-income countries, the most important and cost-effective practice is nutritional enrichment; also, the iron supplementary programs should be improved. Although in low-income countries, iron-fortified foods are more effective than iron supplementary programs, these programs are executed in developed countries. The reason seems to be the omission of some high-risk groups; for instance, no supplementary program is implemented for people during their pubertal age in England (14, 15).
6. Improvement of health indicators is associated with the success of anemia management. Control programs which include accessibility

to safe drinking water are considered to be of high importance (3, 10).

7. In all the studied protocols in this review, the duration of the programs was limited, between 5 to 12 years.
8. The program was free of charge for three high-risk groups of pregnant women, children under two years of age, and high school female students in developing countries of Iran and India. In England, it was free for low-income pregnant women and children under two years of age (3, 14).

Conclusion

Anemia is an indicator of both poor nutriation and poor health condition. The review of iron supplementation protocols in three countries of India, Iran and England showed that the protocols were different regarding the prevalence of anemia in the community, particularly for high-risk groups. The status of public health, availability of safe drinking water, and also prevalence of various diseases like anemia, parasitic diseases, and malaria were the major reasons for the observed differences. Program strategies focus on iron supplementation, and change according to local conditions. This study showed that in low-income countries, the most cost-effective practice is nutritional enrichment, which has already been implemented in developed countries.

Conflict of Interest

No conflict of interest exists.

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