Original Articles

Iron deficiency anemia

A study of risk factors

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ABSTRACT

Objective: To determine the risk factors for iron deficiency anemia among Saudi women of childbearing age.

Methods: This is a case control study conducted at the primary health care clinics of King Khalid University Hospital in Riyadh over a 6-month period. Inclusion criteria included women of childbearing age and hemoglobin level < 120 g/l. Iron deficiency anemia was defined as having iron deficiency and low hemoglobin level < 120 g/l. Controls had hemoglobin level > 120 g/l and were matched with the cases for socio-demographic characteristics.

Results: Eighty-seven patients and 203 controls were enrolled in the study. Low frequency of eating meat, vegetables or drinking juices right with vitamin C increased the risk of having iron deficiency anemia by 2-4 fold (odds ratio = 2.06, 95% confidence interval 1.20-3.54), (odds ratio = 2.86, 95% confidence interval 1.65-4.98) and (odds ratio = 3.75, confidence interval 2.20 - 6.42). Menstrual period duration of ≥ 8 days, history of clots or flooding increased the odds of having iron deficiency anemia by 3-6 fold. The odds of being iron deficient in patients on non-steroidal anti-inflammatory drugs and antacid were 6-9 fold.

Conclusion: Important risk factors for iron deficiency anemia among Saudi women of childbearing age are dietary habits, menorrhagia and history of ingestion of non-steroidal anti-inflammatory drugs or antacids.

Keywords: Anemia, iron deficiency anemia, iron deficiency, risk factors, women of child bearing age, case control study.

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Iron deficiency anemia (IDA) is the most common nutritional disorder in the world, as it is in the Eastern Mediterranean Region (EMR).[1] A total of 149 million people in the EMR are iron deficient or anemic according to the World Health Organization (WHO) criteria.[1] Eighty three million of them are women.[2] In fact the prevalence of anemia in the Gulf Region ranged from 15 to 48% in women of childbearing age.[3] In Saudi Arabia the overall country prevalence was 30 to 56%.[3] A cross-sectional study conducted in Riyadh City among schoolgirls showed that IDA prevalence was 40.5% among female adolescents (16-18) years old.[4] As pregnancy related anemia is linked with a high risk of maternal and fetal deaths as well as increasing perinatal mortality,[5] the control of anemia in women of childbearing age is therefore a public health priority. Fortunately, anemia has received a great deal of attention in international health forums. WHO/UNICEF jointly adopted new goals for the 1990s, aiming amongst other things to control iron deficiency by the turn of the century.[1] The international conference on nutrition (ICN) held in Rome, in December 1992, adopted the nutritional goals of the world summit for children, one of which was to reduce by one third (of the 1990 levels) the

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prevalence of IDA among women of child bearing age.[1] The aim of this study is to determine the risk factors for IDA among Saudi women of childbearing age. A clear understanding of risk factors in this population will help to plan for more effective strategies to control this nutritional deficiency.

Methods. This case control study was conducted at the primary health care clinics (PHCC) for women in King Khalid University Hospital (KKUH) in Riyadh between January 1999 and June 1999 inclusive.

Inclusion and exclusion criteria. The study included non pregnant Saudi females of child bearing age (12 to 50) years with hemoglobin levels < 120 g/l. Other types of anemias were excluded (sickle cell anemia, ß-thalassemia minor, megaloblastic anemia, anemias of infection and of chronic inflammatory disease), post menopausal women, pregnant and lactating mothers, pregnancy related conditions for the last 3 months (abortion and post-partum period), treatment with iron tablets during the last 6 months and females with hysterectomy. Patients satisfying these inclusion and exclusion criteria were recruited for the study.

Definitions of ID, IDA and other variables. Iron deficiency anemia was defined in this study as iron deficiency and a low hemoglobin level of less than 120 g/l. Iron deficiency status was based on 3 laboratory tests: mean cell volume (MCV), serum ferritin (SF), and transferrin saturation (TS). To be diagnosed as iron deficient, the individual had to have an abnormal value of 2 or more of these indicators.[6] The cutoff value for low hemoglobin was less than 120 g/l (according to WHO criteria for diagnosis of anemia).[1] Mean cell value was considered low if the value was less than 80 fl. Accepted lower limits for SF were values less than 12 ug/l for adults.[6] Transferrin saturation was calculated by dividing serum iron by total iron binding capacity, cutoff point was < 16%.[6]

Controls. Controls were Saudi females of childbearing age (12 to 50) years. Two age matched female controls were selected for each case. Inclusion criteria for controls were hemoglobin level > 120g/l (not anemic), not pregnant or lactating, not complaining of pregnancy related conditions and not menopausal. Exclusion criteria included females with hysterectomy.

Data collection form. The data collection form consisted of 2 sections. Section (A) included items on patients' demographic characteristics, clinical presentation, dietary, gynecological, obstetrical, medical and family history. Dietary data was recorded according to the frequency recall technique[7] for the last week. The information gathered was based on self-reported data, but medical records were checked if patients gave vague details. This section was completed by a trained social worker. Patients eligible for the study were medically examined. Section (B) consisted of the results of the laboratory investigations carried out on each subject. The investigations included complete blood count (CBC), hemoglobin electrophoresis, serum ferritin, serum iron and iron binding capacity. One hematologist was assigned to follow, analyze and complete the data of this section.

Data analysis. The data was processed in a microcomputer and the statistical software (SPSS - Version 9) was used for statistical analysis. The chi-square (X^2) test was used to assess differences between cases and controls with any categorical variable. Risk factors were assessed by their odds ratio and their (95%) confidence limit that was calculated by Cornfield's approximation method. The reference category for calculating the odds ratio was the categories with the least risk for each variable.

Results. A total of 325 women were enrolled in the study, 122 anemic patients and 203 controls. Thirteen patients did not fulfill the inclusion and exclusion criteria. One of these patients (1%) had sickle cell anemia, 2 (2%) had Beta-thalassemia minor, 3 (2%) were menopausal and 7 (6%) were taking iron tablets. This suggested that 110 women were eligible for the study. However, 10 patients (1%) did not complete their investigations and another 13 patients (12%) did not satisfy the definition of IDA. Therefore, only 87 patients (71%) were included in the analysis with case:control ratio of 1:2.3. Table 1 shows the socio-demographic characteristics of women with IDA and the controls. The majority of women were aged less than 20 years and >35 years age groups. A sizable proportion were married, and nearly a quarter of house-wives were illiterate. Approximately 60% of spouses or fathers were skilled workers, middle and high professionals. Also, a good majority lived in villas and in urban areas. No significant differences were detected between demographic characteristics of cases and controls. Table 2 demonstrates the frequency distribution of IDA patients and their controls according to dietary habits. A higher proportion of the cases gave a history of a low frequency of red meat consumption, odds ratio 2.06 ($P<0.05$). Infrequent consumption of vegetables was reported in 53% of cases compared to 29% of controls. The odds ratio was approximately 3 fold. Drinking juices containing Vitamin C with lunch was reported less frequently by cases that controls, ($P<0.05$). Similarly the low frequency of drinking laban with lunch increased the likelihood of having IDS by 2 fold. There were no statistical differences between cases and controls as regards to drinking tea, coca-containing drinks directly after lunch, and also following a dietary regime. Table 3 shows the distribution of women with IDA and controls according to gynecological history. Twenty two

Table 1 - Socio-demographic characteristics of women with iron deficiency anemia and the control group.

Characteristics	Cases (87)		Control (203)		Chi-square	P-value
	No	%	No	%		
Age						
<20	25	28	41	20		
20-27	22	25	45	22		
28-35	14	16	36	18		
>35	26	30	79	39	2.69	0.44
Marital Status						
Single	31	36	63	31		
Married	50	57	120	59		
Divorced/Widow	6	7	20	10	1.02	0.60
Education						
Illiterate	23	26	59	29		
Elementary	15	17	40	20		
Intermediate	17	19.5	40	21		
Secondary	19	22	42	11		
University	13	15	22	11	1.23	0.87
Occupation						
Housewife	49	56	127	63		
School teacher	4	5	14	7		
Student	26	30	48	24		
Other	8	9	13	6.5	2.49	0.47
Occupation of Spouse or father						
High professional	19	22	34	18		
Middle professional	8	9	20	11		
Skilled	24	27.5	80	43		
Unskilled	10	11.5	16	8.5		
Others	21	24	36	19	5.32	0.25
Geographical location						
Urban	70	80.5	177	87		
Suburban	17	19.5	26	13	2.18	0.14
Housing						
Villa	60	70	162	80		
Flat	18	21	25	12		
Small House	8	9	13	6		
Others	1	1	3	1.5	4.24	0.12

percent of cases had the duration of their periods ≥ 8 days as compared to 4% of controls (P<0.05). The presence of clots with periods was reported in 22% of cases versus 11% of controls and those with such a history were at a 3 times greater risk of having IDA. History of flooding of periods was present in 33% of women with IDA versus 14% of controls with an odds ratio of more than 4 fold. However, there were no significant differences between cases and controls with regards to frequency of periods, use of oral contraceptive pills and intra-uterine devices. Table 4 demonstrates the distribution of cases and controls according to obstetric history. There were no statistical differences between women with IDA and controls with regards to parity, multiparity, birth interval, or taking iron supplements. Table 5 shows the frequency of subjects with IDA and controls according to medical history. The past history of peptic ulcer, hemorrhoids, parasitic infections, blood disorders, blood transfusion and past history of IDA did not show any statistical significant differences between cases and controls. But the history of drug ingestion such as antacids or non steroidal anti-inflammatory drugs (NSADs) was associated with IDA.

Discussion. This study showed that dietary, gynecological and drug history to be positively associated with IDA in women of childbearing age as in accordance with most other studies.[8-10] Dietary factors such as low consumption of red meat, vegetables, cereals and fruits have been reported to be associated with IDA.[10-11] In this study patients consuming less than 2 servings of red meat and vegetables per week were at increased risk. Haem iron (from meat) provides 10-20% of iron intake while non-haem iron (from vegetables, fruits, and cereals) provides 80-90%. Non-haem iron absorption is influenced by the iron status of subjects and the balance between enhancers and inhibitors much more than haem iron.[5] The main enhancers of non-haem iron absorption are meat and ascorbic acid (vitamin C).[1,5,6] In the present study a low frequency of

Table 2 - Distribution of women with iron deficiency anemia and their controls according to dietary habits.

Items	Cases (87)		Control (203)		Odds ratio 95% CI
	No	%	No	%	
Eating red meat					
Infrequently	47	54	75	37	2.06*
Frequently	39	45	128	63	(1.20 - 3.54)
Eating vegetables					
Infrequently	46	53	58	29	2.86*
Frequently	41	47	148	71	(1.65 - 4.980
Drinking Tea/Coffee Directly after lunch					
Infrequently	52	60	130	4	0.86
Frequently	34	39	73	36	(0.50 - 1.490
Drinking Laban with lunch**					
Infrequently	38	44	56	28	2.08*
Frequently	48	55	147	72	(1.19 - 3.63)
Drinking cocoa containing drinks with lunch					
Infrequently	44	50.5	119	59	0.71
Frequently	43	49	83	41	(0.42 - 1.22)
Drinking Vitamin C containing juices with lunch					
Infrequently	49	56	57	28	3.75*
Frequently	37	42.5	145	71	(2.20 - 6.42)
Following dietary regime					
Infrequently	14	16	50	25	0.58
Frequently	71	82	147	75	(0.28 - 1.17)

Infrequently = ≤ 2 servings per week; Frequently = ≥3 serving per week
* As compared with controls, P<0.05; **Laban is fermentated milk which is rich in calcium

Table 3 - Distribution of women with iron deficiency anemia and controls according to gynecological history.

Variable	Cases (87)		Control (203)		Odds ratio 95% CI
	No	%	No	%	
Frequency of period					
Once/ 2-4 weeks	73	84	175	96	0.83
Once/ 5-12 weeks	14	16	28	3	(0.4 - 1.78)
Duration of period in days					
≥ 8 days	19	22	7	4	6.15*
≤ 7 days	68	78	154	75	(2.3 - 18.0)
Clots with period					
Yes	19	22	17	11	3.2*
No	65	75	186	89	(1.48 - 6.92)
Flooding of period					
Yes	29	33	22	14	4.34*
No	55	63	181	86	(2.21 - 8.5)
Use of oral contraceptives					
Yes	14	16	27	13	1.02
No	73	84	144	71	(0.48 - 2.18)
Use of intra uterine contraceptive device					
Yes	5	6	14	8	0.85
No	79	91	156	92	(0.23 - 2.62)

* As compared with controls, P < 0.05

Table 4 - Distribution of women with iron deficiency anemia and controls according to obstetric history.

Obstetric history	Cases (87)		Control (203)		Odds ratio 95% CI*
	No	%	No	%	
Parity					
No	37	42.5	175	96	1.29
Yes	50	57.5	28	3	(0.75 - 2.22)
Multiparity					
< 5	19	38	7	4	1.00
≥ 5	31	62	154	75	(0.48 - 2.07)
Birth interval in years					
≤ 2	20	23	17	11	0.90
> 2	23	26	186	89	(0.42 - 1.93)
Iron supplements during pregnancy					
Yes	30	34.5	22	14	0.6
No	18	21	181	86	(0.34 - 1.04)
Iron supplements after delivery					
Yes	12	14	27	13	0.93
No	34	39	144	71	(0.42 - 2.01)

*CI - confidence interval

drinking (vitamin C) containing juices with lunch was associated with a 4 fold increased risk of having IDA. This is in accordance with most of the studies.[11,13] Ascorbic acid is known as a powerful enhancer of iron absorption from non-meat foods when consumed within a meal.[1] Important iron absorption inhibitors are polyphenols (gallolyl groups), present in tea, coffee and cocoa. Many studies have reported such an inhibitory effect.[6,11-13] In this study, although infrequent intake showed a reduction in the risk of having IDA, it was not statistically significant. This is possibly because drinking tea and coffee after lunch is a common dietary habit in Saudi Arabia and to detect a significant difference between cases and controls a bigger sample size is needed. Several reports indicate that the intake of calcium can inhibit iron absorption.[6,10] A cross-sectional study among girls and young women in 6 European countries showed that dietary calcium intake had a consistent inverse association with SF. After adjusting the linear regression model for iron intake, calcium was weakly inversely associated with blood iron status.[12] The low frequency of calcium intake with lunch in the form of laban was associated with an increased risk of having IDA. This conflicts with other reports.[10,12] A bigger sample size is needed with linear regression to show whether this association is consistent. Heavy menstrual blood loss is an important risk factor for IDA among women of childbearing age.[6] Our findings suggest that menstrual period duration of ≥ 8 days, history of clots and flooding increased the risk of having IDA. Although giving such a history is very subjective, the risk was increased 3 to 6 fold. This signifies the importance of excluding history of menorrhagia in patients with IDA. The use of intra-uterine devices (IUCD) had been shown to be associated with lower SF, due to increase menstrual blood loss. On the other hand women taking oral contraceptive pills had higher SF and lower frequency of depleted iron reserves than non-users.[6,10] Such associations were not detected in our study, possibly due to the small sample size of patients using IUCD and oral contraceptives. Obstetric risk factors for IDA reported in the literature are multiparity[6] and short birth interval (less than 2 years). Pregnancy creates a large demand for iron, which is needed to develop the fetus and placenta. Additional iron is lost with blood at delivery. When women have 2 or more years between pregnancies they are more likely to enter the subsequent pregnancy with adequate iron status.[1] The present study did not find any significant difference between cases and controls with regards to parity, birth interval, iron intake during pregnancy or after delivery. A bigger sample size might be able to detect such differences. An interesting finding is the increased risk (6.5 to 9.6 fold) of IDA in patients prescribed NSADs or antacids. Non-steroidal anti-inflammatory drugs have been reported to be among important causes of IDA.[9] They may precipitate gastro-intestinal bleeding which as a result causes the anemia. Antacids have been shown to reduce the absorption of iron.[15] Also patients taking antacids for digestive complaints may prove to have gastro-intestinal disease if further investigated by endoscopy. Reports have shown that significant upper gastro-intestinal disease is identifiable among

Table 5 - Distribution of women with iron deficiency anemia and controls according to medical history.

Medical history	Cases (87)		Control (203)		Odds ratio 95% CI
	No	%	No	%	
Past medical history					0.74
Yes	6	7	19	9	(0.23 - 2.0)
No	79	91	187	91	
Hemorrhoids					
Yes	7	8	12	6	1.45
No	77	88.5	191	94	(0.46 - 4.16)
Parasitic infections					
Yes	8	9	8	4	3.59
No	79	91	195	96	(0.40 - 43.38)
Blood disorders					
Yes	2	2	4	2	1.15
No	84	96.5	199	98	(0.10 - 8.23)
Blood transfusion					
Yes	15	17	21	10	1.84
No	69	79	182	90	(0.85 - 4.00
Past history of IDA					
Yes	34	39	70	34.5	1.29
No	50	57.5	133	65.5	(0.74 - 2.25)
Medications					
Antacids					
Yes	14	16	2	1	9.64*
No	73	84	201	99	(2.88 - 41.4)
NSAD +					
Yes	26	30	12	6	6.57*
No	61	70	191	94	(2,96 - 15.10)
Family history of IDA					
Mother					
Yes	24	27.5	23	11	2.92*
No	63	72	176	88	(1.46 - 5.8)
Father of spouse					
Yes	7	8	3	1	5.83*
No	80	92	200	98.5	(1.28 - 35.50
Siblings					
Yes	8	9	4	2	5.04*
No	79	91	199	98	(1.3 - 23.37)
Children					
Yes	9	10	36	18	0.54
No	78	90	167	82	(0.22 - 1.21)

+NSAD - Non steroidal anti-inflammatory drugs
*As compared with controls, $P < 0.05$

most premenopausal women with IDA.[16] A past medical history of IDA had been reported to be a risk factor for a subsequent illness.[6] Although the risk was slightly increased, however ($P > 0.05$). A bigger sample size may detect such an association. A family history of IDA among mothers, siblings, spouses or fathers increased the risk by 3 to 6 fold. This signifies the importance of dietary factors. Dietary habits within a family should be properly investigated to identify the inhibitors and enhancers of iron intake. A dietary record of food intake for one week may be useful to identify such inhibitors and may help to alter some of the poor dietary habits. A study on Russian women's iron intake showed the mean iron intake to be comparable to those of women of reproductive age in the United States of America. When those intakes were adjusted for enhancers and inhibitors of absorption, the iron bioavailability in this Russian group was extremely low.[13] Among the limitations of this study is the scarcity of data linking diet and iron status reflecting the difficulties of evaluating a rapid assessment.

In conclusion, dietary habits, menorrhagia, and history of ingestion of antacids or NSAD were the

most important risk factors among Saudi women of childbearing age. Recommendations. Educational programs to improve public awareness of the causes of IDA and healthy dietary habits. Weekly preventive dose of iron tablets for women presenting with history of menorrhagia. Prescription of antacids/NSAD should be carried out with caution. Endoscopy is recommended for those complaining of digestive complaints or not responding to iron tablets. Future research is needed to evaluate dietary iron adequacy in the Saudi diet.

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