Can date fruits and 7 dates replace iron tablets in increasing hemoglobin levels?

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ORIGINAL ARTICLE

Can date fruits and 7dates replace iron tablets in increasing hemoglobin levels?

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ABSTRACT

Background. Iron suplement programs, as an approach to overcoming anemia, indicate positive impact although many studies have also noted varying levels of success or even a failure. The known and commonly acknowledged side effect of iron supplements, such as constipation, causes a tendency for patients to stop consuming these supplements.

Aim: To examine hemoglobin level and bowel movement differences resulting from an iron suplement program of the government program as well as consumption of the date fruits, and two common products freely available to the Indonesian consumers.

Method. This study is a pilot randomized controlled trial with four groups consist of three treatment groups and one control group. Respondents were anemia adolescent girls with inclusive but not exclusive criteria. 40 respondents were selected using random permutated blocks. Intervention was done for 30 days with weekly assessments. Data analysis used Friedman Test, Wilcoxon Signed Rank and Multiple Linear Regression test.

Results. There is a significant hemoglobin difference before and after intervention on the four groups. The differences seen in week 1, 2, 3, then tends to decline. Strong, significant correlation is found in treatment with hemoglobin and defecation duration (week 4) and bowel problems (week 2, 3, 4); feeding frequency and menstruation with hemoglobin (week 1); feeding frequency and defecation duration (week 2); water intake and defecation duration (week 4). Multiple linear regression analysis results in regression equation and participants' prediction towards dependent variables. There is a positive, significant relationship between treatment (week 2, 3) and bowel problems, water intake (week 4) and defecation duration.

Conclusion. Dates can be used instead of iron tablets and 7dates can be used as a companion iron tablets.

Keywords: Iron tablets, ferrous sulfate, ferrous gluconate, date fruits, 7dates, anemic, hemoglobin, bowel movements, dietary fiber, water intake, bowel problems

INTRODUCTION

Obstetric haemorrhage is the main cause of maternal mortality[1] and it has been estimated to cause 25% of all maternal mortality in the world and over 30% in Asia[2, 3]. In fact, the real number of deaths is beyond the estimation since many death cases caused by postpartum haemorrhage are unreported. However, the absolute risk of death is lower in high-income countries with a ratio estimation of 1: 100,000 childbirths compared to the ratio estimation of 1: 1,000 childbirths in low-income countries[4]. Anemia is an advanced problem that occurs as a result of hemorrhage, but it can also be the indirect cause of hemorrhage[5]. To date, anemia particularly iron deficiency is a serious public health problem in developing countries[6]. Anemia in pregnancy can lead to fetal growth disorders, preterm labor, low birth weight, and haemorrhage[7, 8, 9, 10, 11]. Approximately 16-55% of women have suffered from anemia since early pregnancy[12]. Iron supplementation is the most widely used approach to treat anemia[13]. The iron tablet administration program starting after the first trimester of pregnancy has been applied in many developing countries. Several studies have reported the positive effects of this effort[14, 15, 16, 17] yet the impact is still far from the expectations[12] and it is considered an unsuccessful program[18] due to low adherence of women in consumption of iron tablets. Some studies have reported that gastrointestinal side-effects generally have dropped women compliance in consuming iron tablets[18, 19]. The most common complaints after taking iron tablets are nausea and constipation. This condition is further exacerbated if they are consumed by pregnant women as the body adapts towards pregnancy hormone[20, 21, 22]. Other studies also reported that iron supplementation may cause constipation[23, 24, 25]. Women without a history of bowel problems may experience constipation in the early pregnancy, while women with previous constipation history will experience worse complaints during their pregnancy[20]. The prevalence of constipation reported in pregnancy is 11-38%[26, 27, 28]. Other factors which aggravate constipation are less dietary fiber[21, 29] and low water intake[21]. Moreover, a pregnancy period is a short time period to deal with pre-existing anemia[12]. Therefore, iron deficiency correction should have been done from teenage years or before pregnancy[30].

Iron is a crucial substance for biological function including respiration, energy production, deoxy-ribonucleic acid (DNA) synthesis, and cell proliferation[31] as well as an essential element needed to produce red blood cells which carry all of the nutrients to cells throughout the body[32]. Iron can be acquired from food and beverage. Dates are an example of iron-containing

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nutrients often consumed and favored by the Muslim community[33]. Mariyam et al. reported that Ajwa dates contain the least iron (0.85 mg/100 gr) while the Tunisian dates contain the most iron (7.2 mg/100 g)[34]. In addition to iron, 100 gr of dates also contain 5.2% crude fiber and minerals such as calcium (Ca) 65 mg, phosphorus (P) 72 mg, potassium (K) 521 mg, magnesium (Mg) 20 mg, and selenium (Se) 0.34 mg. Furthermore, the contents of vitamins in dates include vitamin A (0.04 mg), B1 (0.08 mg), B2 (0.05 mg) and nicotinic acid (2.20 mg). All these vitamins have different functions that can help the body to be healthy through carbohydrate metabolism, maintaining blood glucose levels, fatty acids for energy, and assisting in the formation of hemoglobin, leukocytes and red blood cells[32]. Some studies have proven that dates consumption can escalate hemoglobin levels[35, 36]. This study was aimed to examine the divergences of hemoglobin levels and bowel movements among iron supplementation supplied by the government, as opposed to the supplements circulated in the open market and nutritional sources of iron often consumed by the community and to identify an alternative solution to solve anemia.

METHOD OF STUDY

This study is a pilot randomized controlled trial. The independent variables of this study were consumption of ferrous sulfate, ferrous gluconate, date fruits and 7dates while the dependent variables were hemoglobin levels, duration of defecation and bowel problems. Confounding variables for hemoglobin levels were mean of feeding frequency per week and menstruation, whereas for duration of defecation and bowel problems were mean of feeding frequency, dietary fiber and water intake per week. There were four groups, each selected randomly, included three intervention groups (ferrous gluconate, date fruits and 7dates) and one control group (ferrous sulfate).

The control group was iron tablet subsidized by the Bogor District Health Office containing ferrous sulfate excitation 200 mg, while the first treatment group was Sangobion tablet which is an iron tablet commonly consumed by Indonesian people and sold freely over the counter in drugstores containing 250 mg ferrous gluconate. The second treatment group consumed a popular date sold in the Indonesian market, Sayer dates[37]. The third treatment group consumed a commonly available date drink packaged as 7dates. The 7dates election was based on its staple ingredients using dates and water only and it has been certified as a viable product certification from The Assessment Institute for Food, Drugs, and Cosmetics of Indonesian Ulema Council (figure 1).

Respondents in this study were anemic teenage girls in the Bunda Auni community (age 18 to 25 years old) who met the inclusion criteria and were excluded from exclusion criteria. The inclusion criteria were nulligravida and nullipara, having hemoglobin levels 7 to 12 gr/dL (see table 1), having one or more symptoms of anemia, not consuming any iron supplements, and a willingness to consume either iron tablets, dates or 7dates. The exclusion criteria were girls with excess iron (hemocromatosis, hemosiderosis), anemia due to red-cell fragmentation (hemolytic anemia), disorders of red blood cells (porphyria, thalassemia), stomach ulceration (peptic ulceration) and colon ulceration (ulcerative colitis), alcohol drinkers and recipients of routine blood transfusions.

Figure 1. Sayer dates and 7dates

Table 1. Diagnosis of anemia according to WHO

Group	Hb levels (g/dL)
Children aged 6 months to 6 years old	<11.0
Children aged 6-14 years old	<12.0
Adult men	<13.0
Adult women who are not pregnant	<12.0
Pregnant women	<11.0

Source: AlDallal[38]

Before data collection, 6 persons were recruited and trained including 2 officers to measure hemoglobin levels and 4 officers to observe the compliance of respondents in consumption of ferrous sulfate 200 mg (1 tablet per day), ferrous gluconate 250 mg (1 tablet per day), date fruits 70-75 gr (2x35-37.5 gr per day)[39] which contain iron around 2.4 mg/75 gr dates[40] and 7dates (3 bottles per day) for 30 days. Determination of dates doses were based on the recommended consumption of 7 dates per day where Muslims believe that by eating 7 dates each day, a person will be spared from poison and sorcery (Hadith narrated Bukhari no. 356)[41] and considerations of safety aspect where lethal dose (LD) of 50 extract dates are more than 5000 mg/kg[42] whereas the LD of Ferrous Sulfate for adults is 200-250 mg/kg body weight[43, 44]. Data was collected from January to April 2018 in Bojong Kulur village, Gunung Putri district, Bogor regency, West Java province, Indonesia. Data collection method in this study was using primary data taken directly from respondents through observation, interview, and examination.

The selection of research sites was based on considerations of access and technical observation of respondents as most of the girls of the Bunda Auni community reside in dormitories and some live in groups in boardinghouses. Determining the number of samples per group was based on the sample calculation using Federer's formula and 10% addition to anticipate the drop out sample, that was 10 respondents per group or 40 respondents overall. Each member of the groups were chosen by random permutated blocks. A total of 46 anemic girls met the inclusion criteria and were not included in the exclusion criteria and were willing to be involved in the study. However, as many as 6 people dropped out in the first week, 4 of them were unable to tolerate the side-effects of iron supplements and 2 of them moved out, while 40 others remained in the study until the end of the study.

Anamnesis, physical examination and hemoglobin estimation were performed before intervention for screening respondents. Every day the officer reviewed food intake, dietary fiber and water intake, menstruation, bowel movements and bowel problems experienced by respondents followed by weekly examinations including anamnesis, physical examination and hemoglobin estimation that was done by Sahli's method and digital hemoglobin test (hemoglobin testing system quick-check) Easytouch with one prick. The main reason for using Sahli's method is because it is recommended by Indonesian government while digital hemoglobin test is most frequent used by Indonesian midwives. Data analysis was done by using statistical procedure and service solution (SPSS) 19 software. Univariate analysis was performed to describe each variable studied separately. The two-way repeated Anova test could not be done since the data normality and homogeneity were not eligible so the Friedman test was chosen as an alternative test followed by advanced test or post hoc with Wilcoxon signed rank test to identify which group is mutually meaningful. Further, a multiple linear regression was performed to examine the size of the influence between variables.

This study has been submitted to the Ethics of Health Study Committee, The Faculty of Medicine of Universitas Padjadjaran Bandung and obtained approval from the Ethics of Health Study Committee, The Faculty of Medicine of Universitas Padjadjaran number 29/UN6.C10/PN/2018.

RESULT

Friedman test results showed significant differences in hemoglobin levels in all four groups (ferrous sulfate, ferrous gluconate, dates and 7dates) between, before and after intervention (1, 2, 3 and 4 weeks) both using Sahli's method and digital hemoglobin test (table 2).

Table 2. Changes in hemoglobin levels (gr/dL)

	FS*	FG	DF	7D
Shali's method				
Initial	9.7±0.85	10.3±0.83	9.7±1.31	10.7±0.61
1 week	10.5±1.19	11.1±0.86	10.7±0.88	10.8±1.36
2 weeks	11.7±0.92	11.7±0.78	11.4±1.06	12.1±1.10
3 weeks	12.2±0.75	12.3±0.48	12.3±0.61	12.3±0.43
4 weeks	12.4±0.66	11.7±1.52	12.3±0.83	11.9±1.46
P	.000***	.001**	.000***	.002**
Digital hemoglobin test				
Initial	9.8±0.95	10.5±0.60	9.7±1.35	10.6±0.56
1 week	11.2±1.34	12.9±1.22	11.5±1.02	11.3±1.83
2 weeks	13.1±1.63	13.0±1.86	13.1±1.02	12.0±1.81
3 weeks	13.8±1.97	13.5±1.45	13.4±1.38	13.0±0.96
4 weeks	13.2±1.27	13.0±1.91	12.5±1.25	12.1±1.51
P	.000***	.001**	.000***	.008**

Note: Mean±standard deviation; Ferrous Sulfate supplied by local government (FS); Ferrous Gluconate (FG); Date Fruits (DF); 7dates (7D); Friedman test (*p< .05 **< .01 ***p< .001 are significant)

An exponential surge in hemoglobin levels occured in the 1st week to 3rd week while in the 4th week the overall hemoglobin levels tended to decline where the increase was seen only in the ferrous sulfate and dates group by Sahli's method (figures 2 and 3).

The Wilcoxon test result provided a more detail description of the research findings in figure 2 and 3. There were significant differences in hemoglobin levels between before and after treatment (weeks 1, 2, 3 and 4) and between week 1 and in the following weeks (week 2, 3 and 4) that were found in almost all four groups both by Sahli's method and digital test. Furthermore, a significant difference in hemoglobin levels between week 2 and after week 3 and 4 was found only in ferrous sulfate and dates groups by Sahli's method (table 3).

All respondents reported consuming less dietary fiber each week which in the 7dates group reporting the least fiber intake (table 4).

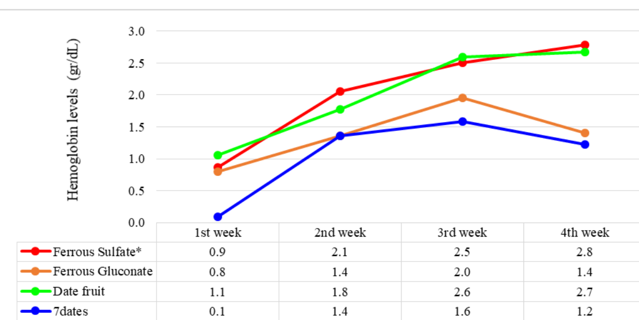

Figure 2. Mean change in hemoglobin levels (g/dL) per week (Hemoglobin estimation by Sahli's method)**
*Iron tablets supplied by local government

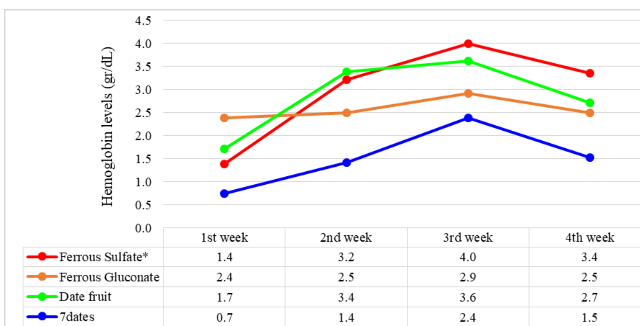

Figure 3. Mean change in hemoglobin levels (g/dL) per week (Hemoglobin estimation by digital hemoglobin test)**
*Iron tablets supplied by local government

Table 3. The result of Wilcoxon signed rank test in hemoglobin levels and bowel movements

	Sahli's method								Digital hemoglobin test							
	FS		FG		DF		7D		FS		FG		DF		7D	
	Z	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*	*Z*	*p*
1 week-initial	-1.632[a]	.103*	-2.092[a]	.036*	-2.196[a]	.028*	-.416[a]	.677	-2.659[a]	.008*	-2.807[a]	.005*	-2.142[a]	.032*	-1.479[a]	.139
2 weeks-initial	-2.805[a]	.005*	-2.654[a]	.008*	-2.652[a]	.008*	-2.805[a]	.005*	-2.803[a]	.005*	-2.599[a]	.009*	-2.803[a]	.005*	-1.683[a]	.092
3 weeks-initial	-2.805[a]	.005*	-2.805[a]	.005*	-2.805[a]	.005*	-2.810[a]	.005*	-2.803[a]	.005*	-2.803[a]	.005*	-2.807[a]	.005*	-2.810[a]	.005*
4 weeks-initial	-2.805[a]	.005*	-2.397[a]	.017*	-2.805[a]	.005*	-1.887[a]	.059	-2.803[a]	.005*	-2.666[a]	.008*	-2.805[a]	.005*	-2.295[a]	.022*
2 weeks-1 week	-2.703[a]	.007*	-2.045[a]	.041*	-1.843[a]	.065	-2.807[a]	.005*	-2.347[a]	.019*	-.051[b]	.959	-2.501[a]	.012*	-.816[a]	.414
3 weeks-1 week	-2.803[a]	.005*	-2.807[a]	.005*	-2.668[a]	.008*	-2.547[a]	.011*	-2.666[a]	.008*	-.663[a]	.507	-2.397[a]	.017*	-2.244[a]	.025*
4 weeks-1 week	-2.805[a]	.005*	-1.173[a]	.241	-2.814[a]	.005*	-1.277[a]	.201	-2.599[a]	.009*	-.102[a]	.919	-2.134[a]	.033*	-1.172[a]	.241
3 weeks-2 weeks	-1.231[a]	.218	-1.897[a]	.058	-2.075[a]	.038*	-.534[a]	.593	-1.599[a]	.110	-.867[a]	.386	-.306[a]	.759	-1.172[a]	.241
4 weeks-2 weeks	-2.462[a]	.014*	-.204[b]	.838	-2.296[a]	.022*	-.051[a]	.959	-.204[a]	.838	-.306[a]	.759	-1.186[b]	.236	-.297[a]	.767
4 weeks-3 weeks	-1.245[a]	.213	-1.122[b]	.262	-.102[a]	.919	-.408[b]	.683	-.867[b]	.386	-1.073[b]	.283	-1.276[b]	.202	-.970[b]	.332

Note: Ferrous Sulfate supplied by local government (FS); Ferrous Gluconate (FG); Date Fruits (DF); 7dates (7D); *Indicates statistically significant change ($p<0.05$); a. Based on negative ranks; b. Based on positive ranks; c. Wilcoxon Signed Ranks Test

Table 4. Consumption of fiber and water weekly by number of respondents

	1 week				2 weeks				3 weeks				4 weeks			
	FS	FG	DF	7D	FS	FG	DF	7D	FS	FG	DF	7D	FS	FG	DF	7D
Mean consumption of fiber in a week																
No fiber consumption	0	2	0	0	1	1	2	2	0	3	1	1	0	0	1	4
Just 1 day	2	0	0	1	1	1	1	3	2	0	0	1	4	3	1	1
2 days	1	0	1	3	1	4	1	2	2	2	3	4	0	0	2	1
3 days	1	3	2	1	1	1	4	1	3	3	3	3	2	4	3	2
4 days	2	2	2	3	3	1	0	1	1	1	1	1	2	2	2	2
5 days	1	1	2	2	3	1	1	1	2	0	1	0	2	1	0	0
Almost every day	3	2	3	0	0	1	1	0	0	1	1	0	0	0	1	0
Every day	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mean intake of water per week																
<1000 mL	1	1	1	2	3	1	4	4	4	3	2	3	5	3	3	4
>1000-1500 mL	6	5	2	3	4	6	2	4	1	6	5	5	3	5	5	4
>1500-2000 mL	2	2	4	3	2	3	2	1	4	1	1	2	2	2	1	2
>2000-2500 mL	1	2	3	1	1	0	1	1	1	0	1	0	0	0	0	0
>2500 mL	0	0	0	1	0	0	1	0	0	0	1	0	0	0	1	0

Note: Ferrous sulfate supplied by local government (FS); Ferrous gluconate (FG); Date fruits (DF); 7dates (7D)

The prominent finding of this study concerns the duration of defecation and bowel problems each week. Even though, the hemoglobin levels of ferrous sulfate and dates groups showed higher levels compare to other groups but there were differences in bowel movements. It can be seen clearly from the table 4 and 5 that even the 7dates group consumed less dietary fiber, but its bowel movements was the smoothest and had the least complaints, followed by the dates group. Meanwhile, many respondents of ferrous sulfate and ferrous gluconate experienced bowel problems. The complaints included inability to defecate, hard stool and diarrhea. Inability to defecate was the most problem complained by respondents of ferrous sulfate and ferrous gluconate groups weekly (table 5).

Table 5. Description of bowel movements experienced by respondents

	1 week				2 weeks				3 weeks				4 weeks			
	FS	FG	DF	7D	FS	FG	DF	7D	FS	FG	DF	7D	FS	FG	DF	7D
Mean duration of defecation per week																
ND for 8 days	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
ND for 7 days	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
ND for 6 days	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ND for 5 days	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0
ND for 4 days	1	1	0	0	0	2	0	0	0	0	0	1	1	0	0	0
ND for 3 days	2	3	0	1	2	0	1	1	1	0	0	0	1	1	1	0
ND for 2 days	1	1	2	1	2	1	0	1	1	4	0	1	0	2	0	0
Routine each 2 days	0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	1
Almost every day	2	0	2	3	1	3	2	1	0	2	2	2	1	0	2	1
Every day	4	4	5	5	5	4	7	7	7	3	8	6	6	4	7	8
Respondents faced bowel problems																
Inability to defecate	4	2	1	0	4	2	1	0	4	2	0	0	4	2	0	0
Hard stool	2	0	2	4	0	0	2	0	0	0	0	0	0	0	2	1
Diarrhea	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No complaints	3	8	7	6	6	8	7	10	6	8	10	10	6	8	8	9

Note: No Defecation (ND); Ferrous sulfate supplied by local government (FS); Ferrous gluconate (FG); Date fruits (DF); 7dates (7D)

Table 6. Correlation: intake factors, menstruation, hemoglobin levels and bowel movements

	1 week		2 weeks		3 weeks		4 weeks		1 week		2 weeks		3 weeks		4 weeks	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Hemoglobin levels	**Sahli's method**								**Digital hemoglobin test**							
Treatment	.043	.396	.095	.279	.075	.323	-.087	.296	-.085	.301	-.213	.093	-.207	.099	-.284	.038*
Feeding frequency	-.269	.046*	-.074	.325	-.125	.220	-.165	.154	-.243	.066	.048	.384	-.037	.410	-.124	.223
Menstruation	.276	.043*	.209	.098	.124	.223	-.086	.299	.004	.491	.243	.066	.179	.134	.192	.118
Bowel problems	**Duration of defecation**								**Bowel problems**							
Treatment	.203	.105	.213	.094	.193	.117	.339	.016*	.238	.070	.333	.018*	.438	.002*	.315	.024*
Feeding frequency	-.034	.418	-.293	.033*	-.003	.492	.163	.157	-.206	.102	-.261	.052	-.193	.117	.188	.122
Fiber consumption	.096	.277	-.128	.216	.012	.470	-.178	.136	-.005	.488	-.135	.202	-.018	.456	-.005	.487
Water intake	.123	.225	.04	.403	.243	.065	.399	.005*	-.085	.301	-.019	.455	.106	.258	.202	.106

Note: Pearson's correlation coefficient (r) and the one-tailed p-values (p); *Significant at .05 level

Table 7. Regression equation and prediction of hemoglobin levels and bowel movements

Hemoglobin levels	**Sahli's method**	**Digital hemoglobin test**
1 week Regression equation Prediction	R^2 = .155, F(3,36)= 2.207, p > .05 Y = 10.652 + 0.022X1 – 0.564X2 + 0.727X3	R^2 = .068, F(3,36)= .880, p > .05 Y = 13.449 - 0.128X1 – 0.698X2 + 0.057X3
2 weeks Regression equation Prediction	R^2 = .052, F(3,36)= .658, p > .05 Y = 10.703 + 0.069X1 – 0.065X2 + 0.526X3	R^2 = .118, F(3,36)= 1.600, p > .05 Y = 10.957 - 0.325X1 + 0.220X + 1.207X3
3 weeks Regression equation Prediction	R^2 = .029, F(3,36)= .361, p > .05 Y = 12.182 + 0.025X1 – 0.131X2 + 0.138X3	R^2 = .082, F(3,36)= 1.067, p > .05 Y = 13.317 – 0.291X1 – 0.171X + 0.625X3
4 weeks Regression equation Prediction	R^2 = .042, F(3,36)= .524, p > .05 Y = 13.651 - 0.111X1 – 0.350X2 – 0.330X3	R^2 = .095, F(3,36)= 1.258, p > .05 Y = 13.324 – 0.298X1 – 0.294X + 0.391X3
Note: df (regression, residual); Y= constant, treatment (X1), feeding frequency (X2), menstruation (X3); a. Predictors: (Constant), menstruation, treatment, feeding frequency; b. Dependent Variable: hemoglogin estimation by Sahli's method and digital hemoglobin test; *p<0.05 **<0.01 ***p<0.001		
Bowel movements	**Duration of defecation**	**Bowel problems**
1 week Regression equation Prediction	R^2 = .068, F(4,35)= .634, p > .05 Y = 6.568 + .360X1 – .270X2 + .170X3 + .219X4	R^2 = .118, F(4,35)= 1.165, p > .05 Y = 3.674 + .274X1 – .535X2 + .053X3 – .159X4
2 weeks Regression equation Prediction	R^2 = .142, F(4,35)= 1.443, p > .05 Y = 9.262 + .319X1 – .904X2 + .040X3 + .203X4	R^2 = .178, F(4,35)= 1.893, p > .05 Y = 3.291 + .357X1 – .559X2 + .034X3 + .074X4
3 weeks Regression equation Prediction	R^2 = .105, F(4,35)= 1.023, p > .05 Y = 7.698 + .311X1 – .307X2 – .028X3 + .545X4	R^2 = .237, F(4,35)= 2.716, p < .05* Y = 3.047 + .394X1 – .495X2 + .017X3 + .209X4
4 weeks Regression equation Prediction	R^2 = .287, F(4,35)= 3.516, p < .05* Y = 7.015 + .535X1 – .498X2 – .132X3 + 1.017X4	R^2 = .135, F(4,35)= 1.363, p > .05 Y = 2.022 + .317X1 + .030X2 + .031X3 + .223X4
Note: df (regression, residual); Y= constant, treatment (X1), feeding frequency (X2), fiber consumption (X3), water intake (X4); a. Predictors: (Constant), water intake, feeding frequency, treatment, fiber consumption; b. Dependent Variable: duration of defecation and bowel problems; *p<0.05 **<0.01 ***p<0.001		

The analysis result on hemoglobin levels shows a strong and significant correlation between treatment (r=-.284, *p*=.038) and hemoglobin levels by digital hemoglobin test at week 4; and between feeding frequency (r=-.269, *p*=.046), menstruation (r=.276, p=.043) and hemoglobin levels by Sahli's method at week 1. While, the result analysis on bowel movements shows a strong and significant correlation between treatment and duration of defecation at week 4 (r=.339, *p*=.016) and bowel problems at week 2 (r=.333, *p*=.018), week 3 (r=.438, *p*=.002) and week 4 (r=.315, *p*=.024); between feeding frequency and duration of defecation at week 2 (r=-.293, *p*=.033); and between water intake and duration of defecation at week 4 (r=.399, *p*=.005) (table 6).

A multiple linear regression analysis was performed to predict hemoglobin levels and bowel movements based on its predictors that produced regression equations and participants' predicted towards dependent variables (table 7).

Based on multiple regression analysis, it was discovered that there is no correlation between hemoglobin levels (both by Sahli's method and digital test) and major confounders (treatment, feeding frequency and menstruation) (table 8).

Table 8. Multiple linear regression analysis using hemoglobin levels as the dependent variable in both estimation

Variables		Sahli's method				Digital hemoglobin test			
		β value	*P* value	95% CI		β value	*P* value	95% CI	
				Lower	Upper			Lower	Upper
1 week	Treatment	.154	.878	-.273	.318	-.596	.555	-.561	.306
	Feeding frequency	-1.824	.077	-1.191	.063	-1.536	.133	-1.619	.224
	Menstruation	1.866	.070	-.063	1.518	.100	.921	-1.104	1.219
2 weeks	Treatment	.501	.620	-.211	.350	-1.446	.157	-.780	.131
	Feeding frequency	-.245	.808	-.602	.472	.512	.612	-.652	1.093
	Menstruation	1.201	.238	-.362	1.414	1.697	.098	-.235	2.649
3 weeks	Treatment	.304	.763	-.143	.193	-1.393	.172	-.716	.133
	Feeding frequency	-.583	.564	-.585	.324	-.302	.765	-1.321	.979
	Menstruation	.632	.532	-.305	.581	1.131	.266	-.496	1.747

Variables		Sahli's method				Digital hemoglobin test			
		β value	*P* value	95% CI		β value	*P* value	95% CI	
				Lower	Upper			Lower	Upper
4 weeks	Treatment	-.586	.562	-.497	.274	-1.243	.222	-.784	.188
	Feeding frequency	-.796	.431	-1.241	.541	-.531	.598	-1.417	.828
	Menstruation	-.659	.514	-1.344	.685	.621	.539	-.887	1.669

Note: Dependent variables, Hb levels by Sahli's method and digital hemoglobin test; CI: confidence interval; *p<0.05 **<0.01 ***p<0.001

However, there is a significant positive correlation between treatment week 2 and 3 and bowel problems after adjusting the effects of major confounders (feeding frequency, fiber consumption, water intake) and between water intake week 4 and duration of defecation after adjusting the effects of major confounders (treatment, feeding frequency, fiber consumption) (table 9).

Table 9. Multiple linear regression analysis using duration of defecation and bowel problems as the dependent variables

Variables		Duration of defecation				Bowel problems			
		β value	*P* value	95% CI		β value	*P* value	95% CI	
				Lower	Upper			Lower	Upper
1 week	Treatment	1.163	.253	-.268	.988	1.560	.128	-.083	.631
	Feeding frequency	-.389	.699	-1.678	1.138	-1.357	.183	-1.335	.265
	Fiber consumption	.804	.427	-.259	.599	.444	.660	-.190	.297
	Water intake	.630	.533	-.488	.927	-.804	.427	-.561	.243
2 weeks	Treatment	1.340	.189	-.165	.803	2.123	.041*	.016	.699
	Feeding frequency	-1.901	.066	-1.870	.062	-1.663	.105	-1.241	.123
	Fiber consumption	.252	.803	-.283	.363	.304	.763	-.194	.262
	Water intake	.774	.444	-.330	.737	.399	.692	-.303	.451
3 weeks	Treatment	1.148	.259	-.239	.861	2.728	.010*	.101	.687
	Feeding frequency	-.387	.701	-1.915	1.302	-1.172	.249	-1.353	.362
	Fiber consumption	-.139	.890	-.438	.382	.160	.874	-.202	.236
	Water intake	1.603	.118	-.145	1.236	1.152	.257	-.159	.577
4 weeks	Treatment	1.969	.057	-.017	1.088	1.813	.078	-.038	.671
	Feeding frequency	-.567	.574	-2.279	1.284	.054	.957	-1.113	1.174
	Fiber consumption	-.652	.519	-.542	.279	.240	.812	-.233	.295
	Water intake	2.578	.014*	.216	1.817	.880	.385	-.291	.737

Note: Dependent variables, duration of defecation and bowel problems; CI: confidence interval; *p<0.05 **<0.01 ***p<0.001

DISCUSSION

The Friedman test result has detected a significant difference in the hemoglobin levels in all four groups between before and after treatment. It is undeniable that iron consumption can improve hemoglobin levels[13, 45, 46, 47] through increasing the serum retinol[48]. Similarly, the consumption of dates can elevate hemoglobin levels[36] through serum iron, serum ferritin, transferrin saturation and total iron binding capacity[49]. This is interesting considering that based on the composition, iron content in 75 gr dates and 3 bottle 7dates are not equivalent to 200 mg ferrous sulfate and 250 mg ferrous gluconate.

Some studies reported that the average iron content in 100 gr dates is approximately 0.24 mg[50, 51, 52] while 100 gr Sayer dates contain 3.21 mg iron (around 2.4 mg/75 gr)[40]. With such a small amount of iron, dates group can elevate hemoglobin levels almost as much as ferrous sulfate group. Ferrous sulfate and ferrous gluconate rely solely on iron for hemoglobin enhancement, in contrast to dates and 7dates which use multiple micronutrients to increase hemoglobin levels since other micronutrient deficiencies will limit the response of hemoglobin to iron supplements[13]. There are some substances in dates contributing to hemoglobin enhancement including iron, vitamin A, vitamin C, zinc, and riboflavin. 100 gr of dates contain vitamins and minerals (the percentage of each minerals in dried dates varies from 0.1 to 916 mg)[53, 54]. The average vitamin content in dates are vitamin A (23.85 μg), B1 (78.61 μg), B2 or riboflavin (116.5 μg), B3 or niacin (1442 μg), B6 (207 μg), B9 (53.75 μg) and vitamin C (3900 μg)[50].

Based on human and animal studies, Hodges et al. concluded that vitamin A is essential for normal hematopoiesis[55]. Experiments in mice show that iron deficiency can decline serum retinol and affect on accumulation of vitamin A in the liver as retinyl esters. This may be related to impaired hepatic acid retinyl ester hydrolase (iron-dependent enzymes)[56]. In case of vitamin A deficiency, iron mobilization from the body's reserve to the circulation and tissues of hematopoietic will be destroyed and cause disorders of erythropoiesis (red cell production)[57]. Supplementation of vitamin A may increase the response of hemoglobin to iron supplementation[13] and increase iron absorption associated with iron concentrations in tissue[57]. Therefore, a combination of iron and vitamin A supplements may further improve iron status[58, 59]. Similar to vitamin A, zinc supplement has also been proven to elevate hemoglobin levels. Allen's study reported that supplement of zinc only or iron only can increase plasma retinol. However, combination of zinc plus iron can enhance plasma retinol more than iron alone[13]. The next micronutrient is riboflavin. Riboflavin deficiency can limit the efficacy of iron supplement, increase iron loss in intestine and interfere iron absorption and intracellular iron mobilization[60, 61, 62]. This condition may also interfere with globin sythesis and activity of NADH-FMN oxidoreductase so that the iron is trapped in ferritin and becomes unavailable for erythropoiesis. NADH is nicotinamide adenine dinucleotide (reduced form) which is an active coenzyme form of vitamin B3 ('niacin') and flavin mononucleotide (FMN) or riboflavin-5'-phosphate is a biomolecule produced from B2 ('riboflavin') by the enzyme riboflavin kinase. NADH-FMN reductase is an enzyme involved in releasing iron from ferritin. Riboflavin supplement may enhance hemoglobin response towards iron supplementation[63] and iron absorption through enhanced gastrointestinal function[64]. Apart from that, riboflavin is also prominent for the synthesis of the globin component of hemoglobin[65]. Hence, riboflavin plus iron supplements can increase hematologic status better than iron alone[66, 67]. The same effect was also reported by other studies that iron supplements or iron-rich foods combined with micronutrients are more effective in increasing hemoglobin levels than iron alone[63, 68]. The combination of substances in dates may trigger activity of phenol compounds which can stimulate erythropoietin production by the liver which has an impact on increasing hemoglobin enhancement[35, 36]. 100 gr fresh dates contains phenolics (134-280 mg of ferulic acid equiv), free phenolic acids (2.61-12.27 mg), and bound phenolic acids (6.84-30.25 mg)[69]. While Biglari et al. reported total phenolic level in 100 gr dates is in range 2.89-4.82 for soft date, 4.37-6.64 for semi-dry date and for dry date at 141.35 milligrammes of gallic acid equivalent per 100 grammes of dry weight (mg GAE/100g dw)[70]. One further matter of interest is that in addition to containing micronutrients, dates also contain macronutrients that can inhibit iron absorption, namely calcium and magnesium[71, 72]. On average, 100 gr dates contains 56-150 mg magnesium[50, 51, 52, 73] and 123-187 mg calcium[73]. In spite of macronutrients contents that can inhibit iron absorption, dates remain capable to raise hemoglobin levels. This is caused by other substances in dates which are able to inhibit the inhibitory effect of iron absorption as reported by Layrisse who stated that vitamin A may reduce the inhibitory effect of polifenol and phytates on iron absorption[74].

Hemoglobin estimation by digital test shows that the four groups tended to experience a downward trend in the fourth week. This is more likely to relate to the body's defense system in which the hemoglobin levels of respondents in four groups had reached a normal level at around 12.0 g/dL to 13.0 g/dL (see table 2). Human body has evolved to keep iron from breakage in various ways including recycling iron after the damage of red blood cells and iron retention if there is no dispense mechanism. However, iron excess can be toxic so that its absorption is limited to 1-2 mg per day and the most iron needed by the body (about 25 mg per day) is provided through recycling by macrophaging agitated erythematic phagocytosis. The two mechanisms are controlled by hormone Hepcidin, which keeps total body iron in the normal range (no deficiency or excess)[75].

Iron supplements have been proven to increase hemoglobin levels. However, high doses of iron consumption (more than 120 mg) significantly increase the risk of constipation, gastric pain, diarrhea,[19, 76] heartburn, nausea and vomiting[19]. This report is in line with the findings that the ferrous sulfate and ferrous gluconates groups experienced more problems in defecation. Constipation is the most frequent chronic gastrointestinal complaint[77]. Patients may report constipation even though they defecate daily. Criteria for constipation diagnosis includes less frequent bowel movements (less than 3 times per week), hard stool and/or difficulty to expel feces,[20, 78] and straining[78]. These complaints are often ignored because these complaints are considered taboo to be discussed and left without treatment until constipation becomes a severe problem for the patient[79]. If constipation persists and the patient does not obtain appropriate treatment, complications will become severe, including feacal impaction (obstruction due to hard stool), further causing faecal incontinence[80]. Straining defecation may also increase the risk of prolapse uterovaginal[81] and cause permanent damage in the form of pudendal nerve damage and impair the supporting function of the pelvic floor muscles[82]. It is not surprising that patients with constipation have a lower quality of life compared to inflammatory bowel disease or gastroesophageal reflux disease[83]. In extreme and rare cases, complication is caused by untreated constipation, such as movement from thrombus vena into vena pulmonary, or sudden cardiac death as a result of straining and cardiac abnormalities[84, 85].

On the other hand, the 7dates and dates groups had fewer bowel complaints than ferrous sulfate and ferrous gluconates groups. This is because dates are the best source of dietary fiber. High fiber consumption decreases the risk of constipation[86] and obesity,[87] increases the amount and frequency of bowel movements, and decreases the average transit time[88]. Recommended daily intake (RDI) of dietary fiber for healthy adults (>20 years) is 25-35 gram per day[85]. Some studies reported that 100 gr dates contains 6.4% to 11.5% dietary fiber,[54, 89] including 0.84 gr soluble dietary fibre, 5.76 gr insoluble dietary fiber and 8 gr total of dietary fiber[69, 90, 91, 92]. Insoluble dietary fiber plays a very significant role in human body. It can protect the body from many diseases, such as diverticular disease and bowel cancer through the increase of fecal weight, and also has a laxative effect[93]. The findings in this study are also supported by Al-Shahib et al. which stated that the consumption of six or seven dates can meet 50-100% of RDI of dietary fiber[90]. The fiber content in dates can help to relieve bowel movements and overcome constipation. It can be used as a natural laxative for patients with constipation[54].

In addition to fiber, the body also needs water. Derbyshire et al. found that water intake significantly decreases the incidence of constipation in women[21]. Given the side-effects of iron consumption and people's habit of consuming less fiber and water, the optimization of natural nutrients can be the recommended as a sound strategy. In many cases, dates and its processed products can be considered as the most ideal food[54] because dates contain many other essential nutrients needed by the human body[90].

CONCLUSION

In the final analysis, dates can be used instead of iron tablets and 7dates can be used as a companion iron tablets. Although ferrous sulfate, ferrous gluconate, dates and 7dates can elevate the hemoglobin levels, both ferrous sulfate and ferrous gluconate have negative side effects while dates and 7dates give positive effects in bowel movements so that both dates and its processed products should be considered as an alternative solution for handling and preventing anemia.

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REFERENCES

1. El-Refaey H, Rodeck C. Post-partum haemorrhage: definitions, medical and surgical management. A time for change. Br Med Bull. 2003;67:205-17. Retrieved from https://academic.oup.com/bmb/article/67/1//330398
2. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Look PFAV. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006;367(9516):1066–74. Retrieved from http://www.hpc4.go.th/director/data/region/WHO_MMR.pdf
3. Haeri S, Dildy GA. Maternal mortality from hemorrhage. Semin Perinatol. 2012;36(1):48-55. Retrieved from https://www.seminperinat.com/article/S0146-005(11)00156-X/pdf
4. Mousa HA, Walkinshaw S. Major postpartum haemorrhage. Curr Opin Obstet Gynecol. 2001;13(6):595-603. [PMID: 11707663].
5. AbouZahr C. Global burden of maternal death and disability. Br Med Bull. 2003;67(1-11):1-11. [DOI: 0.1093/bmb/ldg015]. Retrieved from https://academic.oup.com/bmb/article/67/1/1/330397
6. Toteja GS, Singh P, Dhillon BS, Saxena BN, Ahmed FU, Singh LRP, et al. Prevalence of anemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr Bull. 2006;27(4):311-5.
7. Miller JL. Iron deficiency anemia: a common and curable disease. Cold Spring Harb Perspect Med. 2013;3(7):1-14. Retrieved from http://perspectivesinmedicine.cshlp.org/content/3/7/a011866.full.pdf+html
8. Allen LH. Anemia and iron deficiency: Effects on pregnancy outcome. Am J Clin Nutr. 2000;71(5):1280S–4S. https://doi.org/10.093/ajcn/71.5.s Retrieved from https://academic.oup.com/ajcn/article/71/5/S/4729385
9. Maskey M, Jha N, Poudel SI, Yadav D. Anemia in pregnancy and its associated factors: A study from Eastern Nepal. Nepal J Epidemiol. 2014;4(4):386-92. [DOI: http://dx.doi.org/10.3126/nje.v4i4.11358]. Retrieved from https://www.nepjol.info/index.php/NJE/article/view//9205
10. Haider BA, Olofin I, Wang M, Spiegelman D, Ezzati M, Fawzi WW. Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: Systematic review and meta-analysis. BMJ. 2013;346:1-19. [Doi: 0.1136/bmj.f3443] Retrieved from https://www.bmj.com/content/bmj/346/bmj.f.full.pdf
11. Ononge S, Campbell O, Mirembe F. Haemoglobin status and predictors of anaemia among pregnant women in Mpigi, Uganda. BMC Res Notes. 2014;7(1):712. Retrieved from https://bmcresnotes.biomedcentral.com/track/pdf/10.1186/756-0500-7-712
12. Kurz KM, Galloway R. Improving adolescent iron status before childbearing. J Nutr. 2000;130(2):437S-9S. https://doi.org/10.1093/jn/130.2.437S Retrieved from https://academic.oup.com/jn/article/130/2/437S/4686452
13. Allen LH. Iron supplements: Scientific issues concerning efficacy and implications for research and programs. J Nutr. 2002;132:813S–9S. Retrieved from https://academic.oup.com/jn/article/132/4/813S/4687233
14. Agarwal KN, Gomber S, Bisht H, Som M. Anemia prophylaxis in adolescent school girls by weekly or daily iron-folate supplementation. Indian Pediatr. 2003;40(4):296-301. Retrieved from https://indianpediatrics.net/apr2003/apr-296-301.htm
15. Cook JD, Reddy MB. Efficacy of weekly compared with daily iron supplementation. Am J Clin Nutr. July 1995;62(1):117–20. [DOI: https://doi.org/10.1093/ajcn/62.1.117].
16. Schultink W, Gross R, Gliwitzki M, Karyadi D, Matulessi P. Effect of daily vs twice weekly Indonesian preschool children iron supplementation with low iron status. Am J Clin Nutr. January 1995;61(1):111–5. [DOI: https://doi.org/10.1093/ajcn/61.1.111].
17. Zavaleta N, Respicio G, Garcia T. Efficacy and acceptability of two iron supplementation schedules in adolescent school girls in Lima, Peru. J Nutr. February 2000;130(2):462S–4S, [DOI: https://doi.org/10.1093/jn/130.2.462S]. Retrieved from https://academic.oup.com/jn/article/130/2/462S/4686483
18. Beaton GH, McCabe GP. Efficacy of intermittent iron supplementation in the control of iron deficiency anaemia in developing countries: an analysis of experience. Ottawa, Canada: The Micronutrient Initiative; 1999. Retrieved from https://idl-bnc-idrc.dspacedirect.org/bitstream/handle/10625/29662/117067.pdf?sequence=3
19. Hyder SMZ, Persson LÅ, Chowdhury AMR, Ekström E-C. Do side-effects reduce compliance to iron supplementation? a study of daily- and weekly-dose regimens in pregnancy. J Health Popul Nutr. June 2002;20(2):175-9. Available on http://dspace.icddrb.org/jspui/bitstream/123456789/123/1/2002-JHealthPoulNutr-175-Hyder.pdf
20. Cullen G, O'Donoghue D. Constipation and pregnancy. Best Pract Res Clin Gastroenterol. 2007;21(5):807–18. [DOI: 10.1016/j.bpg.2007.05.005]. Retrieved from https://www.sciencedirect.com/science/article/pii/S1521691807000595
21. Derbyshire E, Davies J, Costarelli V, Dettmar P. Diet, physical inactivity and the prevalence of constipation throughout and after pregnancy. Matern Child Nutr. 2006;2(3):127–34. [DOI: 10.1111/j.740-8709.2006.00061.x]. Retrieved from https://www.researchgate.net/profile/Vassiliki_Costarelli/publication/235450087_Dietary_intake_physical_inactivity_and_prevelance_of_constipation_during_and_after_pregnancy/links/0deec523015be91f26000000.pdf
22. Vazquez JC. Constipation, haemorrhoids, and heartburn in pregnancy. BMJ Clin Evid. 2010;08:1411-28. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3217736/
23. Meier PR, Nickerson HJ, Olson KA, Berg RL, Meyer JA. Prevention of iron deficiency anemia in adolescent and adult pregnancies. Clin Med Res. 2003;1(1):29–36. Retrieved from http://www.clinmedres.org/content/1/1/29.full.pdf+html
24. Milman N, Byg K-E, Bergholt T, Eriksen L. Side effects of oral iron prophylaxis in pregnancy – myth or reality? Acta Haematol. 2006;115:115:53-57. [DOI: 10.1159/000089466].
25. Zygmunt M, Heilmann L, Berg C, Wallwiener D, Grischke E, Munstedt K, et al. Local and systemic tolerability of magnesium sulphate for tocolysis. Eur J Obstet Gynecol Reprod Biol. 2003;107(2):168–75. DOI: https://doi.org/10.1016/S0301-2115(02)00368-8
26. Jewell D, Young G. Interventions for treating constipation in pregnancy (review). Interventions for treating constipation in pregnancy. Cochrane Database of Systematic Reviews. 2012(2):Art. No.: CD001142. [DOI: 10.1002/14651858.CD001142]. Retrieved from http://cochranelibrary-wiley.com/doi/10.1002/.CD001142/full
27. Marshall K, Thompson KA, Walsh DM, Baxter GD. Incidence of urinary incontinence and constipation during pregnancy and postpartum: survey of current findings at the Rotunda lying-in hospital. Br J Obstet

Gynaecol. April 1998;105:400-2. Retrieved from https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1111/j.471-0528.1998.tb10123.x
28. Lederle FA. Epidemiology of constipation in elderly patients: drug-utilisation and cost-containment strategies. Drugs Aging. 1995;6(6):465–9. Retrieved from https://link.springer.com/article/10.2165/00002512-199506060-00006
29. Anderson AS. Dietary factors in the aetiology and treatment of constipation during pregnancy. Br J Obstet Gynaecol. 1986;93:245–9.
30. Deshmukh PR, Garg BS, Bharambe MS. Effectiveness of weekly supplementation of iron to control anaemia among adolescent girls of Nashik, Maharashtra, India. J Health Popul Nutr. 2008;26(1):74-8. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2740684/pdf/jhpn0026-0074.pdf
31. Hentze MW, Muckenthaler MU, Galy B, Camaschella C. Review two to Tango: regulation of mammalian iron metabolism. Cell. July 2010;142(1):24-38. [Doi: 10.1016/j.cell.2010.06.028] Retrieved from https://ac.els-cdn.com/S009286741000718X/1-s2.0-SX-main.pdf?_tid=3a612389-47be-422b-9e0d-dad3be08f13f&acdnat=1528603880_91ff6f066eeb4f34d7e470a9b6807241
32. El-Sohaimy SA, Hafez EE. Biochemical and nutritional characterizations of date palm fruits (Phoenix dactylifera L.). JASR. 2010;6(8):1060-7. Retrieved from https://www.researchgate.net/publication/234027076_Biochemical_and_Nutritional_Characterizations_of_Date_Palm_Fruits_Phoenix_dactylifera_L
33. Indrayani, Rahmadi A, Suharti, Diana O, Zeranika N. How do Muslims consume dates? PJMHS. 2018;12(4):1732-43. [DOI: http://doi.org/10.5281/zenodo.2586225]. Retrieved from http://www.pjmhsonline.com/2018/oct_dec/pdf/1732.pdf
34. Mariyam P, Mary V. Nutritional analysis (macronutrients, potassium, and iron content) of four palm date varieties (Phoenix dactylifera L.) and study of consumption pattern among Muslim and Maharashtrian community. J Food Processing Beverages. 2015;3(1):1-9 Retrieved from http://www.avensonline.org/wp-content/uploads/JFPB-2332-4104-03-0011.pdf
35. Onuh SN, Ukaejiofo EO, Achukwu PU, Ufelle SA, Okwuosa CN, Chukwuka CJ. Haemopoietic activity and effect of crude fruit extracts of Phoenix dactylifera on peripheral blood parameters. Int J Biol Med Res. 2012;3(2):1720-3 Retrieved from https://www.biomedscidirect.com/journalfiles/IJBMRF2011470/haemopoietic_activity_and_effect_of_crude_fruit_extract_of_phoenix_dactylifera_on_peripheral_blood_parameters.pdf
36. Zen ATH, Pertiwi D, Chodidjah. The effect of date (Phoenix dactylifera) juice on haemoglobin level an experimental study in iron supplemented rats. Sains Medika. Januari-Juni 2013;5(1):17-9 Retrieved from http://jurnal.unissula.ac.id/index.php/sainsmedika/article/viewFile/359/298
37. Roektiningroem E, Hastuti PW, editors. Seed's viability of two types of dates (Phoenix dactilyfera L.) from fruit in Indonesian Market. Proceeding of 3rd International Conference on Research, Implementation and Education of Mathematics and Science; May 2016; Yogyakarta, Indonesia: Universitas Negeri Yogyakarta. Retrieved from http://seminar.uny.ac.id/icriems/sites/seminar.uny.ac.id.icriems/files/prosiding/B-05.pdf
38. AlDallal S. Iron deficiency anemia: A short review. J Immunooncol. 2016;2(1):1-6. Retrieved from https://www.omicsonline.org/open-access/iron-deficiency-anaemia-a-short-review-.php?aid=79233
39. Kordi M, Meybodi FA, Tara F, Nemati M, Shakeri MT. The effect of late-pregnancy consumption of date fruit on cervical ripening in nulliparous women. J Midwifery Reprod Health. 2014;2(3):150-6. [DOI: 10.22038/jmrh.2014.2772]. Retrieved from http://jmrh.mums.ac.ir/article_2772_b142d1addcd29393341f33980192b552.pdf
40. Al-Groobi B, Krepl V. Importance of dtae palms as a source of nutrition. Agricultura Tropica et Subtropica. 2010;43(4):341-7.
41. Bukhari. Shahih al-Bukhari, volume 007, book 065, hadith number 356. Beirut: Dar Thauq an Najah; 2001. Retrieved from https://muflihun.com/bukhari/65/356 and http://www.hadithcollection.com/sahihbukhari/98-Sahih%20Bukhari%20Book%2065.%20Food,%20Meals/6409-sahih-bukhari-volume-007-book-065-hadith-number-356.html
42. Agbon AN, Kwanashie HO, Hamman WO, Sambo SJ. Toxicological evaluation of oral administration of Phoenix dactylifera L. fruit extract on the histology of the liver and kidney of Wistar rats. Int J Anim Vet Adv. 2014;6(4):122-9 Retrieved from http://maxwellsci.com/print/ijava/v6--9.pdf
43. Olenmark M, Biber B, Dottori O, Rybo G. Fatal iron intoxication in late pregnancy. J Toxicol: Clin Toxicol. 1987;25(4):347-59. [DOI: 10.3109/15563658708992638]. Retrieved from https://www.tandfonline.com/doi/abs/10.3109/
44. Baranwal AK, Singhi SC. Acute iron poisoning: management guidelines. Indian Pediatrics. 2003;40(6):534-40. Retrieved from https://www.researchgate.net/profile/Arun_Baranwal/publication/10692032_Acute_iron_poisoning_Management_guidelines/links/53fdf9a70cf2dca800042a65/Acute-iron-poisoning-Management-guidelines.pdf
45. Casgrain A, Collings R, Harvey LJ, Hooper L, Fairweather-Tait SJ. Effect of iron intake on iron status: a systematic review and meta-analysis of randomized controlled trials. Am J Clin Nutr. October 2012;96(4):768–80. Retrieved from https://academic.oup.com/ajcn/article/96/4//4576856
46. Muslimatun S, Schmidt MK, Schultink W, West CE, Hautvast JGAJ, Gross R, et al. Weekly supplementation with iron and vitamin A during pregnancy increases hemoglobin concentration but decreases serum ferritin concentration in Indonesian pregnant women. J Nutr. January 2001;131(1):85–90, https://doi.org/10.1093/jn/131.1.85 Retrieved from https://academic.oup.com/jn/article/131/1/85/4686571
47. Tang N, Zhu Y, Zhuang H. Antioxidant and anti-anemia activity of heme iron obtained from bovine hemoglobin. Food Sci Biotechnol. April 2015;24(2):pp 635–42. DOI 10.1007/s10068-015-0083-2 Retrieved from https://link.springer.com/article/10.1007/s-015-0083-2
48. Muñoz EC, Rosado JL, López P, Furr HC, Allen LH. Iron and zinc supplementation improves indicators of vitamin A status of Mexican preschoolers. Am J Clin Nutr. 2000;71(3):789–94. [DOI: https://doi.org/10.1093/ajcn/71.3.789]. Retrieved from https://academic.oup.com/ajcn/article/71/3/789/4729207
49. Youssef HEE-D, Khedr AA. Effect of black dates on iron deficiency anemia of orphanage children. Alex J Agric Res. 2015;60(3):183-91. Retrieved from http://agr.p.alexu.edu.eg/Data/Sites/1/pdffiles/%D8%A7%D9%84%D9%85%D8%B9%D8%AF%D9%84%20%D8%A7E%D9%84%D8%A3%D9%88%D9%84%203202.pdf
50. Al-Farsi MA, Lee CY. Nutritional and functional properties of dates: A review. Crit Rev Food Sci Nutr. 2008;48(10):877-87. [DOI: https://doi.org/10.1080/10408390701724264]. Retrieved from https://www.tandfonline.com/doi/abs/10.1080/
51. Ismail B, Henry J, Haffar I, Baalbaki R. Date consumption and dietary significance in the United Arab Emirates. J Sci Food Agric. 2006;86:1196-201. [DOI: https://doi.org/10.002/jsfa.2467]. Retrieved from https://onlinelibrary.wiley.com/doi/full/10.1002/jsfa.2467
52. Mohamed AE. Trace element levels in some kinds of dates. Food Chem. July 2000;70(1):9-12. [DOI: 0.1016/S0308-8146(99)00232-0].
53. Borchani C, Besbes S, Blecker C, Masmoudi M, Baati R, Attia H. Chemical properties of 11 date cultivars and their corresponding fiber extracts. African J Biotechnol. June 2010;9(26):4096-105. [DOI: 10.5897/AJB09.1497]. Retrieved from https://www.academicjournals.org/article/article1380810378_Borchani%20et%20al.pdf
54. Al-shahib W, Marshall RJ. The fruit of the date palm: Its possible use as the best food for the future? Int J Food Sci Nutr. 2003;54(4):247-59. [DOI: https://doi.org/10.1080/09637480120091982]. Retrieved from https://www.tandfonline.com/doi/abs/10.1080/
55. Hodges RE, Sauberlich HE, Canham JE, Wallace DL, Rucker RB, Mejia LA, et al. Hematopoietic studies in vitamin A deficiency. Am J Clin Nutr. 1978;31(5):876–85. [DOI: https://doi.org/10.1093/ajcn/31.5.876]. Retrieved from https://academic.oup.com/ajcn/article/31/5/876/4650239
56. Rosales FJ, Jang J-T, Piñero DJ, Erikson KM, Beard JL, Ross AC. Iron deficiency in young rats alters the distribution of vitamin A between plasma and liver and between hepatic retinol and retinyl esters. J Nutr. June 1999;129(6):1223–8. [DOI: https://doi.org/10.093/jn/129.6.]. Retrieved from https://academic.oup.com/jn/article/129/6//4721925
57. Roodenburg AJC, West CE, Yu S, Beynen AC. Comparison between time-dependent changes in iron metabolism of rats as induced by marginal deficiency of either vitamin A or iron. Br J Nutr. May 1994;71(5):687-99. [DOI: https://doi.org/10.1079/BJN19940176].
58. Panth M, Shatrugna V, Yasodhara P, Sivakumar B. Effect of vitamin A supplementation on haemoglobin and vitamin A levels during pregnancy. Br J Nutr. September 1990;64(2):351-8. [DOI: https://doi.org/10.1079/BJN19900037]. Retrieved from https://www.cambridge.org/core/services/aop-cambridge-core/content/view/6B427718612384D5B2FE851F72016930/S0007114590001131a.pdf/effect_of_vitamin_a_supplementation_on_haemoglobin_and_vitamin_a_levels_during_pregnancy.pdf
59. Suharno D, Muhilal, Karyadi D, West CE, Hautvast JGAJ, West CE. Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia. Lancet. November 1993;342(8883):1325-8. [DOI: https://doi.org/10.016/0140-

6736(93)92246-P]. Retrieved from https://www.sciencedirect.com/science/article/pii/014067369392246P
60. Thakur K, Tomar SK, Singh AK, Mandal S, Arora S. Riboflavin and health: A review of recent human research. Critical Rev Food Sci Nutr. March 2016;57(17):3650-60. [DOI: 10.1080/10408398.2016.1145104]. Retrieved from https://www.researchgate.net/publication/299509825_Riboflavin_and_health_A_review_of_recent_human_research
61. Powers HJ, Weaver LT, Austin S, Wright AJA, Fairweather-Tait SJ. Riboflavin deficiency in the rat: effects on iron utilization and loss. Br J Nutr. May 1991;65(3):487-96. [DOI: https://doi.org/10.1079/BJN19910107]. Retrieved from https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/riboflavin-deficiency-in-the-rat-effects-on-iron-utilization-and-loss/28E9AA7CB41F0C1F28B781DF4BB46677
62. Fairweather-Tait SJ, Powers HJ, Minski MJ, Whitehead J, Downes R. Riboflavin deficiency and iron absorption in adult Gambian men. Ann Nutr Metab. 1992;36(1):34–40. [DOI: https://doi.org/10.1159/000177696].
63. Powers HJ, Bates CJ, Lamb WH. Haematological response to supplements of iron and riboflavin to pregnant and lactating women in rural Gambia. Hum Nutr Clin Nutr. Mar 1985;39(2):117-29 Retrieved from https://www.researchgate.net/publication/19143205_Haematological_response_to_supplements_of_iron_and_riboflavin_to_pregnant_and_lactating_women_in_rural_Gambia
64. Yates CA, Evans GS, Pearson T, Powers HJ. Absence of luminal riboflavin disturbs early postnatal development of the gastrointestinal tract. Dig Dis Sci. June 2003;48(6):1159–64 Retrieved from https://link.springer.com/article/10.023/A:1023785200638
65. Fawzi WW, Msamanga GI, Kupka R, Spiegelman D, Villamor E, Mugusi F, et al. Multivitamin supplementation improves hematologic status in HIV-infected women and their children in Tanzania. Am J Clin Nutr. 2007;85(5):1335–43. [DOI: https://doi.org/10.093/ajcn/85.5.].
66. Suprapto B, Widardo, Suhanantyo. Effect of low-dosage vitamin A and riboflavin on iron-folate supplementation in anaemic pregnant women. Asia Pacific J Clin Nutr. 2002;11(4):263–7. [DOI: https://doi.org/10.1046/j.440-6047.2002.00310.x].
67. Ma AG, Schouten EG, Zhang FZ, Kok FJ, Yang F, Jiang DC, et al. Retinol and riboflavin supplementation decreases the prevalence of anemia in Chinese pregnant women taking iron and folic acid supplements. J Nutr. 2008;138:1946–50, 2008. Retrieved from https://academic.oup.com/jn/article/138/10/1946/4670060
68. Rosado JL, González KE, Caamaño MdC, García OP, Preciado R, Odio M. Efficacy of different strategies to treat anemia in children: a randomized clinical trial. Nutr J. 2010;9(1):40-9. [DOI: 10.1186/475-2891-9-40]. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2955680/
69. Al-Farsi M, Alasalvar C, Morris A, Baron M, Shahidi F. Comparison of antioxidant activity, anthocyanins, carotenoids, and phenolics of three native fresh and sun-dried date (Phoenix dactylifera L.) varieties grown in Oman. J Agric Food Chem. 2005;53(19):7592-9. Retrieved from https://pubs.acs.org/doi/abs/10.1021/jf050579q
70. Biglari F, AlKarkhi AFM, Easa AM. Antioxidant activity and phenolic content of various date palm (Phoenix dactylifera) fruits from Iran. Food Chemistry. 2008;107:1636–41 Retrieved from https://www.sciencedirect.com/science/article/pii/S0308814607010552
71. Ahn E, Kapur B, Koren G. Iron bioavailability in prenatal multivitamin supplements with separated and combined iron and calcium. J Obstet Gynaecol Can. September 2004;26(9):809-13. [DOI: https://doi.org/10.1016/S701-2163(16)30153-0]. Retrieved from https://www.jogc.com/article/S1701-2163(16)-0/pdf
72. Pallarès I, Lisbona F, Aliaga I, Barrionuevo M, Alférez M, Campos MS. Effect of iron deficiency on the digestive utilization of iron, phosphorus, calcium and magnesium in rats. Br J Nutr. 1993;70:609-20. Retrieved from https://pdfs.semanticscholar.org/a0ad/ff93e9e51cc964b6afc7525a59e9e4c0e36a.pdf?_ga=2.63231847.971562518.1528626651-29673584.376232
73. Assirey EAR. Nutritional composition of fruit of 10 date palm (Phoenix dactylifera L.) cultivars grown in Saudi Arabia. J Taibah Univ Sci. 2015;9:75–9. Retrieved from https://ac.els-cdn.com/S1658365514000703/1-s2.0-S-main.pdf?_tid=b0ec0f03-14fd-47fb-93ce-196ccbbcc49a&acdnat=1528629511_e4d120cd8474a89a6458c17d5c701fea
74. Layrisse M, García-Casal MN, Solano L, Barón MA, Arguello F, Llovera D, et al. Vitamin A reduces the inhibition of iron absorption by phytates and polyphenols. Food Nutr Bull. 1998;19(1):3-5. Retrieved from http://journals.sagepub.com/doi/pdf/10.1177/156482659801900101
75. Camaschella C. Iron-deficiency anemia. N Engl J Med. 2015;372(19):1832-43 retrieved from http://legeforeningen.no/PageFiles/214782/2015CamaschellaNEJM%20Iron-def%20anemia.pdf
76. Müller-Lissner S. General geriatrics and gastroenterology: Constipation and faecal incontinence. Best Pract Res Clin Gastroenterol. 2002;16(1):115-33. [DOI: https://doi.org/10.1053/bega.2002.0269].
77. Norton C. The causes and nursing management of constipation. Br J Nurs. 1996;5(20):1252–8. [DOI: https://doi.org/10.12968/bjon.1996.5.20.1252].
78. Norton C. Constipation in older patients: Effects on quality of life. Br J Nurs. 2006;15(4):188-92. [DOI: https://doi.org/10.12968/bjon.2006.15.4.20542].
79. Norton C. Nurses, bowel continence, stigma and taboos. J Wound Ostomy Continence Nurs. 2004;31(2):85-94.
80. Barrett JA, Brocklehurst JC, Kiff ES, Ferguson G, Faragher EB. Anal function in geriatric patients with faecal incontinence. Gut BMJ. 1989;30(9):1244-51. Retrieved from http://gut.bmj.com/content/gutjnl/30/9/.full.pdf
81. Spence-Jones C, Kamm MA, Henry MM, Hudson CN. Bowel dysfunction: a pathogenic factor in uterovaginal prolapse and urinary stress incontinence. Br J Obstet Gynaecol. 1994;101(2):147-52. [DOI: https://doi.org/10.1111/j.471-0528.1994.tb13081.x].
82. Snooks SJ, Barnes PRH, Swash M, Henry MM. Damage to the innervation of the pelvic floor musculature in chronic constipation. Gastroenterology. 1985;89(5):977–81. Retrieved from https://www.gastrojournal.org/article/0016-5085(85)90196-9/pdf
83. Youssef NN, Langseder AL, Verga BJ, Mones RL, Rosh JR. Chronic childhood constipation is associated with impaired quality of life: A case-controlled study. JPGN. 2005;41(1):56-60. [DOI: 10.1097/01.mpg.0000167500.34236.6a].
84. Kollef MH, Schachter DT. Acute pulmonary embolism triggered by the act of defecation. Chest. February 1991;99(2):373–6. [DOI: https://doi.org/10.1378/chest.99.2.373].
85. Williams CL, Bollella M, Wynder EL. A new recommendation for dietary fiber in childhood. Pediatrics. 1995;96(5):985-8. Retrieved from http://pediatrics.aappublications.org/content/pediatrics/96/5/.full.pdf
86. Dukas L, Willett WC, Giovannucci EL. Association between physical activity, fiber intake, and other lifestyle variables and constipation in a study of women. AJG. 2003;98(8):1790–6. [DOI:10.111/j.572-0241.2003.07591.x]. Retrieved from http://mccordresearch.com/sites/default/files/pdf/Prebiotic-Fiber/Fiber%20and%20Constipation.pdf
87. Burton-Freeman B. Dietary fiber and energy regulation. J Nutr. February 2000;130(2):272S–5S. [DOI: https://doi.org/10.1093/jn/130.2.272S]. Retrieved from https://academic.oup.com/jn/article/130/2/272S/4686350
88. Müller-Lissner SA. Effect of wheat bran on weight of stool and gastrointestinal transit time: a meta analysis. Br Med J (Clin Res Ed). 1988;296(6622):615–7. [PMID: 2832033]. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC545244/pdf/bmj00274-0031.pdf
89. Sawaya WN, Khatchadourian HA, Khalil JK, Safi WM, Al-Shalhat A. Growth and compositional changes during the various developmental stages of some Saudi Arabian date cultivars. J Food Sci. 1982;47(5):1489-92. [DOI: https://doi.org/10.111/j.365-2621.1982.tb04967.x]. Retrieved from https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2621.1982.tb.x
90. Al-Shahib W, Marshall RJ. Dietary fibre content of dates from 13 varieties of date palm Phoenix dactylifera L. Int J Food Sci Tech. 2002;37(6):719-21. [DOI: https://doi.org/10.1046/j.365-2621.002.00615.x].
91. Myhara RM, Karkalas J, Taylor MS. The composition of maturing Omani dates. J Sci Food Agric. 1999;79(11):1345-50. [DOI: https://doi.org/10.002/(SICI)097-0010(199908)79:11<1345::AID-JSFA366>3.0.CO;2-V].
92. El-Zoghbi M. Biochemical changes in some tropical fruits during ripening. Food Chem. 1994;49(1):33-7. [DOI: https://doi.org/10.1016/0308-8146(94)90229-1]. Retrieved from https://www.sciencedirect.com/science/article/pii/0308814694902291
93. Marlett JA, McBurney MI, Slavin JL. Position of the American Dietetic Association: Health implications of dietary fiber. J Am Dietet Assoc. July 2002;102(7):993–1000. [DOI: https://doi.org/10.16/S0002-8223(02)90228-2]. Retrieved from https://jandonline.org/article/S0002-8223(02)-2/pdf