International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 3; Issue 2; January 2017; Page No. 50-54

Efficacy of *Safoof Khabsul Hadeed* in iron deficiency anemia during pregnancy: A randomised controlled trial

[1] Jeelani C, [2] Dr. Ismath Shameem, *[3] Dr. Wajeeha Begum, [4] Wasia Naveed

[1] Incharge Principal & HOD, Dept. of Ilaj Bit Tadbeer, Govt. Unani Medical College, Bangalore, Karnataka. India
[2] Lecturer, Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine, Bangalore, Karnataka. India
[3] Reader & HOD, Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine, Bangalore, Karnataka. India
[4] Ex-Principal & HOD, Dept. of Ilmul Qabala wa Amraze Niswan wa Atfal, Govt. Nizamia Tibbi College, Charminar, Hyderabad, Telangana, India

Abstract

Background and Objectives: Anemia is the commonest medical disorder in pregnancy which exists worldwide especially among the developing countries. Iron deficiency anemia during pregnancy continues to be one of the most prevalent single nutrient deficiencies in the world. The objective of the study was to evaluate the efficacy of *Safoof khabsul hadeed* in the management of iron deficiency anemia during pregnancy.

Methods: A single blind, randomized standard controlled study was carried out at Primary Health Centres in Tavarekere, Hegnahalli and Out Patient Department of the Institute's Hospital. Diagnosed cases (n=60) were included and randomly allocated to test (n=30) or control (n=30) groups. Inclusion criteria were primigravida and multigravida in 2nd and early 3rd trimester of pregnancy with mild to moderate degree of iron deficiency anemia and exclusion criteria were patients with systemic diseases, severe anemia and high risk pregnancies. *Safoof khabsul hadeed* 3 gm/day in capsule form and capsule fefol once a day were administered orally for 45 days in test and control groups respectively. The objective and subjective parameters were assessed for improvement during the study period. The results were analyzed statistically using Student't' test and Chi square test.

Results: In both groups, highly significant ($p < 0.001$) improvement was observed in mean hemoglobin percentage and packed cell volume. Better improvement in peripheral smear was observed in control group than test group. No significant improvement in subjective parameters was observed in either group.

Conclusion: The test drug was as effective as standard drug in improving iron deficiency anemia during pregnancy.

Keywords: pregnancy, iron deficiency anemia, hemoglobin percentage, packed cell volume, peripheral smear, *safoof khabsul hadeed*

1. Introduction

Anemia is a hematological condition characterized by the reduction in the concentration of hemoglobin accompanied by reduced number of circulating RBC [1]. Iron deficiency anemia (IDA) is the commonest nutritional deficiency in pregnant women responsible for 95% of the anemia's during pregnancy [2]. Anemia is defined as a decrease in the oxygen carrying capacity of the blood due to decrease in amount of RBCs or hemoglobin or both. WHO defines anemia in pregnancy as 'hemoglobin levels below 11 g/dl [3]. About half of the global maternal deaths due to anemia occur in South Asian countries; India contributes to about 80 % of this mortality ratio [4]. In India, the prevalence of anemia is high because of low dietary intake, poor iron (less than 20 mg /day) and folic acid intake (less than 70 mg/day); poor bioavailability of iron (3-4% only) in phytate and fibre-rich Indian diet and chronic blood loss due to infection such as malaria and hookworm infestations [5]. There are two known factors which contribute to development of iron deficiency anaemia (IDA) in pregnancy; the first is the woman's iron stores at the time of conception and the second is the amount of iron absorbed during gestation. The fact that anemia frequently occur in pregnancy among women in developing countries is an indication that preexisting iron stores are often inadequate and physiological adaptations to pregnancy are insufficient to meet the increased requirements.[3] Maternal complications include increased incidence of antepartum and post-partum hemorrhage, pre-term labour, pre-eclampsia, sepsis and maternal mortality have been associated with anemia during pregnancy. Adverse perinatal outcome in the form of pre-term and small-for-gestational-age babies and increased perinatal mortality rates have been observed in the neonates of anemic mothers [6]. Risk factors for iron deficiency anemia among pregnant women include a diet lacking adequate iron consumption, obesity, and increased parity. Pregnant women of low socioeconomic status, low educational attainment, and ethnic minority are also at an increased risk for IDA [7]. In India, women having preexisting anemia gets aggravated during pregnancy due to increased demand of iron and nutrients and even excess loss of blood during labour, infections in the antenatal and post natal periods and rapid successive pregnancy will worsen the subsequent pregnancy [3]. Hence, iron supplementation in pregnancy has become a standard and routine practice as a preventive treatment for iron deficiency anemia in pregnancy in developing countries. In classical Unani literature, *Jurjani* states that faulty dietary habits and imbalance (deficient iron nutrients) is the cause of

anemia and he recommends that proper diet and digestion is the key to balance the humours and health and if anemia is left untreated, it may lead to *istesqa* [8]. *Razi* mentions that anemia occurs due to altered temperament of liver resulting in pica and edema and recommended treatment with *muqawiyat jigar* and goat's liver [9]. *Ibn Sina* expressed that the excess of *sauda* produces anemia by stagnating between the liver and stomach and thereby interfering with the normal production of blood and other humours [10, 11]. *Majoosi* mentions that anemia is the result of weakness of *quwate muallide khoon* due to *sue mizaj barid* of liver, which down regulates haemopoiesis; simultaneously *zofe kuliya* exists which alter the filtration, as a result *istesqa* develops [12]. *Rabban Tabri* cited that weakness and edema are clinical features and *muqawiyat* as a treatment for anemia [13]. The other famous *Unani* physicians in their respective books described anemia and attributed the cause to weakness of liver, leading to defective haemopoiesis which in turn results in defective cellular nutrition. In liver, *zofe quwate muallide khoon* leads to reduced haemopoiesis, *ghizae kham* reaches the body parts as a result of partial conversion of food in liver. *Sue mizaj haar* and hemorrhage, due to its ill effects alter the function of liver and changes its temperament to cold, which in turn disturbs the metabolism of food [12]. Hence, it is the need of an hour to correct anemia in the entire women folk of the country which is possible only by improving the socio economic and educational status of women in the society [14]. India was the first developing country to take up a National Programme to prevent anemia among pregnant women by providing free iron and folic acid distribution to all pregnant women through primary health care system so that the vast majority of pregnant women who never seek health care, could benefit from this outreach programme. Anemia prophylaxis programme include pregnant women to receive 60 mg elemental iron and 500 μg of folic acid [5]. The enormous costs of modern medicines indicate that alternative strategies are required for better management of iron deficiency anemia in pregnancy in under privileged and population from below poverty line, which can work out investigations and treatment wise cost effective. Traditional medicines, which include Unani medicine as well, are used throughout the world for a range of obstetrical problems and to study such medicines might offer a natural key to unlock an obstetrical pharmacy for the future [15]. considering the above fact, the present study was carried out in the Dept. of Ilmul Qabalat wa Amraze Niswan, National Institute of Unani Medicine Hospital, Bangalore with an objective to evaluate the efficacy and safety of *Safoofe khabsul hadeed* scientifically in the management of iron deficiency anemia during pregnancy. The hypothesis of the study was use of *Safoofe khabsul hadeed* in one group compared with standard drug in other group will be effective in the management of iron deficiency anemia during pregnancy.

2. Material & methods

2.1 Study Design

A standard controlled randomized single blind study was undertaken in the Dept of Obstetrics & Gynecology, National Institute of Unani Medicine, Hospital, Bangalore. Study has been started after the protocol was approved by Institutional Ethical Committee and completed within the duration of one and half year.

2.2 Participants

The study was conducted on 60 diagnosed cases of IDA in pregnant women attending Out Patient Department of the Institute's Hospital and rural Primary Health Centre's in Tavarekere and Hegnahalli in the vicinity of Bangalore who were randomly allocated by lottery method to test (n=30) and control (n=30) groups.

2.3 Selection Criteria

Pregnant women in second and early third trimester of pregnancy with mild to moderate degree of IDA irrespective of parity were included in the study. Pregnant women with severe anaemia, high risk pregnancies, systemic illnesses, hemoglobinopathies and metabolic diseases were excluded. Participants were subjected to routine investigations like CUE, RBS, TLC, DLC, ESR, Blood grouping Rh typing, VDRL, HIV, Stool for routine and microscopy and USG abdomen before trial. The pregnant women were screened at initial visit & those who were fulfilling the inclusion criteria were made entry in the study and written informed consent was obtained from them.

2.4 Study Procedure

From each included pregnant women, detailed history was elicited regarding the age, literacy status, SES, diet; apart from social history like married life, age of marriage, family income, habitation, source of drinking water etc. Past history was enquired especially for menorrhagia, bleeding piles, chronic infections and worm infestations. Obstetrical history regarding gravida, parity, live births and deaths, last child birth and details of present pregnancy were recorded. Complete physical examination was performed to note pallor, icterus, edema, cyanosis, glossitis, stomatitis, koilonychia, lymph adenopathy & thyroid gland enlargement apart from built, nutritional status and weight. Obstetrical examination was concentrated in detail to determine the gestational age, presentation and position of fetus with obstetrical grips and fetal well being by auscultation of FHS either with Fetoscope or Doppler. All findings were recorded in the CRF designed for the study. Specific investigations such as Hb %, PCV, Peripheral smear (for type of anemia), and Safety profile (SGOT, SGPT, Alkaline Phosphatase, Blood Urea, Serum Creatinine) were performed before & after the trial.

2.5 Intervention

In test group, *Safoofe khabsul hadeed* was used as test drug [16]. The ingredients of *Safoofe khabsul hadeed* are *poste Haleela zard (Terminalia chebula), poste Baleela* (*Terminalia belerica), Amla (Emblica officinalis*), *Filfil syah (Piper nigrum),Filfil daraz (Piper Longum), Sonth (Zingiber officinale),Gudh* (*Jaggery*) each 12 g, *Khabsul hadeed* (*ferroso-ferric oxide)* 24 g. The ingredients of test drug possess tonic, stomachic, digestive, carminative, hepatoprotective, antiulcer, antiinflammatory, antioxidant and immunomodulatory activities etc [17-22] The medicines were provided by NIUM pharmacy, *Khabsul hadeed* was *mudabber* as per the method mentioned in classical text [23]. All ingredients were grinded to make fine powder [16, 23]. And were administered orally in a dose of 3g/day [16] in capsule form (3 capsules of 1 g each) and in control group capsule Fefol (200

mg of ferrous sulphate and 500 µg of folic acid) once daily was administered orally for 45 days.

2.6 Blinding and Compliance
Blinding was maintained as medicine was dispensed in similar pack to one patient at a time. Patients compliance was assessed at each visit by examining the packets in which medicines was dispensed at prior visit.

2.7 Assessment cum Follow up
Patients were followed at 0 day, 21st day, and 45th day. During this period, subjective & objective parameters were assessed for improvement. Patients were also enquired for any adverse effect of drug during the study; Repeat biochemical test were carried out after completion of trial.

2.8 Statistical Analysis
Student't' test and Chi square test were used to analyze the results. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

3. Results

Table 1: Comparison of baseline characteristics

Sl. No.	Base Line Characteristics	No. of Patients (n = 60)
	Mean Age (years)	
1.	Test Group	22.03+3.508
2.	Control Group	21.76+2.431
	SES	
1.	Lower	48(80 %)
2.	Middle	12(20 %)
	Literacy Status	
1.	Illiterate	24(40 %)
2.	Primary	31(51.66 %)
3.	Secondary	5(8.33 %)
	Gravida	
1.	Gravida 1	34(56.66 %)
2.	Gravida 2	20(33.33 %)
3.	Gravida 3	4(6.66 %)
4.	Gravida 4	2(3.33 %)
	Gestational age(wks)	
1.	16- 20 Wks	25(41.66 %)
2.	21- 25 Wks	35(58.33 %)

Table 2: Comparison of subjective parameters in two groups

Sl. No.	Clinical Features	Present / Absent	Test group		Control group	
			BT	AT	BT	AT
			No. (%)		No. (%)	
1.	Pallor	Present	24(80)	23(76.66)	25(83.33)	22(73.33)
		Absent	6(20)	7(23.33)	5(16.66)	8(26.66)
2.	Puffiness of face	Present	12(40)	11(36.66)	20(66.66)	18(60)
		Absent	18(60)	19(63.33)	10(33.33)	12(40)
3.	Pedal edema	Present	5(16.66)	5(16.66)	5(16.66)	4(13.33)
		Absent	25(83.33)	25(83.33)	25(83.33)	26(86.66)
4.	Glossitis	Present	5(16.66)	5(16.66)	6(20)	5(16.66)
		Absent	25(83.33)	25(83.33)	24(80)	25(83.33)
5.	Stomatitis	Present	5(16.66)	5(16.66)	6(20)	5(16.66)
		Absent	25(83.33)	25(83.33)	24(80)	25(83.33)
6.	Early fatigue	Present	10(33.33)	10(33.33)	13(43.33)	12(40)
		Absent	20(66.66)	20(66.66)	17(56.66)	18(60)

Table 3: Comparison of objective parameters in two groups

Mean Hemoglobin (gm %)	BT	AT	P- Value
Test group	8.8	10	<0.001**
Control group	8.6	10	<0.001**
P- Value		0.2818	
Mean PCV (%)	**BT**	**AT**	**P- Value**
Test group	28	32	<0.001**
Control group	28	32	<0.001**
P- Value		0.7801	

Peripheral Smear (%)			
Test group	BT	AT	% change
MHA	18(60 %)	7(23.33 %)	+ 36.67
NHA	12(40 %)	23(76.66 %)	- 36.66
NBP	0	0	
Control group			
MHA	26(86.66 %)	4(13.33 %)	+73.33
NHA	4(13.33 %)	13(43.33 %)	- 30.00
NBP	0	13(43.33 %)	

(MHA- Microcytic hypochromic anemia, NHA- Normocytic hypochromic anemia, NBP-Normal blood picture)

4. Discussion

Base line characteristics

Mean age of the patients was 22.03+3.508 and 21.76+2.431 in test and control groups respectively. Majority of pregnant women, (80%) were belonged to low socio economic status and it was observed that anemia was more prevalent in low SES women due to poor nutrition which is considered as one of the risk factor for IDA in pregnancy.[7] 58.33% pregnant women were in 21-25 weeks and 41.66 % in 16-20 weeks of gestation; literature report says that increase demand of iron occur mainly in second trimester of pregnancy [24]. More over, majority of patients seek ANC during the second trimester when they suffer from clinical manifestation of IDA in pregnancy to receive the treatment. Maximum pregnant women were primi gravida's (56.6%), this probably may be due to young girls who had early pregnancy with poor nutrition.

Subjective parameters

No significant improvement in (pallor, puffiness of face, pedal edema, glossitis, stomatitis and early fatigue) of IDA was observed in both groups. These may be probably due to short duration of treatment and further continuation of the treatment is required to reduce the chronicity of anemia.

Objective parameters

Mean Hb%

Before treatment, it was 8.8 gm% in test and 8.6 gm% in control groups; after treatment, it was improved to 10 gm% in both the groups with $p < 0.001$**, considered highly significant.

Mean PCV

In both groups, it was 28% before treatment which was improved to 32% after treatment with $p < 0.001$**, suggestive of highly significant statistically.

Thus, significant improvement was observed in Hb% and PCV% after 45 days of treatment.

Peripheral smear

Before treatment, microcytic hypochromic anemia was detected in 60% patients which reduced in 23.33% patients after treatment with a percentage change of 36.67% and normocytic hypochromic anemia was detected in 40% patients which improved in 76.66% patients after treatment with a percentage change of 36.67% in test groups; while in control group, 86.66% patients had microcytic hypochromic anemia which reduced in 13.33% patients after treatment with a percentage change of 73.33%, normocytic hypochromic anaemia was detected in 13.33% patients which improved in 43.33% after treatment with a percentage change of 30% and normal blood picture was observed in 43.33% patients after treatment. Better improvement in peripheral smear was observed in control group as compared to test group.

Improvement in objective parameters in test group was attributed to *muqawi jigar wa meda wa tehal* properties of *Safoofe khabsul hadeed* as it is indicated in *zofe meda, zofe jigar,* ascites, splenomegaly and bleeding piles. Further more, ingredients of this formulation possess tonic, stomachic, digestive, carminative, hepatoprotective, antiulcer, anti-inflammatory, antioxidant and immunomodulatory activities [17-22] Moreover, pharmacologically research report reveals that *Sonth* [17] act as a tonic for the digestive system and improve liver functions, *Halela* [18] increases the gastrointestinal motility, *Sonth, Balela,* and *Filfil syah* [17, 19, 22]. act as antithrombotic and thrombolytic, *Amla* is a rich source of vitamin C which helps in absorption of iron and reduces IDA [20] and Jaggery contains30 mg iron/100g apart from Vitamin B_1 and B_2. *Khabsul hadeed* is especially useful in anemia, dysmenorrhoea, menorrhagia, chlorosis, dyspepsia, intestinal worms, kidney diseases and albuminuria. *Maamoon* recommended use of iron rust and its *mu'ajeen* for strengthening the stomach, heart and brain [25]. *Khabsul hadeed* with *tirphala* is a house hold remedy, commonly used as an alternative tonic in the pregnant state [26, 27].

Moreover, the test drug was proved to be safe during pregnancy as the safety parameters were normal and no abnormal clinical manifestation was observed during the study. Finally, it can be inferred that the effect of test drug was comparable with that of control drug in improving IDA in pregnancy; hence, it can be used as an alternate therapy in those pregnant women who have intolerance to oral iron therapy. Strength of the study was this study was first of its kind conducted on pregnant women using Unani formulations, hence cannot be compared with the previous studies. Limitation of the study were short duration of intervention, short follow up, Serum Ferritin and Total iron binding capacity (TIBC) were not done during the study period. Future trials for longer duration with long term follow up are required to confirm the efficacy of test drug formulation.

5. Acknowledgement

The authors are thankful to Prof. M. A. Jafri, Director, NIUM for providing all the required facilities for accomplishment of research work and Dr. G Sofi, Reader in the Dept. of Ilmul Advia, NIUM for performing the statistical analysis.

6. References

1. Veena AV, Jyothi Y, Pokhrel R, Ghosh R, Patidhar R. Comparative anti anemic activity of *Azadirachta indica* leaves and its combination with *Emblica officinalis* in phenyl hydrazine induced anemia using rats. Journal of

Chemical and Pharmaceutical Research. 2015; 7(8):1019-22.
2. Kriplani A, Mahey R, Dash BB, Kulshreshta V, Agarwal N, Bhatla N. Intravenous iron sucrose therapy for moderate to severe anemia in pregnancy. Indian J Med Res July. 2013:78-82.
3. Osungbade KO, Oladunjoye AO. Preventive Treatments of Iron Deficiency Anemia in Pregnancy: A Review of Their Effectiveness and Implications for Health System Strengthening J.Pharmacy. 2012 July.
4. Mudaliar AL, Menon MKK. Clinical obstetrics. Chennai (India): Orient Longman Limited. 1997, 39.
5. Kalaivani K. Prevalence & consequences of anemia in pregnancy. Indian J Med Res. 2009; 130:627-33.
6. Sharma JB, Shankar M. Anemia in Pregnancy. Journal of International Medical Sciences Academy Oct- Dec. 2010; 23(4):253-60.
7. National business group of health. An employer's guide to preventive services. Updated. 10/3/2011.
8. Jurjani AH. Zakheerae Khawarzam Shahi (Urdu translation by Khan HH). New Delhi: Idarae Kitabul Shifa. 2010, 414-15.
9. Razi ABZ, Kitabul Mansoori. New Delhi: CCRUM. 1991; 20:179.
10. Ibn Sina. Al Qanoon Fil Tibb (Urdu translation by Kantoori GH). New Delhi: Idarae Kitabul Shifa; 2010, 884-85.
11. Shah HM. The General Principles of Avicenna's Canon of Medicine. New Delhi: Idarae Kitabul Shifa; 2007, 45.
12. Majoosi ABA. Kamilus Sana'a (Urdu translation by Kantoori GH). Vol I. New Delhi: Idarae Kitabul Shifa, 2010; 161:519-21.
13. Tabri AHAM. Al Moalijatul Bukhratia. Vol III. New Delhi: CCRUM; N.A, 318-19.
14. ICMR (Indian council of medical research).Iron absorption and its implications on strategies to control IDA. 2000; 30(2):15-20.
15. Bhatt RV. Management of pregnancy anemia obsteticians dilemma. J of obst and gynae of India Dec. 1998; 48(6):96-100.
16. Azam khan. Magzanul Mujarribat Qarabadeene Azam. New Delhi: Ejaz Publication house, 2009, 408.
17. Singh SK, Patel JRA, Bachle D. A review on *zingiber officinale*: A natural gift. Int J Pharm Bio Sci. 2014; 5(3):508-25.
18. Rathinamoorthy R, Thilagavathi G. *Terminalia chebula* - Review on Pharmacological and Biochemical Studies. Int J PharmTech Research. 2014; 6(1):97-116.
19. Anindita D, Sikha B, Biswajit D. Pharmacological activities of Baheda (*Terminalia bellerica)*: A review. J Pharmacognosy and Phytochemistry. 2016; 5(1):194-97.
20. Dasaroju S, Gottumukkala KM. Current Trends in Research of *Emblica officinalis (Amla):* A Pharmacological Perspective. Int. J. Pharm. Sci. Rev. Res. 2014; 24(2):150-59.
21. Zaveri1 M, Patel A, Khandhar A, Patel S. Chemistry and Pharmacology of *Piper Longum* L. Int J of Pharm Sciences, Review & Research. 2010; 5(1):67-76.
22. Kadam PV, Yadav KH, Patel FA, Keijiker MJP. Pharmacognostic, Phytochemical, & physicochemical studies of *Piper Nigram* L. Int, Res, J Pharma. 2013; 4(5):189-93.
23. Anonymous. National Formulary of Unani medicine. Vol I. New Delhi: Hukoomat hind, 2003, 445.
24. Dutta DC. Text book of Obstetrics.7th ed. New Delhi: Jaypee brother's medical publishers (P) Ltd, 2013, 55.
25. Prevention and management of severe anemia in pregnancy: Report of a technical working group, 1991. Geneva,WorldHealthOrganization,1994,WHL/FHE/MSM/93.3
26. Prophylaxis against Nutritional Anemia among Mothers and Children. Technical Information, MCH No. 1. Ministry of Health and Family Welfare, GOI, New Delhi, 1970, 3.
27. Nadkarni KM. Indian Materia Medica. Mumbai: Popular Prakashan Pvt. Ltd, 2009, 1205-10.