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Health status and fatigue of postpartum anemic women: a prospective cohort study

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ABSTRACT

Objective: The incidence of postpartum anemia is high. Current therapy consists of iron supplementation or blood transfusions, based on the assumption that these treatments improve health status (HS) and reduce fatigue. The aim of this study was to compare HS and fatigue in postpartum women with and without anemia.

Study design: This prospective cohort study was performed in The Netherlands between April 2008 and August 2010 and involved 112 anemic (hemoglobin [Hb] < 10.5 g/dL) and 108 non-anemic (Hb ≥ 10.5 g/dL) women. The anemic women received oral iron supplementation. Within 48 h and 5 weeks after delivery, HS was measured using the 36 item Short-Form Health Survey (SF-36) and fatigue was measured using the Checklist Individual Strength (CIS). ANOVA for repeated measures was used to compare HS and fatigue scores among groups and across time.

Results: After adjustment for confounding variables, there were no differences in any of the HS and fatigue scores. HS and fatigue seem to be more influenced by a complicated delivery than by anemia. HS and fatigue scores significantly improved over time in all women.

Conclusion: HS and fatigue were not different among women with and without postpartum anemia.

Introduction

Postpartum anemia is a worldwide problem with a prevalence ranging from 22% to 50% in developed countries, and from 50% to 80% in developing countries [1]. Major causes of postpartum anemia include pre-existing iron deficiency and iron deficiency anemia (IDA) in combination with excessive blood loss during delivery [2]. Ferritin, a marker used to diagnose IDA, is not useful in the early postpartum period because of its prominent role in the acute phase response during parturition [3,4]. Therefore, the definition and indication for the treatment of postpartum anemia are based on hemoglobin (Hb) level [3,5,6].

Fatigue is considered the major symptom of anemia [7]. This type of fatigue is not an isolated physical symptom, but involves lethargy, decreased mental alertness, physical weakness, and poor concentration [8]. Uncorrected IDA may have a negative impact on maternal cognition, mood and behavior, and could thereby alter mother-child interactions [9,10]. Therefore, health status (HS), a multidimensional concept that incorporates the self-perceived functioning of physical, psychological, and social aspects of life [11], is regarded as reduced in women with postpartum anemia [1].

To date, few studies have compared HS and fatigue between women with and without postpartum anemia. An observational study examined the natural course of HS and fatigue during the first 6 postpartum weeks in relation to mode of delivery [12]. In addition to physical HS being significantly poorer after a cesarean section than after a vaginal delivery, Hb level was found to be correlated with physical HS and fatigue immediately postpartum. This correlation had disappeared 1 week postpartum. If necessary, women were treated postpartum with oral iron and folic acid. To

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our knowledge, however, HS and fatigue scores have not been compared in women with and without postpartum anemia.

In the present study, we examined differences in HS and fatigue between anemic and non-anemic women during the first 5 weeks postpartum. We also investigated changes in HS and fatigue over time.

Materials and methods

The current prospective cohort study was performed between April 2008 and August 2010 at a large teaching hospital in Tilburg, in the southern part of The Netherlands. The threshold for the definition of anemia in the early postpartum period varies between <11.0 g/dL and <10.0 g/dL [1,3]. Anemia in the current study was defined according to the Dutch guidelines as Hb concentration <10.5 g/dL [5]. The anemic women were part of a randomized controlled trial that showed no between-group differences in Hb, HS, and fatigue after receiving oral iron supplementation with and without folic acid [13]. Non-anemic women (Hb ≥ 10.5 g/dL) received no treatment and were followed prospectively during the study.

Women were eligible for inclusion if they were ≥18 years old, thoroughly understood the Dutch language, and had indications for Hb determination within 48 h after delivery, including estimated blood loss >500 ml, delivery by cesarean section, manual removal of the placenta, and clinical symptoms of anemia. Women were excluded if: their Hb was <6.4 g/dL (because the hospital protocol indicates the need for packed red cell transfusion); they were addicted to alcohol or drugs; they had hematological diseases such as hemoglobinopathies, sickle cell disease, thalassemia, and Hemolysis Elevated Liver enzymes and Low Platelets syndrome (HELLP); they had vitamin B12 deficiency (serum vitamin B12 <100 nmol/L and holotranscobalamin <20 pmol/L); they had chronic inflammatory disease; they were being treated with methotrexate; or they had contra-indications to treatment with folic acid or ferrous fumarate.

The study protocol was approved by the local ethics committee (file number NL21797.028.08). All women received oral and written information about the study, and provided oral and written informed consent.

Maternal venous blood was collected and questionnaires to assess HS and fatigue were completed within 48 h postpartum (T0) and again at the outpatient clinic 5 weeks after delivery (T5). The outcome measures were HS and fatigue improvement among groups and across time.

Hemoglobin was analyzed using an Advia 2120i automated cell counter (Siemens Healthcare Diagnostics, Breda, The Netherlands). Hb, measured as mmol/L, was converted to g/dL by multiplying by 1.6115.

HS was measured using the self-reported standardized 36 item Short-Form Health Survey (SF-36), a generic questionnaire that was chosen because it covers all HS domains and is often used in determining HS in postpartum women, allowing good comparability among studies. The 36 items are organized into eight scales:

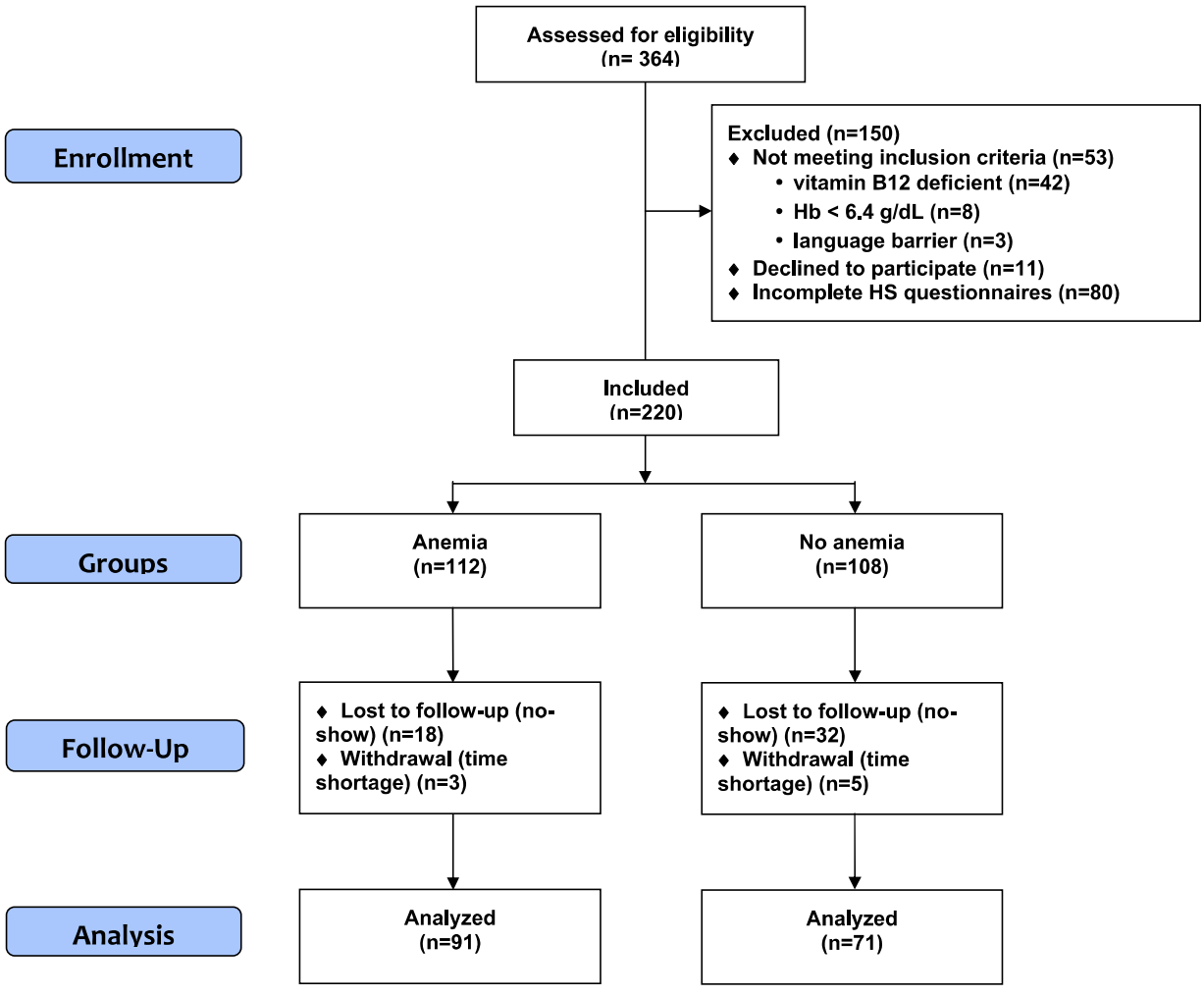

Fig. 1. Flow of participants through the study.

physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Each item has a scoring range from 0 to 100, with higher scores representing better levels of functioning [14]. In addition, the SF-36 provides a physical component summary (PCS) and a mental component summary (MCS). The SF-36 has demonstrated good psychometric properties in postpartum women [15]. Fatigue was measured using the Checklist Individual Strength (CIS), a multidimensional scale that quantifies subjective fatigue and related behavioral aspects [16]. This questionnaire was chosen because fatigue is a symptom of anemia. The 20 items cover four dimensions: subjective experience of fatigue, reduced concentration, reduced motivation, and reduced physical activity level. Each item has a scoring range from 1 to 7, with higher scores indicating greater fatigue. The CIS has been shown reliable and valid in patients with chronic fatigue syndrome, as well as in healthy populations [17].

Statistical analyses were performed using SPSS 15.0. Continuous variables at baseline were compared by independent sample *T*-tests and nominal variables by Chi-square tests. ANOVA for repeated measure was used to compare HS and fatigue scores among groups and across time. We corrected for mode of delivery, as cesarean section has been shown to affect physical HS [12]. Baseline differences were also corrected by including these variables as covariates. We report both the unadjusted and adjusted results, to show the impact of these covariates. To make a more comprehensive assessment of the effect of anemia, the amount of blood loss, and mode of delivery on HS and fatigue, linear regressions were performed with the SF-36 and CIS subscales as dependent variables. We also corrected for the number of tests using the Bonferroni rule. Results are reported as the mean ± standard deviation (SD), mean ± standard error of the mean (SEM), or percentage (%), as appropriate. A *P*-value less than 0.05 was considered statistically significant.

Results

Of the 364 women screened, 53 did not meet the inclusion criteria, including 42 with vitamin B12 deficiency, eight with Hb < 6.4 g/dL, and three due to a language barrier. Eleven women declined to participate. Eighty women did not complete the baseline HS questionnaires for unknown reasons and were therefore excluded.

A total of 220 women were included in the study, including 112 with anemia and 108 without anemia. A total of 50 participants were lost to follow-up after repeatedly not showing up for follow-up appointments. Eight withdrew before the follow-up appointment, mostly because of a lack of time. Thus, 91 anemic women and 71 non-anemic women were analyzed (Fig. 1).

The demographic and clinical characteristics of the participants at baseline are shown in Table 1. The method of delivery differed significantly among the groups, with cesarean sections performed in 37.5% of the women with anemia and 71.3% of non-anemic women ($P < 0.013$). As expected, blood loss was significantly greater in anemic than in non-anemic women ($P < 0.0001$).

Analysis of results on the SF-36 showed that, without adjusting for baseline differences (including delivery method), there were significant differences in physical functioning ($P = 0.008$) and PCS ($P = 0.046$) between anemic and non-anemic women (Table 2). After adjustment for baseline differences, including delivery method, there were no between-group differences in any of the HS and fatigue scores (Table 3).

Both before and after adjustment for baseline differences (including delivery method), there were significant improvements over time in both groups with regard to the SF-36 physical functioning, social functioning, role physical, mental health, vitality, bodily pain, PCS, MCS, and total scores ($P < 0.0001$), and the CIS subscales subjective fatigue, motivation, and activity, and total scores ($P < 0.0001$).

Linear regression analysis showed no association of anemia and the amount of blood loss with any of the SF-36 and CIS scales at both time points. Mode of delivery was associated with scores on the SF-36 scales physical functioning ($P < 0.0001$), social functioning ($P = 0.027$), bodily pain ($P = 0.023$), and PCS ($P = 0.007$) on T0. On T5, mode of delivery was associated with scores on the SF-36 scales physical functioning ($P < 0.0001$), role physical ($P = 0.017$), bodily pain ($P = 0.008$), and PCS ($P = 0.002$), and on the CIS scale reduced activity ($P = 0.002$).

Comments

This prospective cohort study assessing postpartum HS and fatigue found no differences among groups of women with and without postpartum anemia adjusting for baseline differences in mode of delivery, and the amount of blood loss. HS and fatigue scores significantly improved over time in all women.

Cesarean section was significantly more common in women without than with postpartum anemia, a difference that may explain the significant differences in physical functioning and PCS scores between these two groups before adjustment, since cesarean section is known to affect physical HS [12]. The anemic group more frequently delivered vaginally, with increased of blood loss, than the non-anemic group. By contrast, a previous study

Table 1
Patient demographic and clinical characteristics at baseline (T0).[a]

	Anemia (n = 112)	No anemia (n = 108)
Age at entry (years)	30.6 ± 4.7	31.4 ± 4.0
BMI before pregnancy (kg/m^2)	25.2 ± 5.4	25.4 ± 5.6
Twin pregnancies	4 (3.6)	1 (0.9)
Ethnicity:		
Caucasian	97 (86.6)	97 (89.9)
Turkish	5 (4.5)	7 (6.5)
African	5 (4.5)	2 (1.9)
Asian	3 (2.7)	0 (0.0)
South American	2 (1.8)	2 (1.9)
Highest education:		
Lower	6 (5.6)	1 (1.0)
Medium	56 (52.3)	50 (47.6)
High	45 (42.1)	54 (51.4)
Smoking	15 (13.5)	7 (6.5)
Multivitamin use	45 (40.2)	54 (50.0)
Parity at baseline	1.5 ± 0.8	1.6 ± 0.7
Gestational age at delivery (weeks)	40.0 ± 1.5	39.7 ± 1.4
Delivery method:[a]		
Vaginal	70 (62.5)	31 (28.7)
Cesarean section	42 (37.5)	77 (71.3)
Elective cesarean section	12 (28.6)	43 (55.8)
Emergency cesarean section	30 (71.4)	34 (44.2)
Estimated blood loss (ml)[b]	824 ± 416	505 ± 280
Infant feeding:		
Breastfeeding	70 (62.5)	75 (69.4)
Bottle (formula) feeding	42 (37.5)	33 (30.6)

Numbers are mean ± SD or number (percentage).
BMI = Body Mass Index (calculated as weight in kilograms divided by the square of height in meters).
[a] Chi square: $P = 0.013$ between vaginal delivery and cesarean section, $P < 0.0001$ between vaginal delivery, elective cesarean section, and emergency cesarean section.
[b] Independent sample *T*-test: $P < 0.0001$.

Table 2
Health status and fatigue by group at baseline (T0) and at 5 weeks postpartum (T5).[a]

	Anemia		No anemia	
	T0	**T5**	**T0**	**T5**
SF-36				
Physical functioning[b]	41.5 ± 3.5	82.0 ± 1.9	30.0 ± 4.0	75.9 ± 2.2
Social functioning	67.7 ± 2.8	85.0 ± 2.2	63.8 ± 3.2	78.2 ± 2.5
Role physical	34.4 ± 4.0	69.4 ± 4.4	32.2 ± 4.5	55.4 ± 5.0
Role emotional	85.4 ± 3.5	91.4 ± 3.9	81.9 ± 4.0	89.2 ± 4.5
Mental health	78.9 ± 1.6	86.3 ± 1.3	76.8 ± 1.8	84.9 ± 1.5
Vitality	54.7 ± 2.1	66.1 ± 2.6	55.6 ± 2.4	65.4 ± 3.0
Bodily pain	60.2 ± 3.1	84.2 ± 2.1	55.8 ± 3.6	80.8 ± 2.4
General health	80.1 ± 1.5	79.9 ± 1.7	78.4 ± 1.7	76.5 ± 1.9
Health change	44.8 ± 2.1	46.4 ± 2.0	46.8 ± 2.4	44.4 ± 2.3
PCS[c]	53.9 ± 2.3	78.9 ± 2.0	49.4 ± 2.6	72.7 ± 2.3
MCS	71.5 ± 1.8	82.7 ± 1.9	69.4 ± 2.1	79.4 ± 2.1
Total	60.8 ± 1.7	76.9 ± 1.6	57.8 ± 1.9	72.7 ± 1.8
CIS				
Subjective fatigue	35.2 ± 1.3	26.2 ± 1.2	34.8 ± 1.5	29.0 ± 1.3
Reduced motivation	13.1 ± 0.6	8.6 ± 0.4	13.3 ± 0.7	9.9 ± 0.5
Reduced activity	11.8 ± 0.6	8.1 ± 0.5	12.3 ± 0.6	9.3 ± 0.5
Reduced concentration	15.0 ± 0.8	13.4 ± 0.8	15.4 ± 0.9	14.6 ± 0.9
Total	74.8 ± 2.7	56.4 ± 2.3	75.0 ± 3.1	62.8 ± 2.6

Numbers are mean ± SEM.
SF-36 = 36 item short-form health survey, PCS = physical component summary, MCS = mental component summary.
CIS = checklist individual strength.
[a] Repeated measures ANOVA, without adjustments for baseline differences (mode of delivery and estimated blood loss).
[b] $P = 0.008$.
[c] $P = 0.046$.

Table 3
Adjusted health status and fatigue by group at baseline (T0) and at 5 weeks postpartum (T5).[a]

	Anemia		No anemia	
	T0	**T5**	**T0**	**T5**
SF-36				
Physical functioning	36.8 ± 3.5	79.4 ± 1.9	36.8 ± 4.0	79.2 ± 2.2
Social functioning	65.8 ± 2.9	84.0 ± 2.3	67.5 ± 3.4	79.3 ± 2.7
Role physical	32.8 ± 4.3	66.1 ± 4.6	35.2 ± 4.9	59.4 ± 5.3
Role emotional	85.9 ± 3.7	93.6 ± 4.2	80.5 ± 4.3	85.9 ± 4.8
Mental health	79.2 ± 1.7	87.0 ± 1.4	76.1 ± 2.0	84.1 ± 1.6
Vitality	54.7 ± 2.2	66.0 ± 2.8	56.0 ± 2.6	65.8 ± 3.2
Bodily pain	58.4 ± 3.3	81.9 ± 2.2	58.7 ± 3.9	83.6 ± 2.5
General health	79.6 ± 1.6	79.7 ± 1.8	79.1 ± 1.8	76.8 ± 2.0
Health change	44.4 ± 2.3	45.5 ± 2.2	48.2 ± 2.6	45.7 ± 2.5
PCS	51.9 ± 2.3	76.9 ± 2.1	52.5 ± 2.7	75.1 ± 2.4
MCS	71.3 ± 2.0	83.1 ± 2.0	69.8 ± 2.2	78.7 ± 2.3
Total	59.8 ± 1.8	76.1 ± 1.7	59.6 ± 2.1	73.6 ± 2.0
CIS				
Subjective fatigue	35.3 ± 1.4	26.3 ± 1.3	34.6 ± 1.6	28.9 ± 1.5
Reduced motivation	13.0 ± 0.7	8.7 ± 0.5	13.3 ± 0.8	9.8 ± 0.5
Reduced activity	12.0 ± 0.6	8.4 ± 0.5	12.2 ± 0.7	9.0 ± 0.6
Reduced concentration	14.8 ± 0.8	13.2 ± 0.9	15.4 ± 1.0	14.7 ± 1.0
Total	74.8 ± 2.9	56.6 ± 2.5	74.8 ± 3.3	62.5 ± 2.9

Numbers are mean ± SEM.
SF-36 = 36 item short-form health survey, PCS = physical component summary, MCS = mental component summary.
CIS = checklist individual strength.
[a] Repeated measures ANOVA, adjusted for baseline differences (mode of delivery and estimated blood loss).

found that blood loss was greater in women who underwent cesarean section than those who delivered vaginally, although postpartum Hb levels did not differ significantly [18].

To our knowledge, this is the first study to compare all domains of HS and fatigue (physical, mental, and social functioning) in postpartum women with and without anemia. In contrast to previous findings, we observed no association between anemia and fatigue conceptions [7]. In agreement with an earlier study, we found that HS and fatigue scores improved over time in all groups and were not associated with Hb level [12].

A limitation of the present study was the selection bias. Hb and iron status was only determined if indicated. Since all women who underwent a cesarean section were subjected to routine blood analysis, 54% of the enrolled women delivered by cesarean section. We therefore adjusted for mode of delivery in our analyses. Based on the time required for erythroblast maturation, we expected that improvements in Hb concentrations and any differences in HS and fatigue scores among the groups would have been observed after 5 weeks [19]. Others have shown, however, that the average periods required to reach full recovery on physical HS scales were 3 weeks after vaginal delivery, 6 weeks after elective cesarean section, and more than 6 weeks after emergency cesarean section [12]. We performed a subgroup analysis to determine the effect of elective and emergency cesarean section on HS and fatigue and found no differences in any of the HS and fatigue scores between the groups

(data not shown). Another limitation of this paper is that there is no blood measurement before delivery, since prepartum anemia combined with acute bleeding anemia due to blood losses at delivery are the major causes of postpartum anemia [1]. In The Netherlands, blood examination is regularly performed during pregnancy, and not routinely when women are admitted to the hospital for delivery. In accordance with international guidelines, iron treatment is based on Hb measurement at 48 h postpartum [1,3]. Since prepartum Hb was lacking, anemic postpartum women might have been anemic before delivery. It is known that chronically anemic women get used to decreased energy levels; this could explain why no differences were found in HS and fatigue scores between anemic and non-anemic postpartum women. Future research should examine the effect of acute and chronic anemia postpartum on HS and fatigue.

Most studies on postpartum anemia have focused on hematological outcomes after iron supplementation, with many showing that iron had a positive effect on maternal iron status [6]. Our results, however, suggest that iron supplementation may not be necessary in the treatment of postpartum anemia. Since HS and fatigue did not differ among the groups, iron supplementation may only worsen HS because of its known side effects. A prospective longitudinal study is needed to determine the relationships between severity of postpartum anemia and maternal morbidity, HS, and fatigue in women who do and do not receive iron supplementation.

In conclusion, postpartum women with anemia did not show a greater improvement in HS and fatigue when compared with non-anemic women during the first 5 weeks postpartum. All women showed significant improvements in HS and fatigue over time.

Condensation

Postpartum health status and fatigue are not different among anemic women and non-anemic women.

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