ABSTRACT

Objectives. The purpose of this study was to investigate iron status in a population with a high proportion of miners in the northernmost part of Norway.

Study Design. Cross-sectional, population-based study performed in order to investigate possible health effects of pollution in the population living on both sides of the Norwegian-Russian border.

Methods. All individuals living in the community of Sør-Varanger were invited for screening in 1994. In 2000, blood samples from 2949 participants (response rate 66.8 %), age range 30-69 years, were defrosted. S-ferritin and transferrin saturation were analysed in samples from 1548 women and 1401 men. About 30 % (n = 893) were employed in the iron mining industry, 476 of whom were miners and 417 had other tasks in the company. Type and duration of employment and time since last day of work at the company were used as indicators of exposure.

Results. Both s-ferritin levels and transferrin saturation were higher in men than in women. S-ferritin increased with increasing age in women, while the opposite was true for men. Iron deficiency occurred with higher frequencies in women (16 %) than in men (4 %). Iron overload was uncommon in both sexes. Adjustment for smoking and self-reported pulmonary diseases did not show any effect on iron levels.

Miners had non-significant higher mean s-ferritin and transferrin saturation than non-miners. Neither duration, nor time since employment in the mine, had any impact on iron status.

Conclusions. Our analyses did not show any associations between being a miner in the iron mining industry and serum iron levels compared to the general population.

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Keywords: ferritin, transferrin saturation, miners, non-miners, industry, Sør-Varanger
INTRODUCTION

Sixty years ago, investigators claimed that adults and children living north of the Artic Circle had lower haemoglobin levels than in the rest of the country (1). Different causes were suggested. The theory was that haemoglobin levels could be influenced by the intensity of sunlight, as well as by nutritional factors, such as shortage of meat and vegetables in the spring time. As a consequence, vitamin C and iron would be insufficient, or suboptimal, in the late winter and spring seasons. In the 1960s, Natvig published a study showing that the daily supply of vitamin C and iron in the diet was adequate for the population in the municipality of Kirkenes (2). The iron industry was the major employer in the local society. Natvig and co-workers also collected data from a voluntary national industrial health service program, which showed that haemoglobin levels were higher in male wage-earners in the iron and mechanical industries (3). These studies did not measure iron status in the general population. With this background, we wanted to test if geographic localization and iron mining could affect iron status in a population living in the arctic.

In normal subjects, the total average daily loss of iron is about 1-2 mg. These losses are balanced by an equivalent amount of iron absorbed from the diet. Iron is absorbed by the intestinal mucosal cells, which also regulates this absorption. In the plasma, iron is bound to a transport protein, transferrin, which provides the main means of iron transport. S-ferritin and transferrin saturation values are the two most widely used biochemical markers of body iron status. S-ferritin concentration significantly correlates with body iron stores in normal subjects, but s-ferritin is also an acute-phase reactant, elevated during infection, chronic inflammation and liver disease (4).

We had the possibility to use blood samples from a screening study carried out in the Sør-Varanger municipality in 1994, namely the Norwegian-Russian Health Study (5-8). At the time of the screening, A/S Sydvaranger was still the main employer in the municipality.

The aims of this study were (1) to evaluate the iron status in a multiethnic population in the east of Finnmark county in northern Norway, and (2) to investigate whether the iron status of miners was influenced by their work in an iron mine.

MATERIAL AND METHODS

Study location and background
The Sør-Varanger municipality of Finnmark County is situated in the north-eastern part of Norway, north of the Artic Circle at the 70th parallel, close to the common border between Norway and Russia (Fig. 1). In 1994, about 9800 people lived in Sør-Varanger. There has been a mining and iron smelting industry in Kirkenes for the last hundred years, but the mine closed in 1997. The city of Kirkenes was established because of the mining activity. The mine was in Bjørnevatn, and the ore was transported approximately 12 miles to Kirkenes, where iron-pellets were produced and, thereafter, exported by sea. The peak production period was in the 1980s, with an annual production of 24 million tons of iron mineral.
The Norwegian-Russian Health Study focused on possible health effects of nickel pollution from the Russian smelters in Nikel and Zapolyarny, located about 6 and 25 miles from the Norwegian border, respectively (5-7). The study collected information about different diseases, smoking habits and social conditions from questionnaires. Because the original study did not include iron measurements, the questionnaire did not contain questions about vitamin C or iron consumption.

**Screening**

The Sør-Varanger municipality consists of a multicultural population, with inhabitants of Norwegian, Finnish and Sámi origin. In 1994, all adults in Sør-Varanger between 18 and 69 years were invited to participate (n = 6822). In total, 3721 people participated, corresponding to a participation rate of 60.2 %. Participation was higher among women (67.5 %) than men (52.2 %), and increased with increasing age. The response rate for participants in the age range between 30 – 69 years was 66.8 % (5-8), which we regarded as an adequate participation rate for this study. Subjects younger than 30 years have hence been excluded (Figure 2).

Iron status was measured in a total of 1401 men and 1548 women. Among these participants, 893 (30.3 %) were employed at A/S Sydvaranger, of whom 476 were miners and 417 were wage earners with different tasks in the company. We performed stratified analyses for 1) miners, 2) other industry workers at A/S Sydvaranger, and 3) the remaining population. We did not demonstrate any differences in iron levels between the two non-mining groups (group 2 and 3), and they were therefore merged and used as a control.

In 1993, The Sør-Varanger study was accredited by the Regional Board of Research Ethics, and the Norwegian Data Inspectorate.
Registered population
Age 18 - 69 years

Population N=6822

Eligible 6177

Died/moved 303 a) Absent 342 b)

Participants N=3721 (60.2%)

N=2949 (66.8%)

Age >29
Analysed for pollution and iron status

Employed at A/S Sydvaranger N= 893

Miners N= 476

Non Miners N= 417

Not employed at A/S Sydvaranger N= 2056

Figure 2. Flow-chart of survey participants.
gave permission to store personal information about the participants. In relation to the extension of the study in 1999, both the Regional Board of Research Ethics and the Norwegian Data Inspectorate gave new approvals.

All participants gave written, informed consent prior to the screening. They also gave informed consent to link information to hospital databases and the register of death certificates in statistics of Norway.

Non-fasting blood samples were obtained at admission. Serum was stored at -20 °C. S-ferritin, iron and transferrin were measured on a Hitachi 917 analyser from Boehringer Mannheim, Germany. All reagents were purchased from the same company. Iron was measured with a ferrozine method, and calibrated using Cfas (catalogue No. 759350, lot No. 199462). Transferrin was measured with a turbidimetric assay, and calibrated using Cfas Proteins (catalogue No. 1355279, lot No. 196610). S-ferritin was measured with a turbidimetric assay, and calibrated using Cfas Proteins (catalogue No. 1355279, lot No. 196610). In an effort to harmonize s-ferritin levels within Norway at the time, the laboratory used a factor of 0.82 for s-ferritin analysis. Transferrin was reported in g/L, and serum TIBC (total iron-binding capacity) was calculated as s-TIBC µmol/L = 25.1 x s-transferrin. Transferrin saturation (%) was calculated as 100 x (serum-iron/TIBC). Moderate iron overload is defined as s-ferritin > 200 µg/l for men, and s-ferritin > 110 µg/l for women, according to limits used by the Nord-Trøndelag Health Study (9). S-ferritin levels > 699 µg/l are compatible with severe iron overload, according to previous studies (10). Iron deficiency is defined as s-ferritin < 16 µg/l or transferrin saturation < 15 %, according to WHO criteria (11-12). Body mass index (BMI) was based of measurements of weight and height, and calculated as body weight in kilograms/body height in metres^2.

**Record linking**

Kirkenes hospital is the only hospital in this region. The hospital database therefore covers health information for the whole population. The University Hospital is more than 800 kilometres away. In order to find participants with liver and kidney diseases, or alcohol liver damage, we linked the participant record to the Kirkenes hospital database for the years of 1993, 1994 and 1995.

**Statistical analyses**

Analysis was stratified for sex and mining status. The Sharpiro – Wilk test was utilised to examine the normal distribution of data. Distributions for s-ferritin showed positive skewness; therefore, s-ferritin values were logarithmically transformed and replaced by log e (ferritin). S-ferritin values were log – normally distributed. When s-ferritin was used as dependent variable, both log e and non-log-transformed s-ferritin were analysed. There were no differences in the results; therefore, non-logarithmical ferritin was preferred. Transferrin saturation was normally distributed. Analysis of variance (two-way ANOVA) was used for evaluating the changes of s-ferritin and transferrin saturation by age, sex, occupation and pulmonary diseases. The s-ferritin and transferrin saturation interval between the 2.5 and 97.5 percentiles (central 95 % interval) was estimated. We used the SAS statistical software package version (SAS Institute Inc, Cary, NC; Version 8.2).
RESULTS

Study population
Table I shows sex-specific differences in selected characteristics at screening. Both mean s-ferritin and mean transferrin saturation were significantly higher for men than for women. Until 1994, Sør-Varanger had a stable population. About 80% of the population (both sexes) had lived in the municipality for more than 20 years. Two thirds of the participants had BMI values higher than 24 kg/m².

Population distribution of s-ferritin and transferrin saturation
The range of s-ferritin for men was 4 – 1215 µg/l, and for women it was 1 – 1172 µg/l. Figure 3a shows the percentile distributions of s-ferritin by age for men. The distribution of median s-ferritin level in different age groups showed little variation, except for the oldest participants over 60 years. There was a small tendency of decreasing s-ferritin with age for all percentiles, except for the 97.5 percentile. From 50 – 59 years there was a significant decrease in s-ferritin (p < 0.01). Figure 3b presents the percentile distribution of s-ferritin by age for women. The median for all women varied with age from 30 – 60 µg/l. The range of variation was largest in the age group 65 – 69 years and smallest in the age group 35 – 40 years. There was a significant increase in s-ferritin from 45 - 54 and 50 - 59 years (p < 0.0001). Transferrin saturation showed less variation than s-ferritin

Table I. Baseline characteristics of the study population in Sør-Varanger aged 30-69 yrs.

| Characteristics                  | Men (n = 1401) | Women (n = 1548) |
|----------------------------------|---------------|------------------|
|                                  | Mean (95% CI) | Mean (95% CI)    |
| S-ferritin (µg/L)                | 90 (87-94)    | 35 (34-37)       |
| Transferrin saturation (%)       | 26 (26-27)    | 24 (23-24)       |
| Age (yr)                         | 49 (48-49)    | 48 (47-49)       |
| Body mass index (kg/m²)          | 26.9 (26.7-27.1) | 26.4 (26.2-26.7) |
| Smokers (%)                      | 42.2 (39.8-45.0) | 41.0 (38.6-43.5) |
| Percent employment in iron industry all occupations | 53.8 (51.2-56.4) | 13.4 (11.8-15.2) |
| Percent miners of total population | 31.8 (29.3-34.3) | 2.0 (1.4-2.8)    |
| Duration of residence            |               |                  |
| Percent lifelong                 | 43.7          | 36.1             |
| Percent > 10 years               | 88.6          | 87.7             |
| Percent > 20 years               | 80.4          | 77.1             |

Table II. Distribution of s-ferritin in men and women in the Sør-Varanger municipality

| Age   | Men n | Mean (95% CI) | Women n | Mean (95% CI) |
|-------|-------|---------------|---------|---------------|
| 30 - 39 | 370   | 94 (88-100)   | 441     | 28 (26-29)    |
| 40 - 49 | 404   | 94 (87-101)   | 439     | 25 (24-28)    |
| 50 - 59 | 313   | 87 (80-95)    | 344     | 47 (43-51)    |
| 60 - 69 | 314   | 84 (77-92)    | 324     | 58 (53-63)    |
| Total  | 1401  | 90 (87-94)    | 1548    | 34 (34-37)    |

a 95 % Confidence interval (CI)  
b Geometric mean
Mean s-ferritin levels adjusted for age groups (both sexes) are shown in Table II. For men, mean s-ferritin decreased with age, and for women s-ferritin increased with age, especially after 49 years. S-ferritin increased significantly with increasing BMI for both sexes. Transferrin saturation decreased significantly for women, but not for the male population (data not shown).

**General health status of the study population**

The prevalence of self-reported acute pulmonary diseases is shown in Table III. In addition, the hospital database identified one person diagnosed with acute pneumonia in 1993. None of the participants were diagnosed with liver, kidney, or alcohol-associated diseases, according to the database.

**Iron status in miners**

The percentage of miners was 30.0, 32.7, 34.2 and 34.1 % among men aged 30 – 39, 40 – 49, 50 – 59 and 60 – 69, respectively, in total 439 men. Only 37 women were miners, which corresponded to 2 % of female population, hence we limited our analyses to men due to the low number of female miners.

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**Figure 3. S-ferritin by age in men (a) and women (b).**
Iron stores

No differences in s-ferritin were found between male miners and non-miners. S-ferritin tended to decrease with increasing age for both miners and non-miners. Mean transferrin saturation was non-significant in all age groups among miners and non-miners (p < 0.09). Information on smoking habits was available for 413 miners, of whom 200 (48%) were smokers, and for 804 non-miners, of whom 327 (41%) were smokers (Table IV). There were no significant differences between s-ferritin, or transferrin saturation in these four groups.

Prevalence of high and low iron stores

The prevalence of moderate iron overload was 14% among miners and 10% among non-miners in the age group 30–49 years. Moderate iron overload increased slightly with age in men, among both miners and non-miners. In a stratified analysis, no difference in prevalence was found, RR = 1.2/ (95% CI; 0.9 – 1.6).

S-ferritin levels > 699 µg/l were observed in two men, one miner and one non-miner. Among the women, one miner and one non-miner also had severe iron overload.

The prevalence of iron deficiency among the male population was 5.2% for miners and 3.7% for non-miners, respectively. RR = 1.4/ (95% CI; 0.9 – 2.4). No age differences were demonstrated.

DISCUSSION

The subjects available for iron analyses were all participants in a population-based study, with a high proportion being industrial workers in the iron smelting industry (5-6).

### Table III. Prevalence of acute diseases in relation to gender and mining.

|                          | Women                 | Men                 |
|--------------------------|-----------------------|---------------------|
|                          |          % (95% CI) a |          % (95% CI) a |
| Pulmonary disease        |          9.7 (2.0-25.8) |          9.8 (8.4-11.4) |
| Pneumonia                |         19.4 (7.5-37.5) |         13.2 (11.5-14.9) |
| Bronchitis               |          6.5 (0.0-21.4) |          5.0 (3.8-6.2) |
| Coughing                 |          16.1 (5.5-33.7) |          9.2 (7.8-10.8) |
| Allergy                  |          19.4 (7.5-37.5) |          18.3 (16.4-20.4) |
|                          |       95% confidence interval ( CI ) a |

### Table IV. Distribution of ferritin and transferrin saturation among miners versus non-miners and smokers versus non-smokers. The data represent men aged 30 – 69 yrs.

|                          | Miners n = 213 | Non-miners n = 477 | Miners n = 200 | Non-miners n = 327 | P c |
|--------------------------|---------------|-------------------|---------------|-------------------|-----|
| S-ferritin(µg/L) a       | 130 (104-156) | 121 (98-144)      | 123 (99-148)  | 115 (93-137)      | 0.5 |
| Transferrin saturation(%) a | 25.3 (22.4-28.2) | 25.7 (23.2-28.3) | 26.1 (23.2-28.8) | 25.6 (23.2-28.0) | 0.7 |

a 95% confidence interval ( CI )

Multiple-adjusted for age, BMI, length of residence, pulmonary disease, pneumonia

95% confidence interval (CI)

p-value between miners and non-miners
The present analysis did not show significant differences with regard to s-ferritin and transferrin saturation levels, between miners and non-miners.

The s-ferritin level is the most specific biochemical test that correlates with total body iron stores. S-ferritin has been used as key parameter in several epidemiological studies where iron status has been measured (10,13-15). A low s-ferritin level reflects depleted iron stores, while a high s-ferritin can reflect iron overload. S-apoferritin is a part of the measured s-ferritin, and is an acute-phase reactant protein that is elevated in infectious, inflammatory and malignant diseases. Information about liver and kidney diseases and information about alcohol consumption, or medications were not available in this study. When merging the participants’ records with the hospital database it was not possible to point out any differences among miners and non-miners concerning these diseases. There were no differences in self-reported pulmonary diseases between the different subgroups either, indicating that miners in general are not healthier than non-miners.

We found significant sex differences for both s-ferritin and transferrin saturation. Age had a major effect on s-ferritin in women, with values increasing from the age of 40. Previous studies have shown that it takes 7 - 10 years before a new iron balance is established in post-menopausal women (15). The Dan-Monica studies from Denmark demonstrated the same age variations (13,15,16). S-ferritin levels for men remained constant until 50 – 54 years of age, after which they declined with age. Similar variations have been reported for haemoglobin in elderly men (17).

In the present study, transferrin saturation also increased in women after 50 years of age, but not so clearly as for s-ferritin. For men, transferrin saturation remained constant into old age.

The prevalence of iron depletion was lower for men than women. The Danish study also reported considerable differences concerning the prevalence of iron deficiency between men and women, when age groups where compared (15 – 16).

In previous studies, it was reported that s-ferritin increases, and transferrin saturation decreases, with increasing BMI (18). In our study, s-ferritin increased significantly with increasing BMI as well, for both sexes. At the same time, transferrin saturation seemed to decrease, especially when BMI exceeded 29 kg/m², which is defined as obesity by WHO (19). There were no differences in BMI between male miners compared to non-miners.

Mining, as an occupation, had no significant influence on iron status in our study. Nor was it possible to demonstrate any effect related to smoking habits. The iron pellet factory in Kirkenes caused some environmental pollution; hence a major part of the population was, to some extent, exposed to iron-dust particles. However, we regard this exposure to be equal for all inhabitants, miners and non-miners alike.

The miners worked underground, and the slight diversity in iron stores between miner and non-miners could be explained by exposure to the iron ore. At the same time, mining is hard, physical work, and it is known that great losses of sweat during hard manual labour also lead to loss of iron (20). Only tiny amounts of iron are lost by this
route. It is not possible to document if these two effects counteract each other.

In 1994, the activity in the mine was already reduced and only a portion of the industrial workers were still working there. Therefore, it was difficult to draw any conclusions about the issue of iron dust intake and exposure. However, body iron accumulation caused by industrial exposure is not very likely, because this requires several decades of severe contamination (4).

Conclusions

In our study we found the same variations between sex and age groups concerning iron status in the general population as described in previous studies in Denmark. Natvig’s finding from the 1960s, that haemoglobin level was higher among workers in iron metal industry, cannot be verified for the iron status in the same population thirty years later.

The results from this study did not indicate any relationship between iron industry and serum iron levels, neither for environmental exposure, nor for occupational exposure.

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Ann Ragnhild Broderstad
Institute of Community Medicine,
University of Tromsø
N-9037 Tromsø
NORWAY
Email: Ann.Ragnhild.Broderstad@ism.uit.no