

## THE INCIDENCE OF ANEMIA IN THE ADULT WORKING POPULATION OF VOJVODINA

### UČESTALOST ANEMIJE MEĐU ODRASLIM RADNO AKTIVNIM OSOBAMA U VOJVODINI

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#### Summary

**Background:** Anemia is a global public health problem of endemic proportions, especially in women, and with serious health consequences. Anemia was defined according to the World Health Organization criteria as hemoglobin concentration <130 g/L for men and <120 g/L for women. The incidence of anemia varies between regions, so the aim of the study was to determine the incidence of anemia in a randomly selected sample of adult working individuals of both sexes, in Vojvodina.

**Methods:** The study included a total of 6087 subjects (4658 men and 1429 non-pregnant women) aged 18–65 years who presented for a regular checkup at the Public Health Institute of Vojvodina. Blood specimen collection was performed by antecubital venipuncture in all subjects.

**Results:** The results showed that the incidence of anemia in adults in Vojvodina was 7.7%, and it was more frequent in women (20%) than in men (3.86%). The most frequent was normocytic anemia, whereas microcytic anemia was less prevalent. Macrocytic anemia was found in only 3.3% of subjects, exclusively in women. The greatest proportion of anemic subjects, regardless of sex, had hemoglobin levels that indicated mild anemia (Hb 100–119 g/L for women, and 100–129 g/L for men). Only 4% of men and 12% of women

#### Kratak sadržaj

**Uvod:** Anemija je globalan, problem u oblasti javnog zdravlja, endemskih razmera, naročito među ženskom populacijom, sa ozbiljnim posledicama po zdravlje. Prema kriterijumima Svetske zdravstvene organizacije, anemija je definisana kao koncentracija hemoglobina <130 g/L za muškarce i <120 g/L za žene. Njena incidenca varira od regiona do regiona, te je cilj rada bio da se utvrdi učestalost anemije u slučajnom uzorku odraslih zaposlenih osoba oba pola u Vojvodini.

**Metode:** Istraživanje je sprovedeno u 6087 ispitanika (4658 muškaraca i 1429 žena koje nisu trudne) starosti 18–65 godina koji su se javili na periodični sistematski pregled u Institutu za javno zdravlje Vojvodine. Svim ispitanicima je antekubitalnom venepunkcijom uzet uzorak krvi za određivanje krvne slike.

**Rezultati:** Utvrđeno je da na teritoriji Vojvodine incidenca anemije kod odraslih iznosi 7,7%, pri čemu je ona učestalija među ženskom populacijom (20%) u odnosu na mušku populaciju (3,86%). Među anemičnom odrasлом populacijom najveća je bila zastupljenost normocitne anemije, a daleko manja mikrocitne anemije. Makrocitna anemija je bila zastupljena kod svega 3,3% ispitanika i to isključivo ženskog pola.

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*List of abbreviations:* RBCC, red blood cell count; Hb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WHO, World Health Organization.

had Hb levels that indicated the presence of moderate or severe anemia ( $\leq 100$  g/L).

**Conclusions:** Considering the medical, social and economic consequences anemia may produce, identification of risk factors and application of adequate preventive measures should be a public health priority.

**Keywords:** anemia, adults, men, women

## Introduction

Due to its high prevalence and the significant impact it has on the population's health, anemia has been recognized as a public health problem for several decades. However, despite all the efforts that have been made to reverse this, the global prevalence of anemia is still unacceptably high (1). According to the World Health Organization estimates, it is 24.8% (22.9–26.7%, CI 95%), which means that around 1.62 billion (between 1.5 and 1.74 billion, CI 95%) people worldwide are anemic (2–5). In spite of the epidemic proportions of the problem, the prevalence of anemia significantly varies in different populations and among different groups within one population, being the highest in the southeastern Asia and Africa. However, the highest number of people affected with anemia is in the area of western Pacific (2, 3). As regards age, the highest prevalence of anemia is found in preschool-age children, and the lowest prevalence in men. The group with the greatest number of individuals affected is non-pregnant women (2).

Causes of anemia are numerous and may be nutritional and non-nutritional. Nutritional causes are more frequent, and the most important are deficiencies of iron, folate, vitamin B12 (6–9). Iron deficiency is by far the most frequent cause of anemia and also the most frequent nutritional deficit in the world. The most significant non-nutritional factors that may cause anemia include bleeding, infection, chronic illness, various causes (hereditary or acquired) of hemolytic anemias, toxic effects of medication (6, 7), renal dysfunction (10), etc.

The onset of anemia is usually gradual and symptoms are rather vague and obscure, which is why anemia in most cases remains unrecognized and undiagnosed (11, 12). One of the most common symptoms is tiredness, which affects work efficiency and productivity. In addition, health risks involved in anemia are numerous, since anemia can make the symptoms worse or contribute to progression of other comorbid diseases or conditions. The study of Lippi et al. found a high prevalence of anemia and anisocytosis in a population of emergency department patients, whose identification may be important for appropriate treatment and favorable outcome (13). In diabetic patients, through renal hypoxia that stimulates production of different growth factors (transforming

U najvećem procentu anemičnih ispitanika u ovoj studiji, bez obzira na pol, vrednosti hemoglobina ukazuju na blaži stepen anemije (Hb 100–119 g/L za žene, odnosno 100–129 g/L za muškarce). Samo 4% muškaraca i 12% žena je imalo vrednosti Hb koje ukazuju na prisustvo umereno teške ili teške anemije ( $\leq 100$  g/L).

**Zaključak:** S obzirom na zdravstvene, socijalne i ekonomske posledice do kojih malokrvnost može dovesti, identifikacija faktora rizika za pojavu anemije i primena odgovarajućih preventivnih mera bi trebalo da budu u javnom zdravstvu.

**Cljučne reči:** anemija, odrasli, muškarci, žene

growth factor- $\beta 1$ , vascular endothelial growth factor, platelet-derived growth factor) and cytokines, anemia contributes to the development of interstitial fibrosis, i.e., scarring and thickening of the kidney (14, 15). Correction of anemia in these patients significantly reduces the proportion of patients that will have a double increase in serum creatinine levels (16). Furthermore, anemia may lead to increased oxidative stress (17), and may induce or worsen heart disease (18).

In addition, anemia may affect cognitive and mental functions, which may significantly affect the quality of life (9, 19). Especially significant are the adverse effects of anemia in children, since anemia may slow down growth, reduce the ability to learn and lead to poor academic performance, lower the intelligence quotient and increase risk of different psychiatric disorders (unipolar depressive disorder, bipolar disorder, anxiety disorder, autism spectrum disorder, attention-deficit/hyperactivity disorder, tic disorder, delayed development, and mental retardation) (20).

Data about the incidence of anemia in Vojvodina, and particularly among the working population, is sparse. The aim of this study, therefore, was to investigate the incidence of anemia in a randomly selected sample of employed subjects of both sexes, aged 18–65 years, in order to contribute to a more thorough and comprehensive approach to the detection and treatment of this condition.

## Materials and Methods

The study was carried out on a sample of 6,087 subjects (4,658 males and 1,429 non-pregnant females) who were surveyed for the presence of the WHO-defined anemia. The WHO Hb thresholds were used to classify individuals living at sea level as anemic: Hb < 130 g/L for men and Hb < 120 g/L for women. On the basis of the MCV values of > 98 fL, 82–98 fL and < 82 fL, anemias were classified into macrocytic, normocytic and microcytic, respectively (21–25).

Subjects were employees aged 18–65 years who presented for a regular checkup at the Public Health Institute of Vojvodina in Novi Sad in the period from April 2011 to May 2012. All subjects were apparently healthy, without evident infection. Data

were collected from the medical records and the database available at the Hematological Laboratory of the Public Health Institute.

Blood specimens were collected by antecubital venipuncture into tubes (Vacutainer; Becton-Dickenson, Franklin Lakes, NJ) containing the appropriate anticoagulant. Complete blood count was determined on site with fresh blood using a hematology analyzer (Horiba ABX Micros 60 Automated Hematology Analyzer). The HORIBA analyzer uses impedance technology and photometry as measurement methods. The studied parameters were red blood cell count (RBCC), hemoglobin (Hb) and hematocrit (Hct). In addition, erythrocyte indices (mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC)), white cell count, and differential white cell count were determined.

Results are expressed as mean  $\pm$  SD, and median (interquartile range). Differences in distributions of individual parameters between the study groups were

analyzed using the parametric Student t-test and ANOVA test or using the non-parametric Mann-Whitney and Kruskal-Wallis test when a distribution showed a significant deviation from normal distribution. Normality of the data distribution was tested with Kolmogorov-Smirnov test. The variable RBC was normally distributed, while the variables age, Hb and Hct were not. Linear regression analysis and the Pearson coefficient of linear correlation were used to study the correlation between variables. Results are assumed to be statistically significantly different at  $p < 0.05$ . Statistical analysis was performed using Excel 2007 and the statistical software Statistica 12.0.

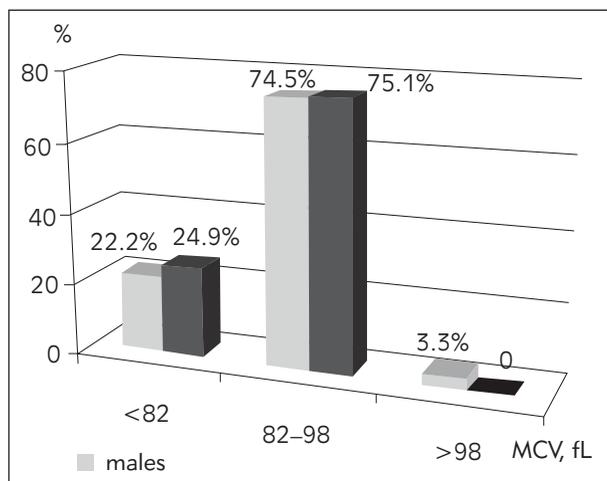
## Results

Out of a total of 6,087 subjects, Hb levels below the WHO threshold were found in 466 subjects (7.7%); in 180 men (3.86%) and 286 women (20%). Average age, erythrocyte and hematocrit counts, and hemoglobin concentrations in the study subjects are shown in *Table 1*.

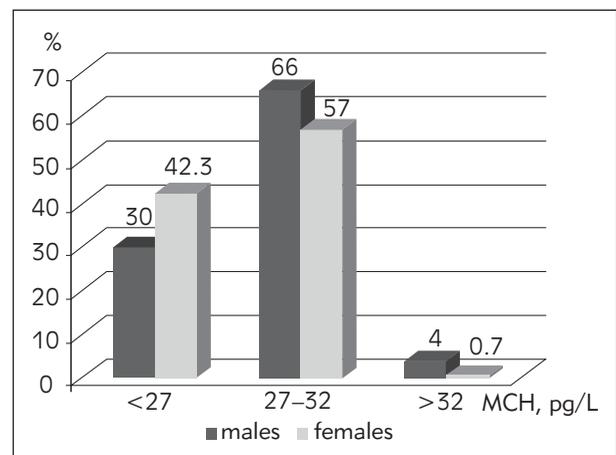
**Table 1** Age, level of hemoglobin, erythrocyte count and hematocrit in all subjects [median (I quartile-III quartile) and mean  $\pm$  SD]

	Males with anemia (n=180)	Males without anemia (n=4478)	Females with anemia (n=286)	Females without anemia (n=1143)
Age (years)	49.0 (38–56)* 46.8 $\pm$ 12.3	42.0 (32–51) 41.7 $\pm$ 11.8	39.0 (30–45)** 38.5 $\pm$ 10.2	42 (32–51) 42.0 $\pm$ 11.7
Hb (g/L)	126 (122–128)* 122.2 $\pm$ 10.3	146 (141–152) 146.4 $\pm$ 9.0	113 (107–117)** 110.1 $\pm$ 9.4	130 (126–136) 131.5 $\pm$ 7.6
RBC ( $\times 10^{12}/L$ )	4.4 (4.2–4.6) 4.4 $\pm$ 0.4*	5.0 (4.8–5.2) 5.1 $\pm$ 3.1	4.1 (3.9–4.32) 4.1 $\pm$ 0.3**	4.5 (4.3–4.7) 4.5 $\pm$ 0.3
Hct (L/L)	0.38 (0.37–0.39)* 0.38 $\pm$ 0.03	0.44 (0.42–0.46) 0.44 $\pm$ 0.03	0.35 (0.33–0.36)** 0.34 $\pm$ 0.03	0.4 (0.38–0.42) 0.4 $\pm$ 0.02

Legend: Hb – hemoglobin, RBC – red blood cells (normal distribution), Hct – hematocrit, \* $p < 0.05$  compared to males without anemia, \*\* $p < 0.05$  compared to females without anemia



**Figure 1** MCV (mean corpuscular volume) in men and women with anemia (%).



**Figure 2** Values of hemoglobin, erythrocyte count and hematocrit in anemic subjects (%).

**Table II** Age, level of hemoglobin, erythrocyte count and hematocrit in all subjects [median (I quartile-III quartile) and mean±SD].

	Hb (g/L)	RBC ( $\times 10^{12}/L$ )	Hct (L/L)
<b>Males</b>			
56–65 years (n=53)	125 (119–127) 121.5±9.9	4.4 (4.1–4.8) 4.4±0.4	0.38 (0.36–0.39) 0.37±0.03
46–55 years (n=53)	125 (122–128) 121.6±12.2	4.3±0.5 4.3 (4.1–4.6)	0.38 (0.37–0.39) 0.37±0.04
36–45 years (n=33)	126 (123–127) 123.8±5.4	4.5±0.4 4.5 (4.3–4.6)	0.38 (0.37–0.40) 0.38±0.02
26–35 years (n=30)	125 (122–128) 121.5±12.8	4.5±0.4 4.5 (4.3–4.6)	0.38 (0.37–0.39) 0.37±0.03
18–25 years (n=11)	127 (124–128) 125.3±4.54	4.5±0.24 (4.4–4.7)	0.40 (0.38–0.41) 0.39±0.02
<b>Females</b>			
56–65 years (n=15)	117 (115–118) 112.5±15.9	4.2±0.34 4.2 (4.0–4.4)	0.36 (0.35–0.37) 0.34±0.04
46–55 years (n=56)	114 (107–116) 110.1±9.4	4.1±0.36 4.1 (3.9–4.3)	0.35 (0.33–0.36) 0.34±0.03
36–45 years (n=92)	113 (105–117)* 109.1±10.5	4.2±0.34 4.2 (3.9–4.3)	0.35 (0.33–0.36) 0.33±0.03
26–35 years (n=98)	111 (106–116)* 110.6±7.1	4.1±0.39 4.0 (3.8–4.2)	0.34 (0.33–0.36) 0.34±0.02
18–25 years (n=25)	114 (111–115) 111.3±6.8	4.2±0.2 4.1 (4.0–4.3)	0.35 (0.34–0.36) 0.34±0.02

Legend: Hb – hemoglobin, RBC – red blood cells, Hct – hematocrit, \*  $p < 0.05$  compared to 55–65 years group

With regard to Hb levels, anemic men were classified into four groups. The greatest number of subjects had Hb values in the range 121–129 g/L (79%), followed by 111–120 g/L (12%), 101–110 g/L (5%), and  $\leq 100$  g/L (4%). Anemic women were classified into three groups: 62% had Hb levels in the range 111–119 g/L, 26% had Hb levels 101–110 g/L, and 12% had Hb levels below 100 g/L.

Figure 1 shows MCV values in male and female subjects. In most subjects, MCV levels were within the range characteristic for normocytic anemia. Figure 2 shows MCH values in anemic subjects of both sexes. A majority of subjects had normochromic anemia and a minority had hypochromic anemia. Table II shows average hemoglobin levels and erythrocyte and hematocrit counts in anemic subjects in relation to age. In males, the highest average Hb concentration was in the age group 18–25 years ( $125.3 \pm 4.54$  g/L), and the lowest in the age group 56–65 years ( $121.5 \pm 9.9$  g/L) but without any significant differences between groups ( $p > 0.05$ ). In females, the highest average Hb concentration was found in the age group 56–65 years ( $112.5 \pm 15.9$  g/L; median 117), and the lowest in the age group 26–35 years ( $110.6 \pm 7.1$  g/L; median 111) ( $p < 0.05$ ). RBC and Hct were similar among the groups of anemic males and females ( $p > 0.05$ ). Linear regression analysis did not show a

correlation between age and Hb levels in anemic subjects.

## Discussion

Anemia is considered an important cause of morbidity and mortality (12). When the prevalence of low Hb values is more than 5% in the population, it is regarded as a public health problem (26). On the basis of Hb concentrations, the WHO established the following criteria for assessing the public health significance of anemia: if its prevalence in the general population is 5–19.9% – low; 20–39.9% – moderate; and  $\geq 40\%$  – severe (1, 5, 8). Due to the varying distribution of social and biological risk factors for anemia and the fact that it can lead to medical, social and economic consequences, epidemiological studies of anemia are becoming increasingly important (27, 28).

We studied the incidence of anemia on a relatively large sample of the working population of Vojvodina. We found a relatively low incidence of 7.7%. According to literature data, the prevalence of anemia ranges from around 9% in developed countries to 43% in developing countries (5), with children and women of reproductive age being the most

endangered categories. On the basis of data obtained, we were not able to determine the prevalence of anemia in the general population, since our study did not include two important categories – children and elderly, which is a major limitation of the study. On the basis of the research carried out in Serbia in 2000, the WHO estimated the prevalence of anemia in Serbia to be 29.5%, which makes it a problem of moderate public health significance (2).

As expected, in our subjects, the prevalence of anemia was higher in women (20% of all studied women). Anemia in women of reproductive age is especially important since maternal anemia bears an increased risk of intrauterine retardation, low birth weight, increased perinatal mortality and maternal morbidity and mortality (3). It is estimated that anemia during pregnancy and delivery leads to death in 3.7% of pregnant women in Africa and 12.8% of pregnant women in Asia (26). Early detection and treatment of anemia in women of reproductive age are therefore of critical importance for preventing anemia in pregnancy (29). The high prevalence of anemia among women is a burden for the women, for their families, and for the economic development and productivity of the country (30). Among men, there were only 3.86% of anemic subjects (180 out of 4,658 subjects), which is comparable with the studies that report the prevalence of anemia in men in the range 1.7–3.5% (23, 31). These results were expected, considering the fewer risk factors for anemia in men.

Average Hb levels in men and women in our study were  $122.2 \pm 10.3$  and  $110.1 \pm 9.4$  g/L, respectively. Average age of anemic men was significantly higher compared with healthy men, as opposed to average age of anemic women, which was significantly lower than average age of healthy women ( $p < 0.05$ ). It has been shown that in men Hb levels decrease with age, while in women they increase after the menopause up to the age of 70, thereafter gradually decreasing (8, 22, 28, 31). While some authors explain it with the decreased erythroid capacity of the bone marrow (31), others point out that anemia should not be considered a normal consequence of ageing (12, 19, 24). Lippi et al. demonstrated that impaired renal function might be a major determinant of anemia in the elderly (10).

In our study, most anemic subjects, both men and women, had hemoglobin levels that indicated a mild degree of anemia. This finding is in accordance with the literature data that indicate that a Hb concentration of  $\leq 100$  g/L is found in 13–21% of women (30, 32).

Unfortunately, the etiology of anemia cannot be determined on the basis of decreased Hb concentration only (8, 26). Screening for iron deficiency based solely on the determination of hemoglobin enables detection of just around 37% of iron-deficient subjects (8). On the other hand, normal hemoglobin concentrations do not exclude iron deficiency. Our results showed that the majority (around 75%) of anemic subjects had normocytic anemia, while around 35% of women and 22.2% of men had microcytic anemia. Microcytic anemia is usually a consequence of iron deficiency, whereas normocytic anemia is most often found in chronic diseases, chronic inflammation and malignancies. Considering the heterogeneity of the age structure of our subjects, the highest prevalence of normocytic anemia found in our study is likely due to the presence of chronic diseases, whereas the probable causes of microcytic anemia may be low intake of iron and chronic blood loss.

Macrocytic anemia was found in only 3.3% of the studied anemic women and none of the men. This finding indicates an adequate intake of necessary vitamins (folates and B complex vitamins) in the studied male population, as well as a satisfactory intake of these vitamins in our female population. In a study by Chandyo et al. (29), out of 12% of anemic women, one half had microcytic anemia and the other half had macrocytic anemia caused by folate and vitamin B12 deficiency, whereas Khatib and associates reported that in their study 7.7% of women had microcytic and 12.6% macrocytic anemia (6). Such discrepant results indicate that there are a great number of different factors affecting critically the prevalence and features of anemia in different countries and regions.

In summary, according to our findings on a random sample of apparently healthy subjects in the Vojvodina region, the incidence of anemia in adults was 7.7%, with more women affected than men (20 vs. 3.86%). The most frequent was normocytic anemia, while microcytic anemia was less prevalent. Macrocytic anemia was rare and found exclusively in women. In most subjects anemia was mild, while moderate and severe anemia were found in only 4% of men and 12% of women.

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### **Conflict of interest statement**

The authors stated that there no conflicts of interest regarding publications of this article.

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