Prenatal care: What supplements do we advise pregnant women?

Jasna Kusturica¹, Lejla Rakovac-Tupković², Aida Kulo¹, Maida Rakanović-Todić³

The aim of the paper was to investigate the types and frequency of supplementation during pregnancy in the city of Sarajevo. This study was conducted in two pediatric outpatient clinics in Sarajevo using a questionnaire. Five hundred women who had been pregnant in the past five years were questioned. The results showed that most pregnancies were unplanned. The prevalence of pre-term delivery was 5.2%, and the prevalence of low birth weight infants was 4%. There were seven cases of birth defects. Multivitamin supplements were taken by one woman before pregnancy and by 55.6%, 31.2% and 18.8% women during the first, second and third trimester, respectively. Simultaneously with multivitamin supplements, folic acid was taken by 10% women. Further efforts in terms of planning pregnancy are needed to improve prenatal care. These efforts should include the continuous education of both health professionals and women of childbearing potential, which should also enable the adequate implementation of the recommended supplementation.

Key words: women of childbearing potential, pregnancy, vitamin-mineral supplements, folic acid

Introduction

Proper nutritional status of women before, during, and after pregnancy is an important element of reproductive health. It maintains maternal health and reduces the risk of adverse pregnancy outcomes, birth defects and chronic diseases in postnatal life. However, questions whether healthy pregnant women can obtain all necessary nutrients from food, and if they need routine multivitamin and mineral supplementation are frequently raised.

There is no clinical evidence in favor of supplementation with multivitamins in pregnancy to be beneficial (1). According to prenatal nutrition guidelines, routine prenatal care should include dietary supplementation with folic acid. Folic acid is a member of the vitamin B group (vitamin B9 or folacin), the synthetic form of folate naturally found in food. Folates obtained from food are not as well absorbed as folic acid is. The active form of folic acid is tetrahydrofolate. It is a coenzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides, and synthesis of DNA (1). The first evidence, from the 1960s, as well as recent randomised controlled trials demonstrate that supplementation with
folic acid in the period around conception reduces the incidence of neural tube defect (NTD) in the offspring of mothers who had previously borne children with defects (1-8). A significant risk reduction was reported for first time occurrence of NTDs too (5, 6, 9). The risk of having a subsequent NTD-affected pregnancy was reduced approximately by 60-70% (8, 10). Supplementation with folic acid has also been shown to reduce the risk of other malformations such as cleft lip, with or without cleft palate, congenital heart defects and imperforate anus (6, 9, 11-13). Maternal use of folic acid supplements periconceptionally and in early pregnancy was associated with a reduced risk of preterm delivery, infant low birth weight, fetal growth retardation, severe language delay in children at the age of 3 and reduced chromosomal defects in sperm. It may also protect the fetus when the mother is struggling with a disease, taking medications, or smoking during pregnancy (14-17).

The National Institute for Health and Care Excellence (2010), besides folic acid recommends vitamin D supplementation (10 mcg/day). Due to unpleasant maternal side effects, iron supplementation is not recommended routinely to all pregnant women. However, pregnant women should be offered screening for anaemia. This screening should take place in early pregnancy and at 28th week of pregnancy when other blood screening tests are being performed as well. This approach will allow enough time for treatment in case of detected anaemia (18). According to Canadian Prenatal Nutrition guidelines, daily multivitamin supplementation containing 16-20 mg of iron is recommended in routine prenatal care (19).

With the focus on folic acid, the aim of this paper was to investigate what supplements are recommended during pregnancy in the city of Sarajevo.

Material and methods

This observational, cross-sectional study examined the types and frequency of supplements used during pregnancy. The study was conducted in two pediatric outpatient clinics in Sarajevo.

The study was conducted through a simply-structured, thought-out questionnaire. The questionnaire consisted of two types of questions: questions related to the infant (gestational age, anthropometric measures at birth, birth defect), and questions on supplements used in pregnancy. After informed consents for the participation in the survey were given, women were questioned during their children's control medical examinations.

The data were collected in a Microsoft Office Excel database and statistically analysed by the MedCalc for Windows program, Version 10.1.2.0 (MedCalc Software, Mariakerke, Belgium). Descriptive statistical analysis presented as arithmetic mean and standard deviation (SD) values was performed. Frequencies were expressed as percentages. Correlation between variables was performed using Pearson’s correlation analysis.

Results

The study included 500 women who had given birth during the past five years. The mean age and standard deviation of included women was $28.42 \pm 4.92$ years. There was 2% of adolescent pregnancies and 1.2% of older women pregnancies (Table 1).

No statistical relationship was detected between maternal age and birth weight (Pearson’s correlation coefficient $r=-0.032$, $p=0.48$). The prevalence of pre-term delivery was 5.2% (gestational age, mean value 34 weeks, minimum value 27 weeks), and the prevalence of low birth weight infants was 4%. The mean weight and standard devia-
The birth weight of low birth weight infants was 3428.82 ± 945.33 g. There were seven cases of birth defects (Table 2).

Multivitamin supplements (Prenatal®, Pregnacare®) were taken by one woman before pregnancy, and 303 women were taking multivitamin supplements during pregnancy (Table 3).

Table 1. Maternal age and infant birth weight

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>N</th>
<th>%</th>
<th>The birth weight (g)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>10</td>
<td>2.0</td>
<td>&lt;2000</td>
<td>4</td>
<td>0.8</td>
</tr>
<tr>
<td>20-24</td>
<td>101</td>
<td>20.2</td>
<td>2001-2500</td>
<td>16</td>
<td>3.25</td>
</tr>
<tr>
<td>25-29</td>
<td>196</td>
<td>39.2</td>
<td>2501-3000</td>
<td>72</td>
<td>14.4</td>
</tr>
<tr>
<td>30-34</td>
<td>132</td>
<td>26.4</td>
<td>3001-3500</td>
<td>230</td>
<td>46.0</td>
</tr>
<tr>
<td>35-39</td>
<td>55</td>
<td>11.0</td>
<td>3501-4000</td>
<td>127</td>
<td>25.45</td>
</tr>
<tr>
<td>&gt;40</td>
<td>6</td>
<td>1.2</td>
<td>4001-4500</td>
<td>43</td>
<td>8.65</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;4501</td>
<td>7</td>
<td>1.45</td>
</tr>
</tbody>
</table>

Table 2. The birth defects

<table>
<thead>
<tr>
<th>Birth defects</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pes equinovarus</td>
<td>1</td>
</tr>
<tr>
<td>Cleft lip and palate</td>
<td>1</td>
</tr>
<tr>
<td>Agenesis bulbi</td>
<td>1</td>
</tr>
<tr>
<td>Microcephalus</td>
<td>1</td>
</tr>
<tr>
<td>Hydronephrosis</td>
<td>1</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>1</td>
</tr>
<tr>
<td>Neural tube defect (spina bifida)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 3. Ingredients of vitamin-mineral supplements and recommended doses

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Prenatal*</th>
<th>Pregnacare*</th>
<th>RDA*</th>
<th>The pregnancy RDA</th>
<th>The lactation RDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A (acetate and beta carotene)</td>
<td>2.4 mg</td>
<td>2 mg</td>
<td>700 mcg</td>
<td>770 mcg</td>
<td>1300 mcg</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>400 I.J.</td>
<td>400 I.J.</td>
<td>5 mcg</td>
<td>5 mcg</td>
<td>5 mcg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>30 mg</td>
<td>4 mg</td>
<td>15 mg</td>
<td>15 mg</td>
<td>19 mg</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>120 mg</td>
<td>70 mg</td>
<td>75 mg</td>
<td>85 mg</td>
<td>120 mg</td>
</tr>
<tr>
<td>Folic acid</td>
<td>800 mcg</td>
<td>400 mcg</td>
<td>400 mcg</td>
<td>600 mcg</td>
<td>500 mcg</td>
</tr>
<tr>
<td>Vitamin B-1 (thiamine)</td>
<td>1.8 mg</td>
<td>3 mg</td>
<td>1.1 mg</td>
<td>1.4 mg</td>
<td>1.4 mg</td>
</tr>
<tr>
<td>Vitamin B-2 (riboflavin)</td>
<td>1.7 mg</td>
<td>2 mg</td>
<td>1.1 mg</td>
<td>1.4</td>
<td>1.6</td>
</tr>
<tr>
<td>Vitamin B-3 (niacin)</td>
<td>20 mg</td>
<td>20 mg</td>
<td>14 mg</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Vitamin B-6 (pyridoxine)</td>
<td>2.6 mg</td>
<td>10 mg</td>
<td>1.3 mg</td>
<td>1.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Vitamin B-12</td>
<td>8 mcg</td>
<td>6 mcg</td>
<td>2.4 mcg</td>
<td>2.6 mcg</td>
<td>2.8 mcg</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>-</td>
<td>70 mcg</td>
<td>90 mg</td>
<td>90 mg</td>
<td>90 mg</td>
</tr>
<tr>
<td>Iron</td>
<td>28 mg</td>
<td>17 mg</td>
<td>18 mg</td>
<td>27 mg</td>
<td>9 mg</td>
</tr>
<tr>
<td>Calcium</td>
<td>200 mg</td>
<td>-</td>
<td>1000 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Zinc</td>
<td>25 mg</td>
<td>15 mg</td>
<td>8 mg</td>
<td>11 mg</td>
<td>12 mg</td>
</tr>
<tr>
<td>Selenium</td>
<td>-</td>
<td>30 mcg</td>
<td>55 mcg</td>
<td>60 mcg</td>
<td>60 mcg</td>
</tr>
<tr>
<td>Magnesium</td>
<td>-</td>
<td>150 mg</td>
<td>310 mg</td>
<td>350 mg</td>
<td>310 mg</td>
</tr>
<tr>
<td>Iodine</td>
<td>-</td>
<td>140 mcg</td>
<td>150 mcg</td>
<td>220</td>
<td>290</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>-</td>
<td>6 mg</td>
<td>5 mg**</td>
<td>6 mg**</td>
<td>7 mg**</td>
</tr>
<tr>
<td>Biotin</td>
<td>-</td>
<td>150 mcg</td>
<td>30 mcg*</td>
<td>30 mcg*</td>
<td>35 mcg*</td>
</tr>
<tr>
<td>Copper</td>
<td>-</td>
<td>1000 mcg</td>
<td>900</td>
<td>1000</td>
<td>1300 mcg</td>
</tr>
</tbody>
</table>

*Recommended Dietary Allowance (RDA): average daily level of intake that is enough to meet the nutrient needs of nearly all (97-98%) healthy people.

**Adequate Intake (AI): established when there is not enough evidence to develop an RDA. It is set at a level that is thought to ensure enough nutrition.
Simultaneously with multivitamin supplements, folic acid was taken by 54 women (Table 4).

### Discussion

Prenatal care is expected to be focused on family planning, lifestyle, nutrition and supplementation. Physicians should be informed about the latest guidelines.

The majority of women included in our study were in the most appropriate age for pregnancy, which is under the age of 30. Women of that age are generally healthy, ready for the new responsibility and change in life. In terms of long-term health, conceiving in one’s 20s decreases the risk for both breast (20-23) and ovarian cancer (24). In contrast, for adolescent pregnancy, in women younger than 19 years, increased risk for obstetric complications is suggested. Teenage pregnancies are usually unintended (in 85% cases) and can be prevented by wide use of effective contraceptives (25). Older women are exposed to risks in pregnancy in a wholly different way than younger women. Those risks include pregnancy-induced hypertension, premature rupture of the membranes, preterm delivery, vaginal bleeding and gestational diabetes. Risks for chromosomal birth defects are also shown to rise (26, 27). Pregnancy in older women is more frequent in developed countries (2.4% in UK) (28).

The gestational age, birth weight and birth defects are indicators of prenatal care and have implications for public-sector services as well (29). According to relevant literature, the preterm births prevalence of 5.2% and 4% as found in our study are lower than expected. Preterm births prevalence in Europe is 6.2% and in the USA 8.9%. For low birth weight infants, the prevalence in Turkey is 11%, in the USA 7.7%, in Albania 7%, in the former Yugoslav Republic of Macedonia and in Serbia 6%, in Bosnia and Herzegovina and in Croatia 5% (30-32). The prevalence and type of birth defects found in our study are in accordance with the literature. The European Surveillance of Congenital Anomalies reported prevalence of congenital heart defects to be 6.5 per 1000 births, of limb defects 3.8 per 1000, of urinary system anomalies 3.1 per 1000 and of nervous system defects 2.3 per 1000 (33).

Considering folic acid supplementation use in our capital city, we’ve found it to be unsatisfactory. The same problem still exists even in developed countries. In the USA, more than 50% of pregnancies are unplanned, and at least the same percentage can be expected in our country. The estimated use of folic acid before pregnancy in Sweden is 5-6% (34), in the Netherlands
37% (35), in Central Pennsylvania 17% for women ages 18-24 years and 27% for women ages 24-45 years (36). Interestingly, folic acid use in this last study was not associated with pregnancy intention in either age group (36). In reducing NTDs, folate from supplements was shown to be more effective compared to folate derived from food sources (37). The reason for this is that folates obtained from food are not absorbed as well as folic acid is. The average consumption of dietary folate by women in the USA has been estimated to be about 0.2 mg per day (38).

In many countries, low folic acid use has led to the introduction of fortification (38). In our study, only one woman was taking a vitamin-mineral complex containing recommended 0.4 mg of folic acid before pregnancy. Considerable advantage of fortification is that it allows intake of folic acid before conception. This is important because closure of the neural tube occurs during the third and fourth week of gestation, at a time when the majority of women are only just aware of their pregnancy. Folic acid fortification, in order to reduce NTDs, is considered to be one of the most successful public health initiatives in the past 50-75 years (39). On the other hand, Nikkila et al. (2006) reported that one of the reasons for marked decline in the prevalence of NTDs is prenatal diagnosis followed by elective abortion (34).

Our study showed that besides a multivitamin complex, folic acid (5 mg/day) was taken during the first trimester by 10% of women who had previously experienced a spontaneous miscarriage, and by 1% in the second and third trimester, respectively. However, is such a high dose of folic acid rational and necessary? For the prevention of NTDs, the recommended oral dose of folic acid for all women of childbearing age capable of becoming pregnant is 0.4 mg/day. For women with a history of a pregnancy resulting in an NTD, the recommended oral dose is 4 mg/day (from one month before pregnancy until the fourth month of pregnancy). The Canadian College of Medical Geneticists recommends a range of 0.8-5 mg/day for the second prophylaxis (9).

These higher doses may be required in the presence of diabetes mellitus, haemolytic anaemia, anticonvulsant therapy, chronic infections, smoking, and alcoholism, in cases of pregnant adolescents or specific socio-economic conditions (9).

To determine the most appropriate dose of folic acid, the red blood cell (RBC) folate concentration can be used. It has been shown that RBC folate concentrations exceeding 906 nmol/L are maximally protective against folate-dependent NTD (40). The dose of folic acid that might cause harm, such as difficulty in identifying cobalamin deficiency, lowering of cobalamin levels, folate neurotoxicity, antagonism of drugs that inhibit folate metabolism, reduced zinc absorption, association with malignant neoplasm, hypersensitivity reactions, increased susceptibility to malaria, is still unknown (41). Campbell et al. (1996) emphasize that data suggesting folic acid supplements were unsafe are weak and based predominantly on case series and reports (41). Since some substances in multivitamins, especially Vitamin A, could be harmful when administered in larger doses, women should be advised not to take more than one multivitamin supplement per day.

When compared with an average of 18% prevalence in the industrial world as a whole (42), the prevalence of iron-deficiency anaemia in the third trimester of pregnancy in our study (0.2%) was very low. It is unclear if this is due to good nutrition or the lack of adequate screening. Although an iron supplementation becomes more important in later pregnancy, the majority of women in our study stopped using this preparation in the second and third trimester of pregnancy. Iron deficiency anaemia is one of the most common pregnancy complications. Despite
its numerous sources, due to the very inefficient absorption of iron, women have difficulty maintaining iron balance using only a healthy diet (43). Generally, iron supplementation is recommended to low-income pregnant women, to pregnant women in developing countries and in cases of documented iron deficiency (44).

The role of vitamin D in maintaining healthy pregnancy has recently become the main focus. The functions of this hormone are widespread and complex. Circulating maternal concentrations of hormonally active vitamin, calcitriol, rise early in the first trimester, doubling by the end of the third trimester of pregnancy. The early rise in calcitriol levels is believed to be necessary for the mother’s immunological adaptation required for the maintenance of a normal pregnancy (45), in modulating the risk of pregnancy complications and in sustaining fetal growth, bone development and immune maturation (46). It has been hypothesized that maternal deficiency in vitamin D may increase susceptibility to pre-eclampsia and childhood asthma (47, 48). Low maternal calcitriol levels are mainly associated with low intake of vitamin D and dressing habits providing ample coverage (49, 50). Fluoride supplementation from the third to the ninth month of pregnancy is shown to be effective in preventing dental caries in the offspring (9).

Despite the extensive research, the exact role of the variety of other micronutrients in fetal growth and development has yet to be explored in detail. According to the literature, supplementation of calcium, magnesium, zinc, selenium, vitamin C and vitamin B6 may be of added value to prevent pre-eclampsia (44, 51, 52). On the other hand, calcium, zinc, copper and Vitamin B-12 supplementations may enhance intra-uterine growth restriction (44, 53). In addition, magnesium, copper, Vitamin E and Vitamin B-6 deficiencies were associated with hematological damage, while iodine and biotin deficiencies have been shown to cause birth defects (44, 53, 54). Moreover, severe iodine deficiency may result in congenital hypothyroidism and neurocognitive deficits (55-57). On the other hand, there are many interactions described. Intake of cereal-based diets rich in phytate, high intake of supplemental iron, or any gastrointestinal disease may interfere with zinc absorption. Since both iron and copper compete with zinc at the absorption sites; zinc supplementation is recommended when elemental iron supplementation exceeds 60 mg/day. Likewise, whenever zinc supplements are used, copper should also be supplemented (42).

As well-balanced diets provide the nutritional Recommended Dietary Allowance (RDA) for pregnant and lactating women, routine supplementation is not recommended (58). However, there is some evidence that 20-30% of pregnant women suffer from some vitamin deficiencies (44). Moreover, consequences could be severe due to often co-existing multivitamin deficit combinations and subclinical depletions (59). A meta-analysis of 17 studies provided evidence of a significant benefit of multiple micronutrient supplementations in pregnant women in developing countries in terms of reducing the prevalence of small-for-gestational age births. In contrast, the iron-folate supplementation showed no significant effect on maternal anaemia in the third trimester (60). Therefore, the decision about supplementation prior to and during pregnancy must be based on economic status, social and cultural environment and personal habits of the mother.

Conclusion

Although folic acid supplementation during the first trimester of pregnancy in our capital city is not satisfactory, the indicators of prenatal care such as gestational age,
birth weight and birth defects indicate good health care of pregnant women. Further efforts in terms of planning pregnancy are needed to improve prenatal care. These efforts should include the continuous education of both health professionals and women of childbearing potential, which should also enable the adequate implementation of the recommended supplements. The prevalence of anaemia in pregnancy in this study was lower than expected, so we suggest further studies to explain this finding.

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