Determination of Some Biochemical Parameters in Women during the First Trimester of Pregnancy (Normal Pregnancy and Missed Miscarriage)

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Abstract—Our study was designed to determine the metabolic changes of some biochemical parameters (cholesterol, triglyceride, Iron, uric acid, Urea and folic acid) and highlight their changes in 57 women of the region Batna, during the first trimester of pregnancy. This practical work was done with 27 women with missed miscarriage, compared with 30 control subjects of normal pregnant women. The assay results revealed a highly significant difference (P = 0.0006) between the two groups in serum iron (64.00 vs 93.54) and in the rate of folate (6.70 vs 9.22) (P <0.001) but no difference was found regarding the rate of Ca (9.69 vs 10.20), urea (0.19 vs 0.17), UA (33.96 vs 32.76), CH (1.283 vs 1.431), and TG (0.8852 vs 0.8290). The present study indicates that iron deficiency and folate are associated with missed miscarriage, but no direct pathophysiological link has been determined. Further in-depth studies are needed to determine the exact mechanism by which these deficits lead to a missed miscarriage.

Keywords—Biochemical parameters, pregnant women, missed miscarriage.

I. INTRODUCTION

IN Algeria, about 40% of pregnant women experience health problems related to pregnancy and 15% of all pregnant women suffer permanent complications that put their lives in danger.

Pregnancy is a period of significant physiological changes characterized by an adaptation of the maternal organism during which fetal needs require regular and balanced inputs provided by the food and maternal stores. These two factors lead to a new nutritional balance that we begin to see now it is possible implications in the smooth running of gestation [1].

If caloric needs are normally met, and even beyond, in developed countries, food is increasingly skewed towards carbohydrates, lipids and inadequate micronutrient whose native reserves are limited or non-existent, causing subcarences, whose effects on the fetus are the subject of many studies, but the impact on fetal growth and development of the pregnancy begins to be known. In addition, fetal eutrophy should not only be analyzed in terms of weight, but the additions to the fetus must provide the basics of postnatal development both physically and mentally [2].

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Therefore, it is recommended that mothers follow the dietary guidelines in force, and also before pregnancy.

Our study consists in: Determine the impact of metabolic changes in some biochemical parameters and highlight their variations on the progress of the pregnancy in the first quarter.

II. MATERIALS AND METHODS

A. Targeted Population and the Place of the Study

Targeted subjects were randomly formed from 57 pregnant women during their first trimester of age between 18 and 47 years, who presented for a consultation at BOUATOURA MERIEM MATERNITY – BATNA during March to November 2013. The women were recruited after giving their informed consent to participate in the study.

B. Blood Samples

Further to an interrogation of descriptive character samples were taken at the antecubital vein using sterile equipment.The blood collected in a heparinized tube was used for performing an assay of some biochemical parameters (iron, calcium, TG, cholesterol, urea, and uric acid). While that collected in a dry tube was used for the determination of vitamin B9.

C. Laboratory Evaluation

The determination of biochemical parameters (iron, calcium, uric acid, urea, triglyceride and cholesterol) was performed manually; the concentration of folate was determined by electroluminescence through immunoanalyseur Elecsys 2010 ™ Roche.

D. Statistical Analyses

The results are expressed on Mean ± SEM. To compare the averages of samples, we used the test "t" student. The number "N" (number of subjects) is <30, the calculations were performed using a Graph Pad Prism 5.00 software. P values <0.05 are considered statistically significant.

III. RESULTS AND DISCUSSIONS

A. Distribution of Pregnant Women by Age Ranges

The mean age for women having a missed miscarriage is 32.44 ± 0.90 years.

It has been described in the literature that female fecundity is highest in 25 years [3], while it decreased from the age of 30 years [4].

TABLE I
DISTRIBUTION BY AGE RANGES

Age ranges	Missed miscarriage	Normal pregnancy
18-23	1 (1.75%)	5 (8.77%)
24-29	5 (8.77%)	14 (24.56%)
30-35	15 (26.32%)	6 (10.53%)
36-41	4 (7.02%)	4 (7.02%)
42-47	2 (3.51%)	1 (1.75%)
Total	27 (47.37%)	30 (52.63%)

B. Distribution of BMI Pregnant Women during Pregnancy

According to [5], the overweight is an independent risk factor for miscarriage in the first trimester of pregnancy.

Among overweight women, there may be a short luteal phase [6], with a cycle of endometrial disorders [7], which may partly explain the embryo implantation failure and the occurrence of FCS [8].

TABLE II
VARIATION IN THE RATE OF BMI AMONG WOMEN PREGNANT

BMI (kg/m²)	Missed miscarriage	Normal pregnancy
< 18	1 (3.70%)	0
18 – 25	7 (25.93%)	11(36.67%)
25 – 30	9 (33.33%)	9 (30%)
30 – 35	7 (25.93%)	8 (26.67%)
> 35	3 (11.11%)	2 (6.67%)

C. Distribution by Passive Smoking

TABLE III
VA DISTRIBUTION OF PREGNANT WOMEN ACCORDING TO PASSIVE SMOKING

	Missed miscarriage	Normal pregnancy
Passive smocking	11 (40.74%)	15 (50%)

Passive smoking increases the risk of occurrence of obstetric complications.

The principal toxicant tobacco smoke, carbon monoxide (CO) which has a very high affinity for hemoglobin than oxygen and knowing that the CO passes the fetoplacental barrier; it most affects the fetal oxygenation.

D. Distribution of Pregnant Women According to Clinical Signs

TABLE IV
DISTRIBUTION OF ANEMIA AND DIGESTIVE DISORDERS ACCORDING TO PREGNANT WOMEN

	Missed miscarriage	Normal pregnancy
Anemia	9 (33.33%)	10 (33.33 %)
Digestive disorders	19 (70.37%)	23 (76.67%)

According to the results, the frequency of anemic pregnant women with normal pregnancy is the same for Missed miscarriage. So, anemia has not an effect on prognosis of pregnancy.

The digestive disorders are not affecting the pregnancy outcome.

E. Determination of Biochemical Parameters in Pregnant Women

TABLE V
DETERMINATION OF BIOCHEMICAL PARAMETERS IN WOMEN WITH A MISSED MISCARRIAGE AND CONTROLS (MEAN ± SEM)

Age ranges	Missed miscarriage	Normal pregnancy
Seric iron (µg/dl)	64.00±4.91a	93.54±6.29**b**
Calcium (mg/l)	9.69±0.49a	10.20±0.47a
Urea (g / l)	0.19±0.01a	0.17± 0.01a
Uric Acid (mg/l)	33.96±2.29a	32.76±1.95a
Triglyceride (g/l)	0.8852±0.06a	0.8290±0.06a
Cholesterol (g/l)	1.283±0.08a	1.431±0.06a
Folic acid (ng/ml)	6.70±0.9 a	9.22±1.27 **b**

a, b: comparison between group means with a significance level (P <0.05).

The assay results revealed a highly significant difference (P = 0.0006) between the two groups in the serum iron and in the rate of folate (P <0.001), but no difference was found regarding the rate of Ca, urea, AU, CH, and TG.

The reason given to explain our results is that iron requirements during pregnancy are significantly increased due to the increase in erythrocyte mass, fetal growth and development of the placenta. Maternal iron stores are used significantly, so that for many women, insufficient reserves, which can lead to deficits and therefore sometimes anemia [9].

Iron deficiency causes a decrease in the synthesis of hem in the erythrocytes in the bone marrow which can cause a decrease in the rate of production of hemoglobin and decreased efficiency mitochondrial system; therefore, it affects the fetal development.

The mean concentration of folate in pregnant women with pregnancy stopped (6.70 ± 0.9 ng/ml) was significantly lower than that of controls (9.22 ± 1.27 ng/ml) with a very significant difference (p <0.001).

Several studies on the relationship between vitamin B complex, particularly folic acid, and spontaneous abortion have been published.

Dansky et al. [10] reported that low levels of folic acid in the blood before and / or in early pregnancy were significantly associated with spontaneous abortion.

However, Neiger et al. [11] in a prospective study revealed that among pregnancies complicated by hemorrhage first trimester pregnancy, a known risk factor for abortion, low folate status was not associated with an increased risk of loss of pregnancy and adverse outcome.

Although folate deficiency is the most common deficiency in pregnant women after iron deficiency, is one of the factors that may cause alterations in the structure of chromosomes in rapidly dividing cells [12].

No mechanism by which low folate levels could cause spontaneous abortion has yet been identified [13].

This deficiency is reported to be associated with many pathologies; however, much less is known about effects of the deficiency on human reproduction. Gao et al. [14] showed that a folate deficiency status did not influence embryo implantation, and the methylation and expression of three molecules essential for uterine receptivity, such as cadherin 1

(Cdh1), the progesterone receptor (RPG) and estrogen receptor 1 (Esr1) [15].

IV. CONCLUSION

Our study showed that iron deficiency and folate deficiency are associated with pregnancy loss but no pathophysiological mechanism has been identified.

The importance of these deficiencies found and their potential impact on the pregnancy outcome suggest prevention by balanced diet diversification and adapted to the specific needs during this period, women's education in preconceptional and gestational period about their eating habits. Moreover, the potential benefits of supplementation should be better characterized.

The missed miscarriages etiologies are multiple and reflect dysfunction of many systems. However, knowledge in this area is still lacunars and need to be deepened by studies that take account of many nutritional, environmental and genetic factors.

REFERENCES

[1] J. Rey, "Adaptation et Grossesse. In: Alimentation des femmes enceintes », *Paris : Cidil* 1986, pp. 13-24.

[2] J. Belaisch-Allart, " Grossesse et Accouchement Après 40 ans ». *EMC – Obstétrique*, 2008, pp.1-8.

[3] RT. Scott, GE. Hofmann, "Prognostic Assessment of Ovarian Reserve". *Fertil Steril*; 1995, pp. 63: 1-11.

[4] P. Lecomte, N. Gervaise, "Troubles de la Fertilité D'origine Endocrinienne". *EMC - Endocrinologie-Nutrition*, 2001, pp.1-25.

[5] Bellver J., Rossal L.P., Bosch E., Zuniga A., Corona J.T., Melendez F., et al. (2003). Obesity and the Risk of Spontaneous Abortion after Oocyte Donation. Fertil Steril; 79 : 1136-1140.

[6] K. D. Helm, R. M. Ness, W. S. Evans, "Physiologic and Physiopathologic Alterations of the Neuroendocrine Components of the Reproductive Axis". *Yen and Jaffe's Reproductive Endocrinology. Philadelphia: Saunders*, 2009, pp. 441–88.

[7] A. Jain, A. J. Polotsky, D. Rochester, S.L. Berga, T. Loucks, G. Zeitlian, et al. "Pulsatile Luteinizing Hormone Amplitude and Progesterone Metabolite Excretion are Reduced in Obese Women". *J Clin Endocrinol Metab*, 2007, pp. 92: 2468-2473.

[8] A. Benammar, N. Sermondade, C. Faure, C. Dupont, I. Cedrin-Durnerin, C. Sifer, S. Hercberg, R. Levy, « Nutrition et Fausses Couches Spontanées: Une Revue de la Littérature ». *Gynecol Obstet &Fertilité*, 2012, pp. 40: 162-169.

[9] F. E. Viteri, "Prevention of Iron Deficiency in Prevention of Micronutritient Deficiencies". In: *Board of international Health*, Food and Nutrition, *éd*. Tools for Policy Makers and Public Health Workers. Washington: *National Academy Press*, 1997, pp. 45-103.

[10] L. V. Dansky, D. S. Rosenblatt and E. Andermann, "Mechanisms of Teratogenesis: Folic Acid and Antiepileptic Therapy". *Neurology*, 1992, pp. 42 (Suppl. 5), 32–4.

[11] R. Neiger, C. Wise, S. A. Contag, M. B. Tumber, J. A. Canick, "First Trimester Bleeding and Pregnancy Outcome in Gravidas with Normal and Low Folate Levels". *Am J Perinatol*; 1993, V, 10(6), pp. 460-462.

[12] E. Baker, and G. R. Sutherland, "A New Folate Sensitive Fragile Site at 1p21.3". *J. Med. Genet*., 1991, pp. 28, 356–357.

[13] J. G. Ray, C. A. Laskin, "Folic Acid and Homocyst(e)ine Metabolic Defects and the Risk of Placental Abruption, Pre-Eclampsia and Spontaneous Pregnancy Loss: A Systematic Review". *Placenta*.; 1999, pp. 20:519-529.

[14] R. Gao, Y. Ding, X. Liu, X. Chen, Y. Wang, C. Long, S. Li, L. Guo, and J. He, "Effect of Folate Deficiency on Promoter Methylation and Gene Expression of Esr1, Cdh1 and Pgr, and Its Influence on Endometrial Receptivity and Embryo Implantation". *Hum. Reprod.* 2012, V. 27 (9), pp. 2756-2765.

[15] J. Fujimoto, S. Ichigo, M. Hori, T.Tamaya (). Alteration of E-cadherin, Alpha- and Beta-Catenin mRNA Expression in Human Uterine Endometrium during the Menstrual Cycle. *Gynecol Endocrinol*; 1996, pp. 10:187-191.