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Effect of Micronutrient Supplements on Female Fertility

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Abstract **Original Research Article**

Introduction: Over the last few decades, fertility has declined globally to unprecedented low levels. ***Objective:*** Main goal was to determine whether the micronutrient supplements have any impact on female fertility. ***Method:*** This prospective observational study was conducted at the Department of Gynae and Obs, Dhaka Medical College Hospital, Dhaka, Bangladesh. Total 142 patients were enrolled in the study, during July 2019 to June 2020. Analysis of different variables were done according to standard statistical tool Spss and calculations were done using scientific calculators & using MS-excel program in computer. The present study was conducted after receiving approval from the Medical and Health Research Ethics Committee (MHREC). ***Result:*** For vitamins C and E, mean nutritional intake surpassed the estimated average requirement (EAR). There were no variations in antioxidant consumption across the groups. In multivariable models, women with a body mass index (BMI) of R25 kg/m^2 had shorter TTP when they took vitamin B6 from dietary supplements. Vitamin C from dietary supplements was also linked to a shorter TTP among women with a BMI of less than 25 kg/m^2. ***Conclusion:*** Women with a BMI of 25 kg/m2 had a shorter TTP when their vitamin C intake increased, while women with a BMIR of 25 kg/m2 had a shorter TTP when their vitamin B6 intake increased.

Keywords: Micronutrient, Supplements, female fertility.

INTRODUCTION

Over the last few decades, fertility has declined globally to unprecedented low levels[1]. Europe has the lowest rates, with 1.6 children per woman, compared to 2.5 children per woman globally[1]. An issue with ovulation cannot be diagnosed in more than 70% of couples, prompting researchers to look for possible modifiable risk factors[2, 3]. In developed countries, particularly Europe, Australia, and North America, a rising number of women put off having children for a variety of reasons, including higher education, job aspirations, or financial concerns-often unaware that fertility falls with age and that assisted reproductive treatments are less effective in older women[1, 4]. Caffeine, alcohol, and environmental contaminants, as well as smoking and obesity, can have a negative impact on fertility[4]. Micronutrients are vitamins and minerals that must be consumed in tiny amounts as part of a balanced diet. Despite the fact that these micronutrients do not produce energy to the human body, they are required for catabolic and anabolic processes and must be obtained from outside sources. The necessity of excellent nutrition during pregnancy has previously been proven, with embryonic and fetal development, and consequently pregnancy outcomes, being influenced[5, 6]. Pre-eclampsia, pre-term births, neural tube defects of the brain or spinal cord (such as spina bifida), and other congenital abnormalities, as well as newborns born small-for-gestational age or with a low birth weight, can all be caused by micronutrient deficiencies in pregnant women. 5 Micronutrient deficiencies during pregnancy may have long-term consequences in adulthood, increasing the risk of non-communicable illnesses[7]. This ‘national consumption research II' (Nationale Verzehrstudie II) employed questionnaires to capture men and women of various ages' daily food consumption and compute the average intake. It also takes into account the loss of micronutrients due to factors such as food storage and preparation. The German, Austrian, and Swiss nutritional societies (D-A-CH) [8] issue a publication

named "reference values for micronutrient supply," which is one of the most important European releases of this data. Dietary recommendations for certain life situations may be determined using this data, such as the increased need for key nutrients during pregnancy[9]. There are several researches in veterinary medicine that explore the impact of vitamin supplementation on cattle fertility. In humans, however, there are only approximately a dozen randomized, placebo-controlled trials, some of which are repeat publications. A recent systematic review used a standardized quality analysis to analyze and evaluate the available research. A final judgment is difficult in general since a lot of research were lacking[10-14]. Another recent clinical trial looked at the impact of vitamin E replacement in the setting of clomiphene-based hormonal stimulation treatment and showed that women who took vitamin E had thicker endometrium's[15]. In-vitro fertilization (IVF) studies suggest a particularly beneficial effect on endometrial thickness following stimulation, albeit the clinical effect was not investigated[16]. This micronutrients may have fertility-improving characteristics: vitamin B6, vitamin C, vitamin D, vitamin E, iodine, selenium, iron, omega-3-fatty acid.

OBJECTIVES

- To determine the effect of micronutrient supplements on female fertility.

MATERIALS & METHODOLOGY

This prospective observational study was conducted at the Department of Gynae and Obs, Dhaka Medical College Hospital, Dhaka, Bangladesh. Total 142 patients were enrolled in the study according to following inclusion and exclusion criteria during July 2019 to June 2020. Women participating in The Fast Track and Standard Treatment (FASTT) trial that reported reliable dietary information and started treatment were included in the present study. Pretested and predesigned pro-forma containing history and examination finding of the patients and operative procedure & follow up were used to collect the data as was approved in the protocol. Analysis of different variables were done according to standard statistical tool Spss and calculations were done using scientific calculators & using MS-excel program in computer. The present study was conducted after receiving approval from the Medical and Health Research Ethics Committee (MHREC).

- **Inclusion Criteria**
  - 12 months of failed conception;
  - Hysterosalpingogram or laparoscopic confirmation of at least one ovary and ipsilateral patent fallopian tube;
  - No pelvic disease, ectopic pregnancy, or past infertility therapy (with the exception of up to three cycles of clomiphene citrate without IUI).
- **Exclusion Criteria**
  - Presence of hydrosalpinges,
  - Stage III/IV endometriosis, use of donor sperm,
  - Or the need for assisted reproductive technology procedures other than IVF.

RESULTS

Out of 142 patients 65 (45.8%) were 15 to 25 years of age, 66 (46.5%) were 26 to 35 years old and only 11 (7.7%) were 36 to 45 years of age. The mean age of the patients was 27.4 years (Table I). Demographic data like education, occupation and BMI of the patients and details data shown in table II. Among 142 patients, 78 (54.9%) had primary infertility and 64 (45.1%) had secondary infertility (Figure I). Among women aged 26–41 years, the majority of subjects above the EAR for pregnancy. In the unadjusted mean intakes for total, dietary, and dietary supplement intake, there were no significant differences between women who had a live birth during the research period and those who did not. Furthermore, there were no statistically significant connections between having fulfilled the EAR or not and TTP resulting in a live delivery among any of the nutrients under examination, and no significant variations in total energy, antioxidant nutrient consumption, age, or BMI were found between participants who reported dietary supplement use vs. those who did not (Table III). Increased vitamin C consumption from dietary supplements was linked to a shorter TTP in women with a BMI of less than 25 kg/m^2. A significant relationship between increasing total vitamin C consumption and shorter TTP was also found when total vitamin C intake was modeled as a continuous variable. However, no significant relationships between tertiles of total vitamin C consumption and dietary vitamin C consumption were found. Increased b-carotene consumption from dietary supplements was linked to a shorter TTP in women with a BMI of more than 25 kg/m^2. There were no significant associations between total b-carotene and dietary b-carotene intakes (Table IV). Out of 142 female patients, 22 patients were able to conceive after taken the micronutrient supplements for 6 to 9 months (Figure II).

Table I: Age distribution of the patients (n=142)

Age of the patients					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	15 to 25 years	65	45.8	45.8	45.8
	26 to 35 years	66	46.5	46.5	92.3
	36 to 45 years	11	7.7	7.7	100.0
	Total	142	100.0	100.0	

Table II: Demographic data of patients (n=142)

Education of wife					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Not education	3	2.1	2.1	2.1
	primary	17	12.0	12.0	14.1
	Secondary	66	46.5	46.5	60.6
	Graduate	20	14.1	14.1	74.6
	Postgraduate	13	9.2	9.2	83.8
	Other	23	16.2	16.2	100.0
Occupation					
Valid	Housewife	121	85.2	85.2	85.2
	Service	20	14.1	14.1	99.3
	Business	1	.7	.7	100.0
BMI (kg/m2)					
Valid	11 to 20 kg/m2	7	4.9	4.9	4.9
	21 to 30 kg/m2	115	81.0	81.0	85.9
	31 to 40 kg/m2	20	14.1	14.1	100.0
	Total	142	100.0	100.0	

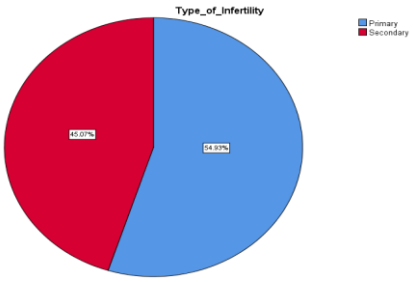

Fig-I: Types of infertility

Table III: Daily energy and antioxidant intake of patients:

	Total (n)	Mean	Median	% meeting EAR	% not meeting EAR
Total energy (kcal)	142	1324	1308	-	-
Vitamin B6					
Total	142	4153	3542	-	-
Dietary	142	3280	2257		
Supplements	109	1370	1280		
Vitamin C					
Total	142	192	192	265	12
Dietary	142	120	120		
Supplements	117	134	134		
Vitamin E					
Total	142	47	29	279	26
Dietary	142	12	9		
Supplements	114	38	18		

Table IV: Ratio of antioxidant intake and BMI (body mass index)

Antioxidant	Supplement intake	Dietary intake		
		T1	T2	T3
BMI <25kg/m2 (n=41)				
Vitamin B6	1.17	1.00	1.07	0.89
Vitamin C	1.06	0.96	0.92	0.98
Vitamin E	1.02	0.73	0.82	0.75
BMI >25kg/m2 (n=101)				
Vitamin B6	1.25	1.04	0.70	1.30
Vitamin C	1.00	1.06	1.20	1.32
Vitamin E	1.06	1.32	0.95	1.08

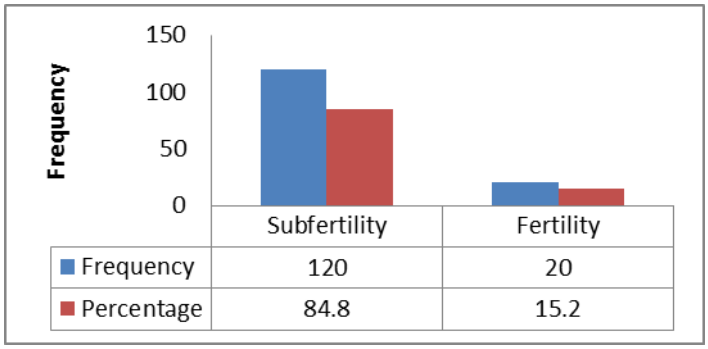

Figure II: Outcome of the patients

DISCUSSION

The results of a study performed by Czeizel et al. [17, 18] on the multivitamin supplement Elevit Pronatal showed an increase in pregnancy rate in the intervention group. Despite questionable assessment strategies, the results were of high or low significance, depending on whether women who conceived in the first month of supplementation were excluded. The number of dropouts differed in the two publications. Ronnenberg et al. [19] conducted a cohort research that found a link between increased vitamin B6 content and an increased relative risk of conception. Methodological restrictions restrict these results, despite a planned research strategy, because vitamin and homocysteine levels were only measured once at the start of the trial. Furthermore, the research was limited to a certain group of people. The intervention trial of Kilicdag et al. [20], which looked at the effects of B vitamins and metformin on women with polycystic ovarian syndrome, could show that, compared to folic acid, vitamin B intake reduced or even prevented homocysteine levels more significantly. Despite its positive methodological approach, the study was only partially useful due to the dubious use of ANOVA and the low number of participants, which was below the predicted needed number of participants in one group. Leeda et al. [21] evaluated the impact of vitamin B supplementation on individuals with a history of preeclampsia and prenatal development retardation, and found that homocysteine levels were significantly reduced. Hemni et al. [22] found a substantial rise in progesterone levels of >10 ng/ml in the intervention group compared to the control group in a cohort trial with a control group in which patients with polycystic ovarian syndrome received high-dose vitamin C supplementation. In this study we found evidence that higher antioxidant consumption is linked to shorter TTP, however the connection was not consistent. TTP was shortened only in women with a BMI of less than <25 kg/m^2 when vitamin C was increased, and in women with a BMI of more than >25 kg/m^2 when vitamin B6 was increased. Consumption of antioxidant elements through dietary supplements, rather than food, was found to be the most important factor. Antioxidants derived through dietary supplements are not physiologically superior to those received from food sources, according to the research. Rather, the use of dietary supplements is likely to have aided FASTT participants in achieving the higher consumption required to trigger an effect.

Limitations of the study

The present study had few limitations such as this study was conducted in a single hospital and had a small sample size that may not reflect the whole scenario.

CONCLUSION

Apart from reducing the chance of deformity by periconceptional folic acid supplementation, other micronutrients, including folic acid, vitamin B6, vitamin C, vitamin D, vitamin E, iodine, selenium, iron, and DHA, may have a favorable influence on infertility therapy. The pathophysiology, clinical trials, and upper limits should all be considered in the multivitamin composition.

REFERRENCE

1. Population Division, Department of Economic Social Affairs, United Nations. World Fertility Patterns 2015—Data Booklet (ST/ESA/SER.A/370). San Francisco, CA: United Nations; 2015.
2. Chavarro JE, Rich-Edwards JW, Rosner BA, Willett WC. Diet and lifestyle in the prevention of ovulatory disorder infertility. Obstet Gynecol. 2007; 110:1050–1058.
3. Gaskins A, Chavarro J. Diet and fertility: a review. Am J Obstet Gynecol. 2017; 218:379–389?
4. Homan G, Davies M, Norman R. The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review. Hum Reprod Update. 2007; 13:209–223.
5. Ramakrishnan U, Grant F, Goldenberg T, Zongrone A, Martorell R. Effect of women's nutrition before and during early pregnancy on maternal and infant outcomes: a systematic review. Paediatr Perinat Epidemiol. 2012; 26:285–301.

6. Cetin I, Berti C, Calabrese S. Role of micronutrients in the periconceptional period. Hum Reprod Update. 2010;16:80–95
7. McMullen S, Langley-Evans S, Gambling L, Lang C, Swali A, McArdle H. A common cause for a common phenotype: the gatekeeper hypothesis in fetal programming. Med Hypotheses. 2012; 78:88–94.
8. Deutsche gesellschaft fu¨ r Erna¨hrung. Referenzwerte fu¨ r die Na¨ hrstoffzufuhr. Umschau-Verlag.
9. Max Rubner Institut. Nationale Verzehrs Studie II 2008 http://www.mri. bund.de/fileadmin/Institute/EV/NVS_II_Abschlussbericht_Teil_1_mit_Ergaenzungsbericht.pdf.
10. Westphal LM, Polan ML, Trant AS. Double-blind, placebo-controlled study of Fertilityblend: a nutritional supplement for improving fertility in women. Clin Exp Obstet Gynecol 2006; 4:205–208.
11. Czeizel AE, Dudas I, Metneki J. The effect of preconceptional multivitamin supplementation on fertility. Int J Vitam Nutr Res 1996; 66:55–58.
12. Cavarro JE, Rich-Edwards JW, Rosner BA, Willet WC. A prospective study of dairy foods intake and ovulatory infertility. Hum Reprod 2007; 22:1340–1347.
13. Cavarro JE, Rich-Edwards JW, Rosner BA, Willet WC. Diet and lifestyle and the risk of ovulatory infertility. Obstet Gynecol 2007; 110:1050–1058.
14. Cavarro JE, Rich-Edwards JW, Rosner BA, Willet WC. Use of multivitamins, intake of b-vitamins and risk of ovulatory infertility. Fertil Steril 2008; 89:668–676.
15. Cicek N, Sarikaya E, Gulerman C, et al. Vitamin E effect on controlled ovarian stimulation of unexplained infertile women. J Assist Reprod Genet 2012; 29:325–328
16. McWilliams GD, Frattarelli JL. Changes in measured endometrial thickness predict in vitro fertilization success. Fertil Steril 2007; 1:74–81.
17. Czeizel AE, Dudas I, Metneki J (1994) Pregnancy outcomes in a randomised controlled trial of periconceptional multivitamin supplementation. Arch Gynecol Obstet 255:131–139
18. Czeizel AE, Dudas I, Metneki J (1996) the effect of preconceptional multivitamin supplementation on fertility. Int J Vitam Nutr Res 66:55–58
19. Rich-Edwards JW, Goldmann MB, Willett WC, Hunter DJ, Stampfer MJ (1994) Adolescent body mass index and ovulatory infertility. Am J Obstet Gynecol 171:171–177
20. Kilicdag EB, Bagis T, Tarim E, Aslan E, Erkanli S, Simsek E, Haydardedeoglu B, Kuscu E (2005) Administration of B-group vitamins reduces circulating homocysteine in polycystic ovary syndrome patients treated with metformin: a randomised trial. Hum Reprod 20:1521–1528
21. Leeda M, Riyazi N, de Vries JIP, Jakobs C, van Geijn HP, Dekker GA (1997) Effects of folic acid and vitamin B6 supplementation on women with hyperhomocysteinemia and a history of preeclampsia or fetal growth restriction. Am J Obstet Gynecol 179:135–139
22. Hemni H, Endo T, Kitajima Y, Manase K, Hata H, Kudo R (2003) Ascorbic acid supplementation and serum progesterone levels in patients with a luteal phase defect. Fertil Steril 80:459–461