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Gynecological and Nutritional Risk Factors for Female Infertility

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ABSTRACT

Backgrounds:
Besides aging, there are a number of modifiable lifestyle risk factors, such as smoking, elevated consumption of caffeine and alcohol, stress, chronic exposure to environmental pollutants, hormonal imbalance and other nutritional habits exert a negative impact on a women's fertility. The aim of present work was to study the gynecological and nutritional risk factors implicated in developing female infertility.

Methodology:
This cross sectional study comprised of 109 women with infertility either primary or secondary . Data were collected using a questionnaire and in face to face interviews. The questionnaire include questions about risk factors, food intake history by 24 hours recall and modified FFQ beside data on anthropometric. Data was presented as either mean ± SD or frequencies and percentages according to the natural of data. Chi-square test was used at $\alpha < 0.05$.

Results:
Of the total samples 109 women with infertility aged between 17-40 years old shown that the peak age at 18-25 years old. The gynecological risk factors shown no significant differences. However, the obtained biochemical result revealed that abnormal high levels of estrogen, TSH, T4, LH, and testosterone, and abnormal low levels of FSH, and T3. The nutritional risk factors have been determined include low levels of serum vitamin D, and serum ferritin. In addition, women with infertility shown to have heavier body weight, overall BMI was 31.5 kg/m2 by which the majorities of women found significant obesity ($P < 0.05$), have high risk of waist circumferences and also WHR ($P < 0.05$). The result of present work found that food intake and food pattern of women have low energy intake and their dietary habits shown lack fruits and fish intake with increased junk food consumption ($P < 0.05$).

Conclusion:
The gynecological risk factors can be modified. The correct balance of energy, vitamin D and iron in the daily diet provides essential benefit for an optimal female reproductive health and reduces the risk of infertility. In this context, the association of certain risk factor to develop of infertility could be ameliorate by increase intake of balance diet or triggers can be eliminated.

KEYWORDS: *Infertility; BMI; Nutrition risk factors; Biochemical data; food intake; modified risk factors*

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INTRODUCTION

Infertility is one of the major problem in modern society and represent as much as 20–30% of the fertile female population (1). The American Society of Reproductive Medicine (ASRM) define the

infertility as the failure the coupling to conceive after one or more years of attempts of natural fertilization (2). The World Health Organization (WHO) reporting that about 80 million women in the world affected by this disease to date, with a prevalence rate of50% of women in developing countries (3).Furthermore, the infertility categorized as primary or secondary. Primary infertility is due to failure to achieve pregnancy after one year or more of regular unprotected sexual. Secondary infertility arise when couples have been pregnant at least once, and later on not able to get pregnant (3).

There are a number of risk factors have been reported among which gynecological, PCOS, systemic diseases, lifestyle factors and environmental conditions such as stressful jobs, unbalanced nutrition and unhealthy diet coincide to interfere with reproduction safety in women (4). In addition, heavier body weight (increased BMI) and energy imbalance in terms of restrictions or excesses, as well as dietary enrichment in carbohydrates, proteins, fatty acids, vitamins and minerals all of which exert their detrimental impact on reproductive system (5).

Regarding Nutritional factors affecting human infertility still receiving a lot of challenges, some researchers suggested that improve female infertility by consuming some micronutrient (6, 7). While, some studies have shown that micronutrient supplements attributed to higher pregnancy rates even if they have fertility disorders (8). Furthermore, about 15% of infertile women are considered idiopathic, which may be caused by oxidative stress (9). Therefore, many studies have investigated intervention strategy of micronutrient supplementation in oxidative status of infertile women (10-12). However, there is recent evidence demonstrated that micronutrients have play role in ovarian hormones secretion and uterus structure (13). There are a number of studies reported that some foods have protective role against infertility such as fish, poultry, fruits and vegetables and whole-grains reduce (14). On the other hands high western style diet with high saturated fat, trans fat and refine sugars have linked to high risk of infertility (15).Besides the aforementioned risk and causative factors there also hormonal imbalance (LH, estrogen, progesterone, testosterone, FSH, TSH and T3 (16, 17). In number of studies also found endometriosis, fallopian tube dysfunction, vaginitis and uterus polyps also contribute to female infertility (18-20).

Given the tight interconnection between nutritional factors and reproduction, this study, attempt to find the risk factors for female infertility include hormones factors, dietary habits, body weight status and also figure out if there is any risk factors implicated in women infertility. Therefore, the aim of the present work is to study Gynecological and nutritional risk factors attributed to female infertility.

Materials and methods

Study population

A cross sectional descriptive study carried out from beginning of October 2019 to the end of March 2020 on an infertility center at Alhwaary hospital in Benghazi the second largest city in Libya.

Approached of our study is aged groups attending the infertility center. The samples 109 subjects and the age of patients ranging between 17-40 years were married and have either primary or secondary infertility were involved in the study. After obtaining written consent, the subjects were requested to fill out a questionnaire and proceed to a private area to have their height and weight measured. Although we approached different number of subjects and the final completed questionnaires in hand were 109. Hence, our overall response rate was 99%.

Questionnaire

The questionnaire for this study based on 36 items divided into four sections. It contained questions about personal information, demographic and socioeconomic characteristics, and also gynecological risk factors include personal habit, family history of causes of infertility, biochemical investigations, history of disease, anthropometric data and dietary history.

Measurements

Weight and height were measured after completion of the questionnaires and hand in by two researchers. Height was measured to the nearest 0.1 cm using standard calibrated scale attached to the balance against a wall. Weight was measured to the nearest 0.2 kg using weighing machine. All measurements were collected with participants in barefoot light cloth. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters and categorized according to the World Health organization (21). WC was measured at the narrowest level of the hip at the maximum level over light clothing, using an unstretched tape meter, without any compressing to body surface and measurements were recorded to the nearest 0.1 cm. A waist circumference >35 inches (88 cm) in women and >40 inches (102 cm) in men (22).

Dietary history

Food intake was recorded by either 24 hours recall or food frequency questionnaires. The 24 hours dietary recall aimed to calculate macronutrients and energy intake, while food frequency questionnaire, have had modified and specified in short form include major

food stuff intake which will indicate dietary pattern of the subjects. Modified food frequency questionnaire (MFFQ) analyzed accordingly food intake daily weekly and monthly.

Biochemical tests

The laboratory tests were obtained from women include testing of hemoglobin, vitamin D, calcium and lipid profiles and hormonal assay . Data were collected by interviews or from medical records of patients.

Ethical statement

This study was granted approval by the local Ethics Committee of the Benghazi province. Informed written consent was obtained through a consent form that was given to the participants along with the questionnaire.

Statistical analysis

The data from the questionnaires was entered using Excel. Data set was exported to SPSS v.22 and Epi-info for complete analysis. Statistical analysis was carried out for the complete sample which were created according to measured BMI: underweight, normal and overweight. Mean values and standard deviation for all continuous variables: weight, height, BMI, age, genders and other variables for all groups were obtained. Frequencies for each categorical variable were calculated for each group as well. To determine the differences regarding each categorical variable in the groups, Chi-square test was performed. $p \leq 0.05$ was considered to be statistically significant. This study only descriptive study.

Result:

There were 109 women undergoing fertility treatment by which mean ± SD of the age was 30± 6 years old, in which 48.6% of the women have age groups between 18-25 years old, followed by age groups 26-40 years old 45% and age less than 18 being the least 6.4% (Table 1)

Table 1: Age distribution of the subjects:

Ages categories		N	N %
Ages in years	< 18	7	6.4%
	18-25	53	48.6%
	26-40	49	45.0%
	Total	109	100.0%

In table 2, most women treated for infertility have had married during the last 5 years 49%, followed by those married between 6-10 years while those between 11-15 years and even more than 15 years represent by 10. 1% and 5.5% respectively (Table 2).

Table 2: socioeconomic factors of the subjects:

		N	N %
years of marriages	1-5 years	49	45.0%
	6-10 years	43	39.4%
	11-15 years	11	10.1%
	more than 15 years	6	5.5%
	Total	109	100.0%
job	House wife	55	50.5%
	Government job	54	49.5%
	Total	109	100.0%

Risk factors for infertility have been shown in table 3, None of the risk factors found significant higher rather all presented less than 30% include family history, poly cystic ovaries syndrome, vaginitis, obstruction of fallopian tubes and etc. (Table 3).

Table 3: Gynecological Risk factors for infertility

		N	N %
Family history of infertility	Yes	17	15.6%
	No	92	84.4%
	Total	109	100.0%
polycystic ovarian syndrome	Yes	29	26.6%
	No	80	73.4%
	Total	109	100.0%

inflammation of vaginal (vaginitis)	Yes	21	19.3%
	No	88	80.7%
	Total	109	100.0%
do you suffer having polyps	Yes	12	11.1%
	No	96	88.9%
	Total	108	100.0%
problem in the fallopian tube	Yes	16	14.7%
	No	93	85.3%
	Total	109	100.0%
disorders of menstrual cycle	Yes	26	23.9%
	No	83	76.1%
	Total	109	100.0%
Member of family of suffering from the same disturbances	Yes	11	10.1%
	No	98	89.9%
	Total	109	100.0%

In the next, the serum biochemical of the subjects have been investigated and found that, have abnormal high levels of estrogen, TSH, T4, LH, and testosterone, and abnormal low levels of FSH, T3, vitamin D, and serum ferritin (Table 4).

Table 4: Biochemical laboratory results:

	Mean± SD	*Reference values
estrogen	69.56±8	0-40 ng /ml
progesterone	10.157± 5	0.2-16 ng/ml
prolactin	20.35± 11	<25 ng/ml
FSH	16.73± 5	20-50 mU/ ml
TSH	5.58 ± 3	0.4-4.2 ng/ ml
T3	1.33± 0.5	80-180 µg/ dl
T4	82.82±17	4.6-12 µg/ dl
LH	14±4	1-12 mU/ ml
vit D	16±9	30-80 ng/ ml
S. ferritin	3.88±	10-120 ng /ml
Testosterone	46.32	< 15ng/ ml

*The reference values are based on local result of references.

Nutritional status of subjects have been determined by anthropometric measurements, and dietary history. In table 5, mean ± SD of body weight, BMI, waist circumferences and WHR shown 77 ± 1.6 kg, 31.7± 2.1 kg/m2, 95 cm, 0.83% respectively. In addition, categorization of BMI revealed that more women significantly have obesity (*P*=0.04), high risk for abdominal fat deposition (WC) (*P*=0.000) and high risk for development of chronic disease (WHR) (*P*=0.000) (Table 6).

Table 5: Anthropometric index of the subjects:

	Mean ± SD
Weight	77.0±1.6
BMI	31.69± 2.1
waist circumference	95.0± 1.4
WHR	0.86± 0.1

Table 6: Anthropometric categorization of the subjects:

		N	N %	P values
BMI	Underweight	1	0.9%	
	Normal	25	22.9%	
	overweight	32	29.4%	
	obesity	51	46.8%	0.04
	Total	109	100.0%	

Waist circumferences	Normal	39	35.8%	
	At risk	70	64.2%	0.000
	Total	109	100.0%	
WHR categories	normal	12	11.0%	
	at high risk	97	89.0%	0.000
	Total	62	100.0%	

Chi-square test have been performed between groups of BMI, WC and WHR and at $\alpha < 0.05$ considered significant.

Furthermore, nutritional status of women with infertility also investigated by dietary history through 24 hours recall and modified food frequency questionnaire (MFFQ). The MFFQ, in table 7 A-C determined that high daily intake of milk, meat, eggs, vegetable, and cereals ($P < 0.05$) while other foods such as legumes shown significantly consumed weekly ($P < 0.05$). There also some foods reported to consumed less frequently include fish, and fruits. In regard junk foods, include coffee and tea and desserts found highly daily basis consumed ($P < 0.05$) while the soft drinks and fries foods presented weekly consumed ($P < 0.05$) but fast foods not preferred to consumed (Table 7 C).

Table 7 A: Summarized food intake by food frequency questionnaire:

		N	N %	P values
Milk and dairy products	daily	88	80.8%	0.000
	weekly	18	16.5%	
	Monthly	3	2.8%	
	Total	109	100.0%	
Fish	No	31	28.4%	
	Daily	5	4.6%	
	weekly	22	20.2%	
	Monthly	51	46.8%	0.00
	Total	109	100.0%	
Meat	No	4	3.7%	
	Daily	73	67.0%	0.000
	Weekly	28	25.7%	
	Monthly	4	3.7%	
	Total	109	100.0%	
Eggs	No	3	2.8%	
	Daily	67	61.5%	0.000
	Weekly	38	34.9%	
	Monthly	1	0.9%	
	Total	109	100.0%	

Chi-square test have been performed between yes and no response in each food stuffs and at $\alpha < 0.05$ considered significant.

Table 7 B: Summarized food intake by food frequency questionnaire:

		N	N %	P values
Vegetables	No	2	1.8%	
	Daily	86	78.9%	0.000
	Weekly	20	18.3%	
	Monthly	1	0.9%	
	Total	109	100.0%	
Fruits	No	2	1.8%	
	Daily	48	44.0%	
	Weekly	58	53.2%	0.09
	Monthly	1	0.9%	
	Total	109	100.0%	

Legumes	No	4	3.7%	
	Daily	20	18.3%	
	Weekly	65	59.6%	0.000
	Monthly	20	18.3%	
	Total	109	100.0%	
Cereals	Daily	84	77.1%	0.000
	Weekly	23	21.1%	
	Monthly	2	1.8%	
	Total	109	100.0%	

Chi-square test have been performed between yes and no response in each food stuffs and at $\alpha < 0.05$ considered significant.

Table 7 C: Summarized Junk food intake by food frequency questionnaire:

		N	N %	P values
Soft drinks	No	18	16.5%	
	Daily	28	25.7%	
	Weekly	52	47.7%	0.000
	Monthly	11	10.1%	
	Total	109	100.0%	
Coffee and tea	No	12	11.0%	
	Daily	69	63.3%	0.000
	Weekly	26	23.9%	
	Monthly	2	1.8%	
	Total	109	100.0%	
Sweets and desserts	No	10	9.2%	
	Daily	56	51.4%	0.01
	Weekly	39	35.8%	
	Monthly	4	3.7%	
	Total	109	100.0%	
Fries foods	No	4	3.7%	
	Daily	17	15.6%	
	Weekly	69	63.3%	0.000
	Monthly	19	17.4%	
	Total	109	100.0%	
fast food	No	22	20.2%	
	Daily	5	4.6%	
	Weekly	38	34.9%	0.08
	Monthly	44	40.4%	
	Total	109	100.0%	

Chi-square test have been performed between yes and no response in each food stuffs and at $\alpha < 0.05$ considered significant.

Diary history by 24 hours recall revealed low calories intake have found (1100). However, all macronutrient intake (fat, protein and carbohydrate) and also their energy intake were fall in normal range of recommended daily allowance (Table 8).

Table 8: Macronutrients calculated from 24 hour dietary recall:

	% Of calories	Mean ± SD
Total fat (gm)		36± 17
Calories from fat (Kcal)	327%1100= (30%)	327±70
Total CHO (gm)		145±51
Calories from CHO (Kcal)	579/ 1100= (53%)	579± 123
Total protein (gm)		41± 12
Calories from protein (Kcal)	165/1100= (17%)	165± 26
Total calories (Kcal)		1071± 240

Discussion:

Good nutrition and healthy life style are an essential component of attaining a healthy pregnancy and birth outcome. In the current work, include women in the reproductive ages from 17-40 years old those women either have primary or secondary infertility, so that no significant differences have been found between all ages of the participate and this finding were similarities with number of researches conducts in USA (23), Uk (24) and India (25).

The gynecological risk factors for infertility was also determined in the study but none of the risk factors (PCOS, endometriosis, vaginitis and etc.) contribute to infertility have been found significantly increased so that, in various studies published elsewhere found that infertility caused by deregulated ovarian function (26), tubal infections (27), endometriosis (28), cervical factor and uterine factors (28). Lack of significant in the present study could be in part of presences of another factors such as hormonal imbalances and obesity or due to small sample size.

There were other risk factors contribute to female infertility include hormonal imbalance and deficit serum levels of some nutrients. In fact those risk factors have been reported in numbers of studies which include increase testosterone, estrogen, TSH, T4, LH (29). Moreover, those factors play a role in reproduction include for menarche, maintenance of normal ovulatory cycles and production of ova (30). On the other hands there were low abnormal levels of FSH, T3, vitamin D, and serum ferritin have been found. Similarly serum FSH and T3 have a play a significant role in ovulation (17). The present study also revealed that vitamin D deficiency was common and considered as another risk factors led to infertility. In the study conduct by Al-Jaroudiet al (31, Fung et al (32),Lerchbaum et al (33) and Li (34) found that Low levels of vitamin D have been linked to pregnancy complications, congenital rickets and fractures in the newborn and poor outcomes in assisted reproduction. Generally, experts believe that serum levels < 20 ng/ mL are deficient and serum levels < 32 ng/mL have been considered inadequate. A cross-sectional study evaluates the prevalence of vitamin D deficiency in an infertile women and the data of the result revealed that the median vitamin D levels of patients were 27 ng/mL; besides, 68.6% and 22.2% of patients were considered insufficient and deficient, respectively. Furthermore, there were some evidence has linked vitamin D deficiency to PCOS phenotype (35). Several studies have been demonstrated that vitamin D levels in patients with PCOS wereless than that in controls (36, 37). In addition, deficiency of vitamin D may be associated with insulin resistance, obesity, and metabolic syndrome, all of which can result in ovulatory dysfunction. Serum ferritin was also found less than normal ranges, it well known that iron is stored as in form of ferritins. Numerous studies have shown that iron may be involved in ovulatory function and fertility (16, 38). One of the high-risk groups for this condition is women of reproductive age (16). In addition, our study highlighted that serum ferritin deficiency was common risk factor for infertility.

The result of the anthropometric measurement revealed that mean ± SD of BMI was 31kg/m2 which indicated that women participate in the study have obesity. Furthermore BMI classification also revealed majorities of women were either obesity or overweight. Many studies reported that there were relationship between body mass index (BMI) and infertility (4, 39).Indeed, the effect of body mass on infertility appeared to be bimodal. Morbidly obese women (BMI > 30 kg/m2) was associated two fold greater risk of ovulatory disorders (4,5). The impact of BMI on reproduction led to a sex dimorphism in the mechanisms linking reproduction and metabolism. Furthermore, being overweight attenuate the fertility in women more than it does in men (39). In many studies found that increased waist circumferences has been associated with increase infertility in women (40).

Dietary pattern of women with infertility has been investigated by two different approach, one is FFQ and the another is 24 hours recall. For 24 hours recall aim to determined macronutrient and energy intake of women. In general the mean ± SD of energy intake was low as much as 1100 kcal/day. However distribution of this kcal was as the following 29% from fat, 17% from protein and 54% from CHO. The first part of the results showed that daily dietary intake of energy was low and this of course altered energy balance is directly correlated to the reduced ovulatory maturation in women (41, 42).Because the data obtained from 24 hours could has limitation due to recall bias as one of disadvantages of this methods. In regard FFQ, the data obtained and analyzed found that, high daily intake of milk, meat, eggs, vegetable, and cereals ($P< 0.05$) while other foods such as legumes shown significantly consumed weekly ($P< 0.05$). There also some foods reported to consumed less frequently include fish, and fruits. In regard junk foods, include coffee and tea and desserts found highly daily basis consumed ($P< 0.05$) while the soft drinks and fries foods presented weekly consumed ($P< 0.05$) but fast foods not preferred to consumed. Presences of low levels or consumption of fish and fruits and high consumption of junk foods could be

enough as other nutrition risk factors for infertility. On the other hand, protective foods against infertility such as fish, poultry, fruits and vegetables and whole-grains reduce the risk female infertility by various mechanisms of action (8). While a high saturated fat, trans fat and sugar is associated with a high risk of infertility, whereas prudent diet that contains much more vegetables, fruits, grains and fish is associated with a low risk of infertility.

Overall, in this study women impose numbers of factors include heavier body weight high waist circumferences, serum nutrient deficit, hormonal imbalance, and imbalance dietary pattern led to women gynecological disorder related to infertility. One of the major limitation of this study was sample size and this study need to be validated in large samples.

Conclusion:

The result of the present study revealed that, women with infertility have high abnormal levels of f estrogen, TSH, T4, LH, and testosterone, and low abnormal levels of FSH, T3, vitamin D, and serum ferritin. Furthermore, heavy body weight, high body mass index (obesity), high risk both waist circumferences and waist hip ratio have been found in the women with infertility. Low total calorie intake and FFQ revealed that some foods not regular consumed and increased consumption of junk foods . The data of this work suggested that, female infertility is complicated by overlapping factors and precise investigation need to be carried out. Therefore, its recommended that regular checkup of all patients and strongly advocated in order to keep down the risk of infertility.

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Conflict of Interest

No conflict of interest.

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