Is Diet A Contributing Factor To Infertility?

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Abstract

Objective: To evaluate the effect of dietary trans-unsaturated fatty acids (TFAs) on ovulatory infertility in young unmarried females.

Methods: This cross-sectional study was conducted from 1 august 2023 to 31 December 2023 at the Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center Karachi. All healthy unmarried females aged 15-25 were included in the study. Females with family history of infertility, having existing comorbidity, history of irregular menstruation cycle or hormonal replacement therapy, were excluded. Based on Food frequency questionnaire score, 300 subjects were divided in 3 groups, Group A were low trans fats Consumers (Score 0-170), Group B were moderate trans fats consumers (Score 171-340) and Group C were high trans fats consumers (Score 341-500). The analysis of results was carried out on SPSS Software version 22.

Results: The study's 300 respondents, who ranged in age from 16 to 25, had a mean age of 21.8 years. Fifteen percent of those in group "A" had abnormal HDL, 22% had bad LDL, and 23% had abnormal TGA, while 17% had abnormal cholesterol. An abnormal TGA, abnormal HDL, abnormal LDL, and abnormal 31% of the participants in group "B" exhibited abnormal cholesterol levels. Significant correlation between oxidative stress and hormonal indicators was found in three groups: "A" (13%) had aberrant LH, "20%" had abnormal FSH, "11%" had abnormal serum estrogen, "10%" had abnormal serum progesterone, and "C" (49% had abnormal LH, FSH, estrogen, and progesterone). Food frequency questioner (FFQ) scores had a 25% positive correlation with cholesterol, a 40% negative correlation with HDL, a 31% positive correlation with LDL, and a 39% positive correlation with biochemical and hormonal indicators.

Conclusion: Trans fats diets significantly increase the risk of ovulatory infertility and reproductive failure in young females.

Key Words: Diet, Unhealthy, Trans Fats, Lipids, Infertility, Females

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Introduction

Infertility is a multifactorial disease that affects 23% of couples in the reproductive age range in Pakistan, with 5% responsible for primary infertility and 18% for secondary causes[1]. Infertility is increasing at a rate of 4% annually, affecting between 60-68 million people worldwide. Diet plays a significant role in infertility, as it provides energy for life processes from respiration to reproduction[4].Fatty acids, which are building components of body fat, play various biological functions, including regulating membrane shape and function, intracellular signaling pathways, transcription factor activity, gene expression, and the synthesis of bioactive lipid mediators[2-4]. Consuming trans unsaturated fatty acids (TFAs) has been linked to increased ovulatory infertility, negative impacts on gestation length, and developmental abnormalities[5-7]. Consuming TFAs may also increase the risk of developing diabetes, Alzheimer's disease, breast cancer, endometriosis, and cholelithiasis, as well as reproductive problems.

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Oxidative stress (OS) affects various reproductive processes in females, including folliculogenesis, oocyte maturation, endometriosis, and embryo development. Studies on the link between trans fats consumption and infertility in humans are limited, contrasting with animal studies[8]. Trans fats, found in commercial products, have been linked to inflammation, insulin resistance, and type 2 diabetes. This study investigates the link between oxidative stress and infertility in Pakistan and the increasing overweight and obesity among reproductive-age women. According to reports, OS and infertility go hand in hand. Studies examining the link between oxidative stress brought on by trans fats consumption and infertility in humans are very rare as compared to information obtained from animal studies[5]. It is well established that regular FSH and LH cycle fluctuations are necessary for healthy follicular maturation. During the development of follicles, remarkable genetic, cytoplasmic, and epigenetic alterations are intended to take place for productive fertilization and the generation of progeny[9]. This mechanism is based on the interaction of granulosa cells with oocytes, which ensures the synchronization of all oocyte processes caused by endocrine and paracrine stimuli. Due to redox reactivity, the reproductive system's two primary drivers of life expectancy and oocyte quality which also affect female fertility decline with age[7,10]. Trans fats are typically found in commercially fried and baked goods. In light of this, present study was design to investigate whether oxidative stress brought on by trans unsaturated fatty acids (TFAs) increases the likelihood of ovulatory infertility. Although many low- and middle-Income Countries (LMICs), including Bangladesh, Sri Lanka, and India, have previously addressed the issue of the rising prevalence of obesity among women of reproductive age, the issue has been underappreciated in Pakistan due to a lack of pertinent data and a lack of a focused policy[9]. This study aims to evaluate the effects of Trans fats diet on reproductive life of young unmarried females. To the best of our knowledge studies evaluating the effect of dietary TFAs on ovulatory failure in young female has not been conducted in Pakistan.

Methodology

It was a cross sectional study, and non-probability purposive sampling was used. The subjects were selected according to predetermined criteria and ethical clearance was obtained from the institutional review committee of the Basic Medical Sciences Institute, JSMU, Karachi. This study was carried out from 1st august 2023 to 31st December 2023 after the approval of the synopsis and obtaining ethical clearance at the Department of Physiology (BMSI), JPMC Karachi in collaboration with multiple departments of JPMC. The sample size is calculated using Online Open Epi Sample Size Calculator version (http://openepi.com/Menu/OE), keeping the mean prevalence of infertility as 22%, with 80% power, margin of error 5% with confidence interval of 95%, the calculated sample size is 264, but we have taken 300 subjects. 300 subjects were divided into 3 groups, where taking n=100, The groups were formed according to the score of FFQ, Cronbach's alpha and correlation coefficients for FFQ validity was done to validity the efficacy and accuracy of FFQ. Both in English and the native tongue, written consent was obtained. The consent form was filled out, signed or thumbprint. Later coded and secured. Data obtained during the study is kept confidential. All subjects fulfilling the inclusion criteria were registered and interviewed in detail regarding their general information, demographic data like name, age, address, ethnicity etc., history regarding their medical and surgical ailments, variables regarding their Reproductive system, Family History of Infertility, Drug History were recorded as per designed format on the prescribed questionnaire by the researcher. All healthy unmarried females between age 15-25 years were included in the study while female with family history of infertility, history of irregular menstruation cycle or hormonal replacement therapy, autoimmune or endocrine disorders, hyperlipidemia and liver or gastrointestinal diseases were excluded. Food Frequency Questionnaire were filled by subjects. Anthropometric parameters, like BMI was calculated as Kg/m2, weight (Kg), and height (m) while the subjects barefooted and in loose clothing. Blood pressure, both systolic

and diastolic were recorded after 15 min of rest and mean of 3 readings were taken. Every subject provided their verbal and written agreement in English and Urdu, duly signed or thumb printed.

Results

The study involved 300 participants, aged and weight matched, divided into three groups based on Food Frequency Questionnaire (FFQ) scores: Low Trans Fats Consumers (0-170), Moderate Trans Fats Consumers (171-340), and High Trans Fats Consumers (341-500). Data was collected using Performa and Food frequency questionnaires. The study surveyed 300 individuals aged 16-25 years, with a mean age of 21.8 years. The majority were students, day scholars, and hostlers. The mean height was 162.61 cm, weight was 56.52 kg, and the mean BMI was 21.45 kg/m2 (table 1). Table-2 shows a significant association between biochemical parameters and studied groups. In group "A", 17% had abnormal cholesterol, 15% had abnormal HDL, 22% had abnormal LDL, and 23% had abnormal TGA. In group "B", 31% had abnormal cholesterol, 22% had abnormal HDL, 30% had abnormal LDL, and 34% had abnormal TGA. The study found a significant association between hormonal and oxidative stress markers in three groups: "A" (13%) with abnormal LH, 20% with abnormal FSH, 11% with abnormal serum estrogen, and 10% with abnormal serum progesterone, and "C" (49% with abnormal LH, FSH, estrogen, and progesterone). Table-4 shows a correlation analysis of FFQ scores with biochemical and hormonal parameters. Results show a 25% positive association with cholesterol, 40% negative association with HDL, 31% positive association with LDL, 39% positive association with TGA, 25% negative association with LH, 24% positive association with FSH, 20% negative association with Estrogen, and 53% negative association with Progesterone. The study compared biochemical and hormonal parameters between two groups: "A" and "B". The mean cholesterol was 161.8 units, while the mean HDL was 44.1 units, LDL was 113.7 units, TGA was 98.1 units, LH was 5.5 units, FSH was 6.3 units, Serum Estrogen was 70 units, and Serum progesterone was 8.4 units. In group "C",the the mean cholesterol was 198.5 units, HDL was 34.3 units, LDL was 146.5 units, TGA was 197.5 units, LH was 3.6 units, FSH was 9.2 units, Serum Estrogen was 62.8 units, and Serum progesterone was 2.1 units (table-5).

Table 1. Descriptive on Demographic Data & Physical Parameters (n=300)

Characteristics		n	%
Age Group	16 - 20 years	112	37.3
	21 - 25 years	188	62.7
	Mean (±SD)	21.8	±2.2
Hostler / Day Scholar	Day scholar	208	69.3
	Hostler	92	30.7
Height (cm)	Mean (±SD)	162.61	±9.0
Weight (kg)	Mean (±SD)	56.52	±9.3
BMI (kg/m^2)	Healthy weight	218	72.7
	Obese	10	3.3
	Overweight	28	9.3
	Underweight	44	14.7
	Mean (±SD)	21.45	±3.93

Table 2. Association of Biochemical Parameters with Studied Groups

Parameters	FFQ Group	A (n=100)	B(n=100)	C(n=100)	p-value
Cholesterol	Abnormal	17	31	60	<0.01*
	Normal	83	69	40	
HDL	Abnormal	15	22	64	<0.01*
	Normal	85	78	36	
LDL	Abnormal	22	30	60	<0.01*
	Normal	78	70	40	
TGA	Abnormal	23	34	50	<0.01*
	Normal	77	66	50	

*p<0.05 was considered statistically significant using Pearson Chi Square test

Table 3: Assessment of Hormonal levels across the Studied Groups

Parameters		FFQ Group A (n=100)	B(n=100)	C(n=100)	p-value
LH	Abnormal	13	20	49	<0.01*
	Normal	87	80	51	
FSH	Abnormal	20	28	49	<0.01*
	Normal	80	72	51	
Serum Estrogen	Abnormal	11	18	47	<0.01*
	Normal	89	82	53	
Serum progesterone	Abnormal	10	15	43	<0.01*
	Normal	90	85	57	

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*p<0.05 was considered statistically significant using Pearson Chi Square test

Table 4. Correlation Analysis of FFQ with Biochemical and Hormonal Parameters

Parameters	FFQ Group	P-value	P-value
Cholesterol	0.25	<0.01*	<0.01*
HDL	-0.40	<0.01*	.<0.01*
LDL	0.31	<0.01*	<0.01*
TGA	0.39	<0.01*	<0.01*
LH	-0.25	<0.01*	<0.01*
FSH	0.24	<0.01*	<0.01*
Serum Estrogen	-0.20	<0.01*	<0.01*
Serum progesterone	-0.53	<0.01*	<0.01*

Table 5. Mean Comparison of Biochemical and Hormonal Parameters with Studied Groups

Parameters	FFQ Group				p-value		
	A (n=100)		B(n=100)		C(n=100)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Cholesterol	161.8	43.7	172.4	59.1	198.5	65.2	<0.01*
HDL	44.1	7.6	44.0	8.9	34.3	11.2	<0.01*
LDL	113.7	26.1	117.7	27.2	146.5	44.5	<0.01*
TGA	98.1	69.0	111.7	82.8	197.5	86.2	<0.01*
LH	5.5	3.1	4.9	3.2	3.6	3.7	<0.01*
FSH	6.3	3.4	8.0	3.5	9.2	5.1	<0.01*
Serum Estrogen	70.0	60.8	32.3	32.6	62.8	73.0	<0.01*
Serum	8.4	7.0	3.3	1.9	2.1	1.9	<0.01*

*p<0.05 was considered statistically significant using one way ANOVA

Discussions

Diet plays a crucial role in life, but trans fats (TFAs) can have harmful effects on fertility, particularly ovulatory infertility. High TFA intake, more than 1% of energy consumption, is a risk factor for infertility in both sexes. Oxidative stress, a byproduct of lipid peroxidation of PUFAs, contributes to various reproductive disorders, including endometriosis, tubal pathologies, and peritoneal pathologies.

Recognizing risk factors and altering lifestyle choices is crucial for preventing infertility, as globally unhealthy diets vary across societies[11-16]. Diet significantly influences life processes, as fatty acids, the building blocks of fat, play a crucial role in regulating membrane shape, intracellular signaling pathways, transcription factor activity, gene expression, and lipid mediator synthesis, it is necessary to sustain life processes, all these mechanisms are influenced by diet [17-19]. This study examines the impact of diet on infertility and reproductive health, focusing on young unmarried females who consume trans fats and compare reproductive hormone levels with trans-fat consumption patterns. The research also aims to identify potential causes of infertility before diagnosis, as trans-fat consumption in commercial baked and fried goods is linked to increased inflammatory responses, insulin resistance, and type 2 diabetes. The study explores the impact of trans fats and oxidative stress on fertility in unmarried girls, revealing unhealthy diet habits among younger age groups and higher oxidative stress levels among hostel residents, despite healthier diets, and irregular hormones in 60% of these individuals. Another study found that individuals with irregular menstruation patterns, oligomenorrhea, amenorrhea, hirsutism, acne, and alopecia have high trans-fat intake, high levels of OS, and routinely eat one or two meals a day[25]. The present study also, reports the descriptive count (percent) on baseline demographic and physical parameters of the studied samples, subjects aged 16 - 20 years were 112(37.3%), and those aged 21 - 25 years samples were 188(62.7%). Our study suggests that the younger (15-21) age group has more habits of consuming unhealthy diet. A study conducted at North-East of Scotland[17], reported teens to have more unhealthy diet patterns. Another study conducted by an American[11], showed older age group has an unhealthier diet. According to Edio Maldonado et al., 2023; Age-related changes include decreased ATP synthesis, increased ROS generation, and a decrease in antioxidant defense. Increased ROS levels can lead to oxidative stress and harm to DNA, lipids, proteins, organelle membranes, and cells. Hence with progressing age, the level of oxidative stress also increases. Based on ethnicity and area, the major subjects selected for study from Sindh were 209 (77.7%); followed by Punjab 43(16%); KPK 8(3%); Gilgit 4(1.5%); and Baluchistan province 5(1.9%). We concluded from our study that, participants from Balochistan have little or no oxidative stress, as they regularly take food rich in antioxidants (nuts, dry fruits), which detoxify their bodies, along with Polyunsaturated Fatty Acids (PUFA). Our study suggests that residents of hostels are found to have more oxidative stress and consumption of Trans Fats, a similar

study conducted at Lahore[21] tells the hostilities were eating more high-calorie junk foods when stressed as compared to the day scholars. While another study narrated dormitory residents have more Healthy Diet patterns compared to Day Scholars. Another study of Pakistan conducted about diet patterns and found That meal snacks habits are more common in hostler. Our study found trans fats induce OS in the body, despite the absence of any other co-morbidity. A study showed excessive intake of trans fatty acid accelerates oxidative stress in a mouse model of hyperlipidemia[19]. Another study conducted by Sweden[16] showed intake of trans Fatty Acids has Little Effect on OS in Humans. Our study also concluded that high trans fats consumers are found to have more OS generated due to Trans Fats, and approximately 60% are found to have irregular Hormones, but unfortunately, no study has been conducted so far about OS and Trans Fats with reproductive hormones involvement. To find an association of OS and Trans Fats with female reproductive hormones, very keen details were obtained from subjects concerning their reproductive life, details as the age of menarche and duration of menstrual cycle (Days) are found to have no association with OS, as nonspecific raised in oxidative stress was found in both extreme ages of subjects, nor duration of menstrual cycle showed any significant finding. Details like irregular patterns of menstruation, oligomenorrhea, amenorrhea, hirsutism, acne, and alopecia were asked during selection to rule out the possibility of PCOs among selected participants, later when compared to their Trans fats intake and OS levels, it was found that those with an irregular pattern of menstruation have high trans fats in their daily life. Subjects with complaints of Acne and Alopecia were found to have high levels of OS, they were also found to have 1 or 2 meals a day in routine with escaping breakfast in most cases. When these parameters were analyzed with FFQ groups, groups A and B were statistically insignificant ($p>0.05$) using the Pearson Chi-Square test. Again, no study has been conducted so far concerning OS and trans fats with female reproductive hormones to compare our results. If a person has a strong background of disease in their family, it is most likely for that person to develop that problem. Our study looked at the association of a family history of infertility, diseases like diabetes, hypertension, endocrine disorder, autoimmune disorder, significant past medical history, significant past surgical history, and family history of obesity with studied groups. In all three groups, a significant association was found with a history of infertility. If someone has a strong background with raised OS and a high intake of trans fats in the diet will face fertility issues in the future. The responses on infertility give a significant association with studied groups ($p<0.05$) using the Pearson Chi-Square test. The present study revealed that more than 100 subjects were found to have raised lipid profiles, and oxidative stress levels. The subjects with raised OS levels were found to have raised FSH levels. The subjects with Raised FSH levels were found to have low LH, estrogen, and progesterone levels along with very low HDL levels. Another study found the same results in infertile females, the study differs from ours, in two ways, the targeted population was diagnosed with cases of infertility[23], while the present study was done on unmarried girls before any fertility complications. A study conducted in North Korea[18], reported an association of elevated OS levels with raised FSH in hypothalamic dysfunction. Most studies are being done globally on different causes and risk factors for infertility, but not much research has been done on common and crucial risk factors like diet.

Conclusion

An unhealthy diet in the presence of oxidative stress generated by the body can increase the risk to human health and especially to the reproductive health of females by double fold. High trans fats consumers are at increased risk of raised LDL levels, decreased HDL levels, and irregular hormones. Present study recommends evaluating fat-based variables for hormonal imbalance specially in young unmarried females.

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