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Study some of Allergic Markers and food allergy in sub-fertile women

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Abstract: Background: risk factors for women's sub fertility are multiple however still many undiscovered causes might have direct or indirect role for sub fertility. Food allergy may be a cause of sub fertility and their relation still not well understood.
Objective: to assess the effect of food allergy in the female at reproductive age group and to design a map for common food allergens in AL-Najaf Province as a step to complete the map of food allergens in Iraq.
Method: A case control study conducted in fertility center at Sader- town in al Najaf Province , Iraq, from first of March 2014 to first of June 2014 Data obtained for (130) responder from age of 18 to 45 years (65 of them females whose were diagnosed to have sub fertility and 65 of them were fertile) they fulfilled well design questionnaires and allergic markers that includes (specific IgE antibodies for common food items, Anti Gliadin Antibody & AntiTissue Transglutaminase antibodies) were also pulled.
Results:In this study 16.9% (11/65) of sub fertile women had food allergy to different food items with significant p value (0.024) , OR (4.21). Peanut is on the top of items causing allergy in sub fertile group (22.7%)).In this study 3.1%(2:11)of case group had positive serum antibody for tissue trans glutaminase(TTG) and also 3.1% (2:11) of case group had same results for gliadine (AGA) and 2 cases are positive for AntiTissue Transglutaminase (ATT) and had both IgA ,IgG while 2 cases are positive for AGA ,one of them IgA and another one was IgG. All of food allergic infertile are primary infertility (45/65)=(44 unexplained +1 endometriosis).
Conclusions :food allergy had an essential effects in pathogenesis of sub fertile female with worthy proportion in unexplained infertility. Peanut were on the highest of food items that cause food allergy and a strong relationship between sub fertility and undiagnosed celiac disease.

Key words: food allergy, subfertility, immunity.

Introduction

Subfertility could be a world public health concern; despite the medical reason behind sub- fertility, ladies receive the main blame for the generative difficulties and that they suffer personal grief and frustration, social stigma, ostracism and heavy economic deprivation[1].

World Health Organization (WHO) reported that in 2010 (48.5) million couples worldwide were unable to possess a baby[2].

In Kuwait The common length of subfertility was four years, 65.7% of ladies and seventy six percent of men suffered from primary subfertility[3].

Primary subfertility calculable by National Health Survey (NHS) was (2.8%) and by National Infertility Survey (NIS) 3.4%. Tehran study calculable the prevalence of primary sub-fertility to be (21.9%)[4].

Sub fertility isn't always a woman's downside. Each women and men can have issues that cause sub fertility. regarding third of sub-fertility cases by females' problems and the other one third of fertility problems are owing to the males. The opposite cases are caused by a mixture of male and female issues or by unknown causes[5].

Approximately one in 5 couples will expertise unexplained subfertility despite finishing a full subfertility work-up. The term "unexplained subfertility" extremely reflects the current limitations of bioscience. The actual fact is that current technology doesn't have the tools for revealing the explanation for subfertility thus it simply hasn't been uncovered nevertheless[6].

The reason for unexplained subfertility is probably going to be heterogeneous, with projected causes starting from (endocrinology, immunologic and genetic factors)[7].Allergy to some types of food may be explained merely as many varieties of adverse immunologic response to food proteins resulting in inflammatory reactions with a T-helper sort a pair of cell and allergen-specific immunoglobulin E predominance[8, 9]

The binding of IgE to sure molecules gift in a food triggers the immunologic response. That that fluctuates from delicate to in rare cases severe and life threatening reaction referred to as hypersensitivity reaction[10]. Though allergic reaction was definitely noted, it remained uncommon and not detected notably in developing countries[11].

In child and youngsters the foremost common food varieties that sensitivity area unit are egg ,milk , peanut , tree nut ,soy , wheat whereas in adult the foremost common square measure shell fish , peanut , tree nut , fish such as salmon. Foods that area unit eaten up habitually increase the probability that someone can develop allergies thereto food[12].

Eating disorder& food allergy may might thought to be an attributing issue for subfertility , though there aren't any current clinical studies proving a definitive association between allergic reaction and subfertility however the inflammatory reaction is a vital interface between diet and immunity[13].

Autoimmunity could be a hot topic generative drugs recently. Autoimmunity primarily suggests that abnormal immunological reaction to eliminates our bodies. hypersensitive reactions fall to 1 facet of this spectrum, and what happens in all told of those disorders is that the immune system loses its ability to discriminate between "safe" and "harmful."[13].

Elevated levels of immune markers like anti-phospholipid antibodies, associate degreed degreeticardiolipin antibodies area unit thought to be related to an immune response to an implanting embryo. different markers of potential medical specialty fertility factors embody anti-nuclear protein , premature elevations of follicle stimulating hormone, lupus anticoagulant, and different clotting factors. Since the method of conception and physiological condition involves a suppression of the T-helper reaction so the girl will carry the craniate to term, any preponderant of this suppression for examples by air born allergic reaction or allergic reaction will cause the embryo or craniate to abort. the idea behind treating medical specialty fertility disorders is to reprogram the system to not react to self-tissue, and to permit the conventional suppression concerned in implantation to occur[13, 14].

Late section immunologic responses related to chronic inflammation notably chronic abdominal and girdle organs inflammation that resulting in sequent adhesion, damaging or maybe obstruction like blockage of Fallopian tube[15]. whereas food allergen itself irritate and inflame the the liner of digestive system that interfere with absorption of nutrient significantly small nutrients that are necessary for gametogenesis and are essential before and when gestation like vitamin B9, iodine and iron (exaggerated intake even before the start of gestation is usually recommended[15, 16]. additionally allergen act as a free radicals (oxidative stress) that outline as imbalance between pro-oxidants and antioxidant capacity affecting whole half in the body has been

concerned in sub optimal reproductive performance that regarded as one reason for subfertility with effect on gametes that are susceptible to oxidizer attack with sequent reduction of male and feminine fertility[17].

While trial for daily rejection of allergic reaction for interference or decrease its sign and symptom ,made the patient brook daily stress that have direct link on gonadotropin releasing hormone (GnRH). Stress causes an increase in glucocorticoids, that suppresses (GnRH) and ovulation[17, 18].

The final outcome for absorption defect , stress or Oxidative stress end in weight disorder that have some impact on ovulation ,menstruation and fertility[`19, 20]

Aim of study:

Assess the effects of food allergy in the Sub fertile female and to design a map for common food allergens in AL-Najaf Province as a step to complete the map of food allergens in Iraq.

Material and Methods :

Case control study was conducted at fertility center of AL –Sader Medical City in AL-Najaf province. Our study was done, throughou the period from first of March to June 2014.

The approval of the ethics committee within the hospital was obtained and approval of ethical committee of community and family medicine department , college of medicine , Babylon University

All patients were informed about the character of the study. They were additionally informed that their participation during this study is voluntary and that they the right to withdraw at any time without any penalization and their refusal to participate and withdraw will not affect their treatment at the Center. The patient browse and signed the consent type

Data assortment tools: A specially designed information sheet was used that contain:

I- Questionnaires:

History of food allergy , type of symptoms (skin, respiratory, gastro- intestinal or others), history of atopy or chronic disease like asthma, allergic rhinitis, diabetes mellitus, celiac disease, eczema, cardiovascular disease, thyroid disease, GIT problems or any other chronic disease &family history of food allergy were also take.

III- Allergic Markers :

With the patient's permission, the patient's file was examined to accumulate the investigations .Antibodies of class IgE against food allergens test instruction for the EUROLINE Food Gulf[21,22]

Anti-Gliadin IgA

Antigliadin IgA antibodies , Antigliadin IgG , Anti-Tissue-Transglutaminase IgA , and Anti-Tissue-Transglutaminase IgG were measured in serum for all subjects according to the instructions of manufacturer company (Orgenetec Madeby - Germany) .

Data Analysis:

Recording data was checked for missing values and entry errors. Statistical analysis was performed using "Statistical Package for Social Science software" (SPSS, version 20) and" Microsoft office Excel 2010". Variables were described using frequency distribution and percentage according to their characteristics and mean(X) with standard deviation (SD) for continuous variable .The Chi square test, was used for categorical data, and independent sample t-test used for numerical data. P-value of less than 0.05 was significant statistically.

Results:

Current study consist of 130 women, 65 of them were sub fertile (cases) while the other 65 were fertile (control). The mean age of cases was (31.6±6) years while mean age of controls was (33.8±6.7) years with no significant difference between them (p=0.052).

Table 1 shows (15.4%) of cases had history of food allergy with significant p –value (0.005)and OR (11.636), while (16.9 %) of them had family history of food allergy with p- value(0.002) and OR (13.037).

Patients' symptoms of food allergy showing (72.7%) had skin manifestations.

In the past medical history , most of cases had co-morbid medical problem like allergic rhinitis (24.6 %), allergic bronchitis(33.8%), allergic skin diseases(13.8 %). In a current study the symptoms vary from GIT problem(54.5%) like (abdominal pain, bloating, vomiting), respiratory symptoms (45.4%) and even skin manifestation as(itching , swelling , urticarial) was (72.7%) of patient (infertile) group.

There were 11from 65 (16.9%) of infertile female in this study had food allergy diagnosed by investigation, while 3 from 65 (4.6%) of control had positive serum antibodies with a significant p- value (0.024) and OR (4.21).In this study 3.1%(2:11)of case group had positive serum antibody for tissue trans glutaminase(TTG) and also 3.1% (2:11) of case group had same results for gliadine (AGA) .(tab.8).And 2 cases are positive for ATT and had both IgA, IgG while 2 cases are positive for AGA ,one of them IgA and another one was IgG.

Table(1) Distribution of study groups according to personal and family histories of food allergy:

Variable		Case N0=65(%)	Control N0=65(%)	χ^2	P value	OR	95%CI
History of food allergy	Present	10(15.4%)	1(1.5%)	8.044	0.005*	11.64	1.4-93.8
	Absent	55(84.6%)	64(98.5)				
Family history of food allergy	Present	11(16.9%)	1(1.5%)	9.181	0.002*	13.04	1.6-104.2
	Absent	54(83.1)	64(98.5)				

In current study on the top of food items that cause food allergy among study group was a peanut with distribution of (22.7 %) for cases and(33.3%) for control.

According to the infertility types (45from 65)of patient had primary infertility and (11)of primary infertile patients had food allergy while (20 from 65) of patient had secondary infertility with no serum antibodies for previously numerated food items and 4.2% of sub-fertile women had food allergy (Figure2,3).

Table 2 shows the majority of infertile patient had unexplained infertility 67.7% followed by tubal obstruction 16.9% then PCO 13.9% & endometriosis 1.5% and 20.45% of unexplained infertile females had food allergy.

Discussion:

It is unknown what percentage individuals really suffer from allergic reaction or food intolerance, and the way how many people are avoiding food that cause allergic symptom[23].

In a current study the symptoms vary in this study from GIT problem(54.5%) like (abdominal pain, bloating, vomiting), respiratory symptoms (45.4%) and even skin manifestation as (itching, swelling, urticarial) was (72.7%) of patient (infertile) group. The classic disorder syndrome had steatorrhea and malnutrition

coupled with multivitamins deficiency states may be less common than unknown celiac disease and often mono-symptomatic shows of the disease. Diverse problems such as dental anomalies, short stature, osteopenia bone disease, lactose intolerance, sub fertility and non-specific abdominal pain among several others may be the only manifestations of celiac disease. The rate at which celiac disease is diagnosed depends on the level of suspicion for the disease. Though diagnosing depends on intestinal biopsy, serologic tests are important as screening tools and as an adjunct to diagnosis[24, 25].

About 46.8% (37/65) of infertile study group have allergic diseases including allergic rhinitis 24.6% , allergic bronchitis 33.8% ,skin allergy 13.8%. Almost any food or food additive will cause hypersensitive reaction. Cross-reactivity between food and nonfood allergens exists, and sensitization might occur as an example, patients with oral allergies (typically, pruritus, erythema, and swelling of the mouth when fruits and vegetables are eaten) might are susceptible by exposure to pollens that square measure antigenically the same as food antigens[26, 27]

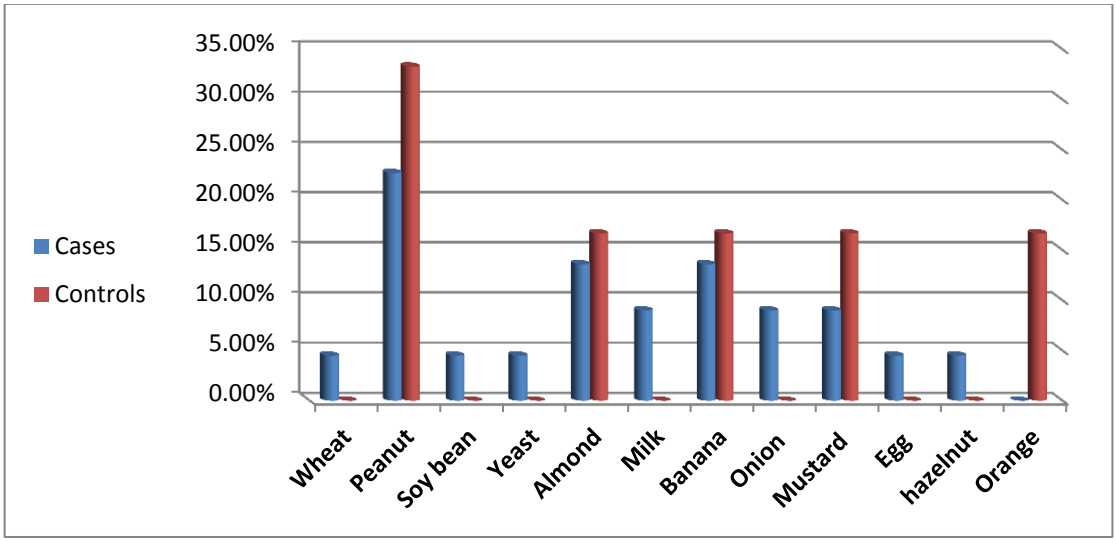
The distribution of study groups according to antibodies results (IgE, Anti Tissue Transglutaminase antibody, Antigliadin antibody) as shown in table 2 express the distribution of 16.9% (11/65) of infertile women had food allergy to different food items with significant p-value (0.024), OR (4.21), these result agree with study done in Royal Free Hospital in UK that show food allergen itself irritate the gut mucosa which is considered as an important protective barrier against entry of the food antigen (Ag) into mucosa leading to sensitization of gut associated lymphoid tissue by antigen and lead to disturbance of digestion and absorption of micronutrient like folic acid, iodine, selenium, zinc, iron and vitamins which are essential before and after pregnancy and essential for reproductive health[16].

Table (2) Distribution of infertile women according to cause of infertility

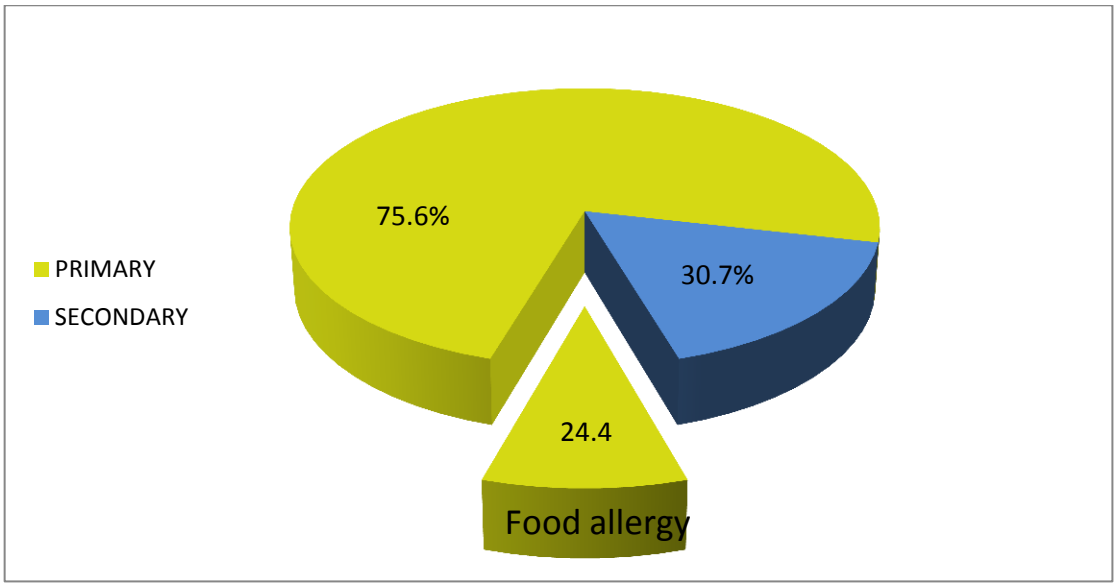
Cause	Number N=65(%)	Food allergy N=11 (%)
Tubal obstruction	11(16.9)	0
PCO	9(13.9)	1(9)
Endometriosis	1(1.5)	1(9)
Unexplained	44(67.7)	9(82)
Total	65(100)	11(100)

Vitamin A is important for embryonic development ,spermatogenesis ,while vitamin D linked to ovulatory dysfunction and sub fertility along with vitamin E that is essential for reproductive health that support the fertility for both male and female and vitamin K is vital to the health of a developing fetus ,low level of vitamin K result in fetal development with deformity like spinal column ,nose ,upper jaw defects , with prolong Prothrombin Time which is of great concern for pregnant ladies with unknown allergy that will increase the chance of miscarriage [28]. When compare this above results with control group we found that the food allergy in this group was 4.5% and the percentage of food allergy in control group is consistent with Food Allergy Facts and Statistics for the United State in 2011 that explain 4%of adults have food allergies .we found 6.2% of case group are sensitive for both tissue trans glutaminase and gliadine (3.1% TTG ,and 3.1% AGA)so these patient are non IgE mediated wheat allergy(coeliac disease)and this result is agreewith research done in Iraq,Diyala in which 7.4% of case group have coeliac disease[29]. While the percentage of celiac disease and uexplained female sub fertility in Islamic Republic of Iran was 3.5% , other research has also shown that women with unexplained sub fertility have a (2.5 to 3.5) times larger incidence of celiac disease than girls with normal fertility[30].

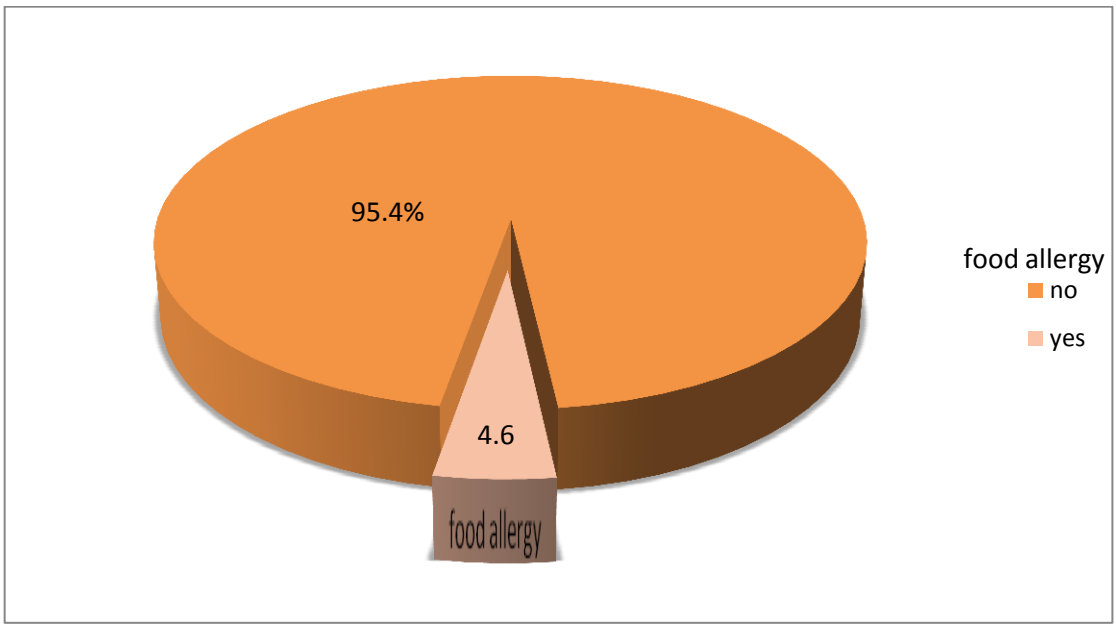
While the distribution of study groups with serum antibodies against food items as in (Figure 3) expressed (4.5%) of cases had IgE wheat allergy, gluten and wheat allergy may be a leading cause of sub fertility and several studies indicate that in gluten sensitivity there will be impacts of the bowels,there are a large vary of health problems stemmed from the disease that may negatively impact reproductive health . ladies with celiac disease carry a higher risk for malnutrition, hormone imbalances, poor egg health, and atrophy of the reproductive organs. Women with celiac also are at higher risk for late on set of menarche, early menopause, endometriosis and pregnancy's complications including recurrent miscarriage, still birth and poor fetal development known as intrauterine growth retardation (IUGR) &elevated levels of prolactin[31].



Figure(1) Distribution of study groups with serum specific IgE antibodies against food items:



Figure(2) Relation between type of sub fertility and food allergy



Figure(3) Relation between fertile women and food allergy:

Although, the process of inflammation is truly useful and protected process wherever takes place within the body during which the white blood cells and other chemicals come together and cause inflammation to fight against infection caused by micro-organisms. But, sometimes the immune system triggers inflammation when there is no infection from any micro-organism in the body. This is often truly a health disorder that's known as hypersensitive reaction. Wheat allergy are like to those of other food allergies, Wheat is highly acid-forming and inflammatory agent, that fast to spark the inflammatory cascade. Foods that never bothered us before, like dairy and wheat, might trigger chronic low-grade indigestion or other seemingly minor symptoms that place our immune system on guard , with further inflammatory concerns to follow, becoming aware regarding foods that cause inflammation and eliminating these foods from diet will facilitate to stop several inflammatory conditions and its complications[32].

Peanut was on the top of items causing allergy in infertile group (22.7%), followed by Almond (13.6%), and Banana(13.6%) then, Milk (9%), Onion (9%),and Mustard(9%), hazelnut (4.5%), egg (4.5%), Backer's yeast (4.5%),and Soy bean(4.5%). Cow's milk has adverse effects on the reproductive system in male mice, While soybean had sturdy capability to disrupt functions of sexual hormones. Hence, its indiscriminate use might increase the chance of sub fertility in males. Thus additional studies are needed to clarify the particular effects of milk and soybean on feminine generative health[33,34].

Regarding mustard, it cause each acute and chronic injuries to completely different elements of the genitourinary system which may interfere with fertility[35].

Figure (2) showed the percentage of food allergy in infertile women was 16.9%(11/65) and all of them are primary sub fertility(45/65)=(44 unexplained +1 endometriosis) so this provide a hint about a strong association between primary sub fertility with food allergy so it is important to identify a lightweight on a relationship of unexplained sub fertility and allergic food disease in which44/65 (67.7%)were unexplained sub fertility and 20.45% (9/44) have food allergy and most of patients stricken by IgE-mediated food allergies that result from exposure to the allergen stimulates the production of allergen-specific IgE antibodies by plasma cells in prone people. No symptoms occur throughout the sensitization phase but, once that phase is completed, the individual is primed to react to the offending allergen. prone people might kind allergen-specific IgE to at least one or many substances in their setting together with food allergens resulting in uncontrolled inflammatory responses. In different words, allergic diseases could also be thought to be the results of ill-adapted Th2 responses[36].

So the inflammation can result in impairment or delay conception in affected woman by unwell understood mechanisms and this might be justify why many infertile women have a chronic illness process like endometriosis or PCOS and this long inflammatory sequences of events lead by way or another to delay fertility[37].

Conclusions:

Food allergy had a vital effects in pathologic process of sub fertile female and worthy proportion of unexplained sterility had food allergy. Peanut were on the highest of food items that cause food allergy among study and control groups and a powerful relationship between sub fertility and undiagnosed celiac disease.

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