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Correlation Between Celiac Disease Patients and Infertility

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Abstract

Celiac disease (CD) an autoimmune disorder triggered by gluten,can indeed have complex relationship with in fertility in both women and men .The inflammation and damage in the intestines can disrupt hormone levels ,potentially interfering with ovulation and the menstrual cycle.

The present study was designed to investigate some biochemical aspects of patients with (CD) in Al habobi Hospital in al-nasirya in Thi-Qar provine The present work included some Celiac disease patients who are already diagnosed as CD patients that by the consultant medical staff, according to clinical examination, symptoms,during the period from October 2024 to march 2025. Samples of the study included 20patients which female and 20 healthy control to study Vitamin D3 , S. Ferritin levels and Concentrations of the sex hormones prolactin, testosterone, estradiol, follicle-stimulating hormone, and luteinizing hormone were measured from the serum samples of recumbent patients with age range of (18-36 years).

The recorded results indicated that their where Vitamin D3 levels were significantly higher in the control group (37.47 ± 10.18) compared to the (CD) patient group (16.27 ± 7.04). A strong statistical significance at P. value 0.01, suggesting that (CD) patients may have a notable deficiency in vitamin D3. S. Ferritin was also much higher in the control group (49.45 ± 23.47) than in (CD) patients (11.01 ± 4.36), with a strong statistical difference at P value 0.01 . This could indicate iron deficiency or altered iron storage in the (CD) patient group. FSH (Follicle Stimulating Hormone) and LH (Luteinizing Hormone) levels were both significantly lower in the (CD) patient group compared to controls. FSH was(5.41 ± 2.13) in controls vs. (3.74 ± 1.96) in patients, and LH was (6.71 ± 2.49) in controls vs. (4.90 ± 1.65) in patients at P. value 0.05 . These hormones are crucial for reproductive function, and their reduction might reflect hormonal imbalance. Prolactin levels were higher in the (CD) patient group (12.51 ± 4.47) compared to the control group (7.04 ± 2.80) at P. value 0.01. Elevated prolactin can affect menstrual cycles and fertility. Testosterone was also significantly elevated in the (CD) patient group (1.76 ± 0.98) compared to controls (0.52 ± 0.57) at P. value 0.01. This may suggest a condition like polycystic ovary syndrome (PCOS), which is often associated with elevated androgens. Estradiol levels were similar between the two groups, with no statistically significant difference (39.98 ± 15.91) in controls vs.(41.11 ± 8.75) in (CD) patients).The Pearson correlation analysis for (CD) patients group revealed a moderate negative correlation between Vitamin D3 and both seurm ferritin (r = -0.435) and prolactin (r = -0.433), suggesting that lower vitamin D3 levels may be associated with higher ferritin and prolactin levels. Other correlations involving vitamin D3—such as with FSH, LH, testosterone, and estradiol—were weak and not likely meaningful. Estradiol showed a weak negative correlation with ferritin, and a moderate positive correlation with LH (r = 0.378), possibly indicating a hormonal link. Prolactin showed a moderate positive correlation with ferritin (r = 0.481) and weak negative correlations with FSH and LH. The remaining correlations across testosterone, FSH, and LH were weak and did not demonstrate strong linear relationships. The Pearson correlation analysis in control showed weak to moderate

relationships among the studied parameters in control group. Vitamin D3 levels were negatively correlated with FSH and testosterone, suggesting a possible inverse relationship, while its correlations with other hormones were weak and likely not significant. Estradiol showed a moderate negative correlation with ferritin, indicating that higher estrogen levels might be associated with lower iron storage. Testosterone levels were negatively correlated with ferritin but positively correlated with FSH, reflecting some hormonal interaction. Other correlations, such as those involving prolactin, LH, and FSH, were generally weak and did not suggest strong linear relationships.

Keywords: Celiac Disease, Infertility, Vitamin D3 Deficiency, Serum Ferritin, Sex Hormones, Prolactin
Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH)

1.1. Introduction

Celiac disease CD is an immune-mediated inflammatory disease of the small intestine caused by gluten proteins ingestion in individuals with a genetic predisposition to human leukocyte antigen HLA) DQ2 or DQ8. Ingestion of these proteins promotes immune-mediated mucosal inflammation of the proximal small intestine with villous atrophy and crypt hyperplasia,leading to malabsorption and gastrointestinal symptoms[1,2].

The chronic inflammation may also play a role in the development of anemia [3,4]. The prevalence of this disease is higher among persons who have first-degree relatives with celiac disease (10 to 15%) [5].

Celiac disease is seldom considered in the evaluation of infertility, and the link between the two has been referred to many times in the literature as a ‘neglected clinical association’. It is estimated that approximately 7.4–14% of women are infertile in North America, with 15% of this infertility attributed to unexplained factors after hormonal and anatomical causes have been ruled out [6,7]. While women with CD may present with amenorrhea, menstrual irregularities, multiple spontaneous abortions, iron deficiency anemia or the host of other symptoms, Similar to fertility, the effect of CD on BMD is multifactorial. One clear factor is the vitamin D and calcium deficiencies commonly seen in CD patients owing to villous atrophy and dietary restrictions [8].

Infertility has become a significant public health concern worldwide. It is defined as the failure to achieve pregnancy after 12 months of regular, unprotected intercourse, or within 6 months for women over 35 years old. This condition affects around 15% of couples of childbearing age. The global lifetime risk of infertility varies, with estimates ranging from 2.6% to 31.8% [9].

many women are only diagnosed around the time of menopause. Thus, the entire span of reproductive life may be disrupted in women with undiagnosed CD.The Celiac disease is one of the most common lifelong disorders on a worldwide basis affecting 0.5-1% of the general population in the USA and other developed countries [10]. The clinical manifestations of CD can be directly related to autoimmunity or can indirectly derive from intestinal inflammation [11].

2.1. Celiac disease

Is one of the most common autoimmune disorders, in many countries the overall prevalence of CD in the general population ranges from 0.5% to 2%, with an average of approximately 1% [12]. With the exception of areas showing low frequency of CD-predisposing genes and low gluten consumption [13].

Celiac disease is common throughout the world, and its prevalence has significantly increased over the past 20 years. There has been a substantial increase in the numbers of new cases of celiac disease, partly due to better diagnostic tools and thorough screening of individuals considered to be at high risk for the disorder [14].

Celiac disease is now known to affect all age groups, including the elderly; more than 70% of new patients are diagnosed above the age of 20 years

[15]. The risk of having celiac disease is much greater in first-degree relatives (up to 10%) and lesser in second-degree relatives, as well in individuals with type 1 diabetes mellitus and other autoimmune diseases, Down syndrome, and a number of other associated diseases [16].

Clinically severe manifestations may occur during pregnancy or during the puerperium in up to 17% of female patients [17].

2.2. Pathogenesis

CD is a unique autoimmune disease in that its key genetic elements (human leukocyte antigen (HLA)-DQ2 and HLA-DQ8), the auto-antigen involved (tissue trans- glutaminase (tTG)), and the environmental trigger (gluten) are all well defined . The triggers for CD are specific immunogenic peptides that are present only and exclusively in the dietary gluten proteins, from wheat and similar structural cereals such as rye and barley[18] .

These peptides are resistant to digestion by gastric and pancreatic enzymes and find their way into the lamina propria of the small bowel, presumably after some changes occur in the intercellular tight junctions with an increase in the intestinal permeability. One such peptide is a 33-amino acid sequence, which is a potent activator of specific T-cell lines from patients with CD[19] .

The subsequent infiltration by CD4 (+) T lymphocytes into the lamina propria and CD8 (+) into the intestinal epithelium, are a hallmark of active CD. The recognition of HLA-bound gluten peptides by T cells, leads to their activation and clonal expansion of B cells that produce antibodies . Other cytokines released by activated CD4 T cells that involve the adaptive immune response, promote various inflammatory mechanisms and produce the intestinal lesion . The expression of the interleukin-15 cytokine appears to play a central role in driving various processes that lead to the increased number of intraepithelial lymphocytes (IELs) as well as in the destruction process of the epithelial cells and the mucosal damage[20] .

The resulting deaminated and thus, negatively-charged peptides, have much higher affinity for the HLA- DQ2 and DQ8 molecules, and have a key step in the immune response in CD[21]. In summary the CD is a complex disorder that results from an interplay of several genetic, immunological and environmental factors, with many aspects for which the final pathogenetic mechanisms[22].

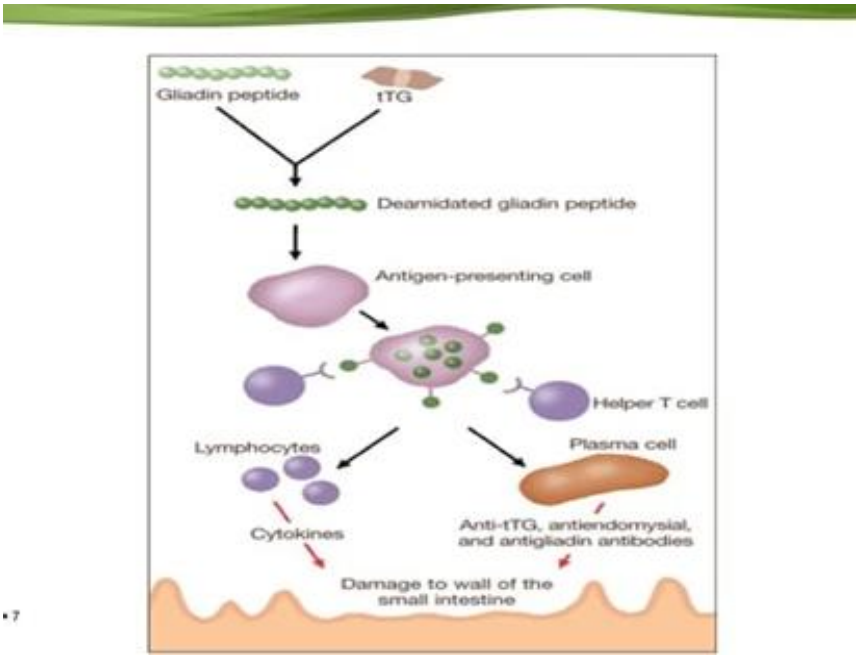

Fig (2-1): Immune response inCeliac disease (Presutti *et al.*,2007*)*

3.1. Genetic Factors

3.1.1. HLA-DQ2 and DQ8

One study found human leukocyte antigens(HLA)-DQ2 and DQ8 present in 98.4% of patients with CD and a presence of 89.6% in their families, suggesting a genetic component to the disease [23]. Antigen-presenting cells, such as dendritic cells, present the peptides to gluten-specific T cells, triggering both the innate and adaptive immune response. The innate response releases interleukin (IL)-15, leading to the destruction of gut epithelial cells by CD8+(cytotoxic) T-lymphocytes [24]. The role of IL-17 in the pathogenesis of CD is still under investigation [25], found lower levels of IL-17-producing T cells in the intra- epithelial lymphocyte (IEL)compartment of CD patients.

They speculate that these changes negatively affect the homeostasis of the mucosal barrier while contributing to the altered permeability of the gut mucosa. In addition, the adaptive response generates inflammatory cytokines, activating either interferon-gamma (IFN-γ) producing T helper (Th)1 cells or Th2 cells that promote B-lymphocyte development into plasma cells. In turn, plasma cells produce anti-gliadin and anti-tissue-transglutaminase antibodies [26]. The effects of gluten on the gut mucosa of susceptible individuals vary but can include gut inflammation, villous atrophy, crypt hyperplasia, and CD4+ and CD8+ T-cell lymphocytic invasion of the intraepithelial tissue [27].

3.2. Gluten Exposure

3.2.1. Gluten Exposure in CD Patients

The pathogenesis of CD at any age requires exposure to gluten. The CD prevalence can still be related to the consumption of cereal that contains gluten(mainly wheat) in the population [28]. The quantity of gluten in an infant's diet may affect the risk for the clinical expression of CD or at least the earlier timing of its onset. In a prospective observational multinational study of more than 6605 children with genetic predisposition for CD due to their HLA antigen genotype, the quantity of gluten exposure during the first years of life was associated with development of celiac autoimmunity 5 and confirmed CD[29]. By 3 years old, the absolute risk for developing celiac autoimmunity and CD was and 21%, respectively, among children who consumed the 28% reference amount of gluten mean intake 3.7 g/day), compared with 34% and 28% among those who consumed an additional 1 g/day of gluten. Time to the initiation of gluten ingestion, breastfeeding duration, and the avoidance of cow's milk were not related to the risk of developing CD [30].

4.Presentation

4.1. Clinical Manifestations of CD

The clinical manifestations of CD are variable and involve multiple organ systems. Symptoms can be broadly classified as intestinal or extraintestinal, and the symptoms that appear vary according to age [31]. In the past, CD usually presented in infants and young children with malabsorption and failure to thrive. Recently, however CD has tended to present later, between 10 and 40 years old, with milder gastrointestinal or nongastrointestinal manifestations . This change in the presentation may be due to the increased recognition of asymptomatic and mild cases due to advances in serological screening [32]. The distinctive difference between children and adults is the clinical manifestations at the time of the diagnosis Symptoms in infants are usually different from those in older children. Diarrhea, anorexia, abdominal distension, and abdominal pain are usually seen in younger children. If the diagnosis is delayed, failure to thrive, irritability and severe malnutrition can be seen. Gastrointestinal symptoms, such as diarrhea, nausea vomiting, abdominal pain, dominal distension, weight loss, and constipation, may occur in older children, depending on the gluten intake .Extraintestinal symptoms are frequent in adult CD cases and may appear associated with other digestive symptoms, such as asthenia, oral sores, osteoporosis, or skin

lesions [33]. CD patients may present extraintestinal anifestations as well as neurological disorders, often with seropositivity for antineuronal and antiganglioside antibodies [34]. Patients with CD can show a delay in the diagnosis, with a median delay of one year for children and more than four years for adults [35,36].

5. The CD Diagnosis

5.1. Diagnostic Method

The diagnosis of CD is based on a high index of clinical suspicion, serological markers,and small bowel biopsies. CD guidelines recommend serological screening for CD inpatients with questionable symptoms or high-risk patients, provided they are on agluten containing diet. Screening of asymptomatic patients without risk factors. A tentative diagnosis of CD is made in patientswith a positive result of a specific antibody test and characteristic histologicchanges in theintestinal mucosa on a gluten-containing diet [37,38].

5.2. Serological Testing

One of the most common screening tests for the diagnosis of CD is the detection of IgA tTG while consuming a normal diet. The sensitivity and specificity of tTG is excellent and 96%, respectively) for identifying CD cases, and it is currently recommended as a 95% screening test by both the NASPGHAN and ESPGHAN. [39]. Antideamidatedgliadin antibody and anti-EMA are preferred. In cases with IgA deficiency, IgG-based tTG and deamidated antigliadin antibodies are the recommended markers, although the sensitivity is not high[40]. A gluten-free diet increases false negative results, so the test should ideally be performed during a period of consuming a gluten-containing diet . Guidelines recommend that serologic testing for CD be followed on a gluten-containing diet for at least six weeks [41].

5.3. Biopsy Testing

Endoscopic small bowel biopsies are considered the gold standard for the diagnosis of CD [42]. Individuals with positive tTG-IgA or EMA- IgA findings should undergo an intestinal biopsy to confirm the diagnosis of CD. Multiple biopsies, should be taken including four from the distal duodenum and at least one from the duodenal bulb, as the disease may have a patchy distribution or initially be confined to the duodenal bulb. Biopsies are evaluated according to the modified Marsh–Oberhuber classification [43]. Results range from mild alterations characterized only by increased intraepithelial lymphocytes (Marsh type 1 lesion) to flat mucosa with total mucosal atrophy, complete loss of villi, enhanced epithelial apoptosis, and crypt hyperplasia (Marsh type 3 lesion). Marsh type 3 is classified as 3a, 3b, or 3c depending on the severity of villous atrophy .Patients with abnormal findings (Marsh type ≥2) should undergo serology and treatment with a gluten-free diet to confirm CD [44].

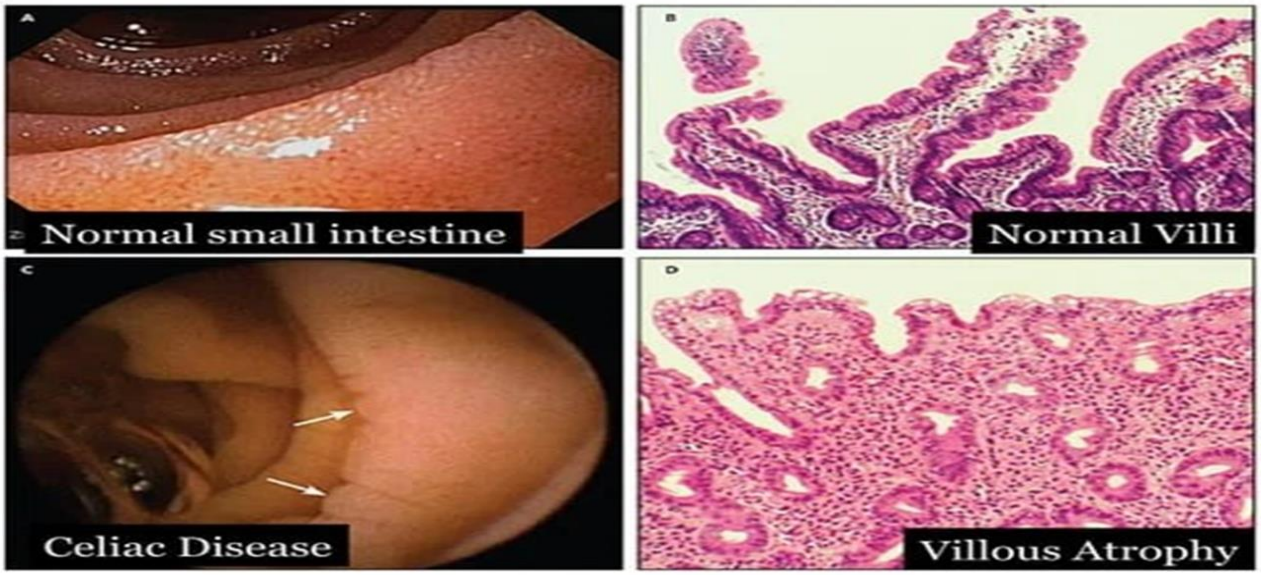

Fig (2-2): Celiac Disease of the small intestine with villous atrophy (Hadithiet *al.,* 2007).

6. Infertility

Infertility and subfertility affect a significant proportion of human beings (45). Infertility is defined as failure to achieve clinical pregnancy after 12 months of regular unprotected sexual intercourse. In general, 8 to 12% of couples of reproductive age suffer from infertility worldwide (46). According to a World Health Organization report, more than 10 percent of women are affected by infertility (47). In addition to the medical problems, infertility can cause numerous personal and social problems. It can be seen as a developmental crisis (48).

7.Celiac Disease and infertility

According to the World Health Organisation, the definition of infertility is a failure to conceive after 12 months of regular unprotected intercourses .It is estimated that 8–12% of couples in the world have reproductive problems. What is significant, approximately 30% of them are diagnosed with unexplained infertility, which means that there is no apparent cause for this condition [49]. For the first time the relation between CD and infertility was described in 1970 by Morris [50].

The connection of autoantibodies and reproduction problems is a very interesting and still analyzed issue. It is proved that dysfunction of ovaries and even premature ovarian insufficiency occurs more often in women with autoimmunization [51]. It all explains the interests in understanding how CD, which is an autoimmune condition, impacts fertility. Also, macro- and micronutrients deficiency could be the reason for reproduction problems in CD [52]. The elements and vitamins with most common deficiency in this condition are iron (Fe), zinc (Zn), calcium, (Ca) vitamin D, vitamin B12 and folic acid . Lower plasma zinc concentration in women is correlated with longer time to pregnancy [53]. It needs to be emphasised that zinc is an important element for the good semen quality. Based on those facts a hypothesis can be made that CD impacts also men's fertility [54]. Another crucial element is folic acid which is essential for proper cell divisions. Its deficiency could be a cause of anovulation and short menstrual cycles [55]. The best described deficiency in CD is iron deficiency resulting in anaemia. If a patient suffers from iron deficiency anaemia and reproduction problems serological assays for CD should be performed [56].

In 2019 meta-analysis was published, whose main aim was to resume publications in this topic and make conclusions . Results show approximately three times more frequent TTG and EMA antibodies in women with infertility. The most significant group among them are women with unexplained infertility

[57]. Data show that women suffering from CD but on GFD have the same risk of infertility and adverse pregnancy outcomes like the general population [58]. What is important, authors indicate that studies about association between CD and infertility use low sample size, which makes them insufficient to be base for recommendations. Another reason for absence of routine tests for CD in infertility diagnostics. Examples are Canadian and Danish [59] papers. It is worth noting that despite many Danish studies about CD and reproduction problems, the prevalence of CD in this geographic region is lower than in the general population (approx. 0.5%)[60].

In literature some authors point out a link between untreated CD and delayed menarche and early menopause [61]. A shorter reproductive period is a consequence. When a patient has a history of delayed menarche it can be suspected that the reason for her problems is CD . Early menopause in case of CD could be associated with decrease of AMH, and in result decrease in ovarian reserve compared to healthy women [62]. It is worth mentioning that in the study which indicates correlation between decrease of AMH and CD, there is no information about using GFD in the analyzed group . In conclusion, there is no information about the influence gluten intake has on AMH concentration. It is worth knowing that CD is not the only one autoimmune condition which results in the decrease of AMH [63].

8. Vitamin D and Female Fertility

Vitamin D, a secosteroid hormone synthesized in the skin upon UVB exposure, plays a critical role in calcium metabolism, immune function, and cellular growth. It also has a substantial influence on the reproductive system due to the widespread presence of Vitamin D receptors (VDRs) in reproductive organs (64).

8.1.Biological Role and Mechanisms

• Ovarian Function: Vitamin D modulates follicular development and ovulation by influencing anti-Mullerian hormone (AMH) expression. AMH levels are directly correlated with ovarian reserve (65).

• Endometrial Receptivity: Vitamin D enhances endometrial receptivity by regulating implantation-related genes like HOXA10 and integrins, which are essential for embryo attachment and successful implantation (66).

• Hormonal Regulation: Vitamin D interacts with the hypothalamic-pituitary-ovarian (HPO) axis, affecting luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion, which are vital for ovulatory cycles (67).

8.2.Risk Factors for Deficiency

Common risk factors for Vitamin D deficiency include:

• Limited sun exposure due to geographical location or lifestyle.

• Dark skin pigmentation, which reduces UVB absorption.

• Obesity, where Vitamin D becomes sequestered in adipose tissue.

• Malabsorption syndromes (e.g., celiac disease, IBD).

• Cultural or religious clothing that limits sun exposure (68).

8.3.Reproductive System Integrity

Vitamin D deficiency compromises the functional integrity of the reproductive system, leading to:

• Altered folliculogenesis and poor oocyte quality

• Impaired endometrial development

• Inflammatory uterine environment due to unregulated immune responses (69).

• Reduced ability of the endometrium to support implantation, contributing to early pregnancy loss (70).

9. Ferritin and Female Fertility

Ferritin is the principal iron-storage protein and a proxy indicator of total body iron stores. Iron is

crucial for DNA synthesis, mitochondrial respiration, and cellular proliferation—all vital for reproductive tissues and embryonic development (71).

9.1.Biological Role and Mechanisms

• Oocyte Development: Iron is essential for mitochondrial activity in oocytes, which require high energy for maturation and meiosis (72).

• Endometrial Function: Iron supports cell proliferation and vascularization of the endometrial lining, ensuring it is sufficiently thick and receptive during implantation (73).

• Embryogenesis: Adequate iron is vital during the early stages of embryonic development, especially for neural tube closure (74).

9.2.Risk Factors for Deficiency

Risk factors include:

• Heavy or prolonged menstrual bleeding (menorrhagia).

• Vegetarian or vegan diets lacking heme iron.

• Gastrointestinal conditions that impair absorption (e.g., ulcers, celiac disease).

• Frequent blood donations or underlying chronic illness (75).

9.3.Reproductive System Integrity

Iron deficiency compromises reproductive integrity through:

• Impaired oocyte maturation and lower fertilization potential (76).

• Inadequate endometrial proliferation, reducing chances of implantation (77).

• Increased oxidative stress leading to follicular apoptosis.

• Higher incidence of early miscarriage due to insufficient endometrial support (78).

10. Combined Deficiency Effects and Synergistic Impact

When Vitamin D and ferritin deficiencies co-occur, the impact on female reproductive health may be magnified.

Interdependent Mechanisms

• Both nutrients are involved in immune modulation. Deficiencies can create a pro-inflammatory environment in the uterus that is hostile to implantation (79).

• Oxidative stress is exacerbated in combined deficiencies, damaging oocytes, granulosa cells, and endometrial tissue.

• Hormonal imbalances become more severe, particularly in women with PCOS or endometriosis, where Vitamin D and iron dysregulation are commonly observed (80).

Study population

This study has been conducted on a group of patients at Al habobi Hospital in al-nasirya in Thi-Qar provine / South of Iraq - during the period from October 2024 to March 2025. The target population was 40 samples which were include (20) patients who are already diagnosed as (CD) patients by the consultant medical staff with age ranged (18-36) year and Control groups is composed of (20) healthy people with the same age range (women). the practical side was completed in the Clinical Biochemistry and the blood diseases Laboratories.to study Vitamin D and S. Ferritin levels and Concentrations of the some hormones prolactin, testosterone, estradiol, follicle-stimulating hormone, and luteinizing hormone were measured from the serum samples of recumbent patients .

Collection of Blood samples

Blood samples (7 ml) were obtained from by vein puncture using a sterile disposable syringe from patients and the control group. The samples were separated individed to two parts groups, the first group samples for the purpose of testing S.Ferritin and Vitamin D3 levels .The second group for the purpose of testing hormones.The blood designed to

study hormones was dispensed in a gel tube and left for 10 minutes at room temperature to clotting sample. Then, it was centrifuged at 5000 rpm for 10 minutes to collect serum and kept in the freezer (-20 °C) until use unless used immediately to analyze hormonal parameters.

Statistical Analysis

The data of the current study were statically analysis by using Excel software version 2016, and software SPSS version 26 by using statistically lows including (Pearson Correlation Coefficient for parameters and T.test).

4.Results

4.1. Compares several hormonal and biochemical parameters between a control group and a patient group.Vitamin D3 levels were significantly higher in the control groups (37.47 ± 10.18) compared to the (CD) patient groups (16.27 ± 7.04). A strong statistical significance at p.value 0.01, suggesting that (CD) patients may have a notable deficiency in vitamin D3. S. Ferritin was also much higher in the control group (49.45 ± 23.47) than in (CD) patients (11.01 ± 4.36), with a strong statistical difference. This could indicate iron deficiency or altered iron storage in the (CD) patient group. FSH (Follicle Stimulating Hormone) and LH (Luteinizing Hormone) levels were both significantly lower in the (CD) patient group compared to controls. FSH was (5.41 ± 2.13) in controls vs (3.74 ± 1.96) in patients at p.value 0.05, and LH was (6.71 ± 2.49) in controls vs.(4.90 ± 1.65) in patients at p.value 0.05. These hormones are crucial for reproductive function, and their reduction might reflect hormonal imbalance. Prolactin levels were higher in the (CD) patient group (12.51 ± 4.47) compared to the control group (7.04 ± 2.80). Elevated prolactin can affect menstrual cycles and fertility. Testosterone was also significantly elevated in the (CD) patient group (1.76 ± 0.98) compared to controls (0.52 ± 0.57) This may suggest a condition like polycystic ovary syndrome (PCOS), which is often associated with elevated androgens. Estradiol levels were similar between the two groups, with no statistically significant difference (39.98 ± 15.91) in controls vs. (41.11 ± 8.75) in (CD) patients.

Table (4-1) Compares concentration of FSH, LH, Prolactin, Testosterone and Estradiol and levels of ferritin and Vit-D3 in CD patients and control groups

Parameters	Control group	Patients group
Vitamin D3	37.47 ** ±10.18	16.27 ±7.04
S.Ferritin	49.45 ** ±23.47	11.01 ±4.36
FSH	5.41 * ±2.13	3.74 ±1.96
LH	6.71 * ±2.49	4.90 ±1.65
Prolactin	7.04 ±2.80	12.51 ** ±4.47
Testosterone	0.52 ±0.57	1.76 ** ±0.98

Estradiol	39.98 ±15.91	41.11 ±8.75
* correlation is significance at the 0.05 level (2-tailed) ** correlation is significance at the 0.01 level (2-tailed)		

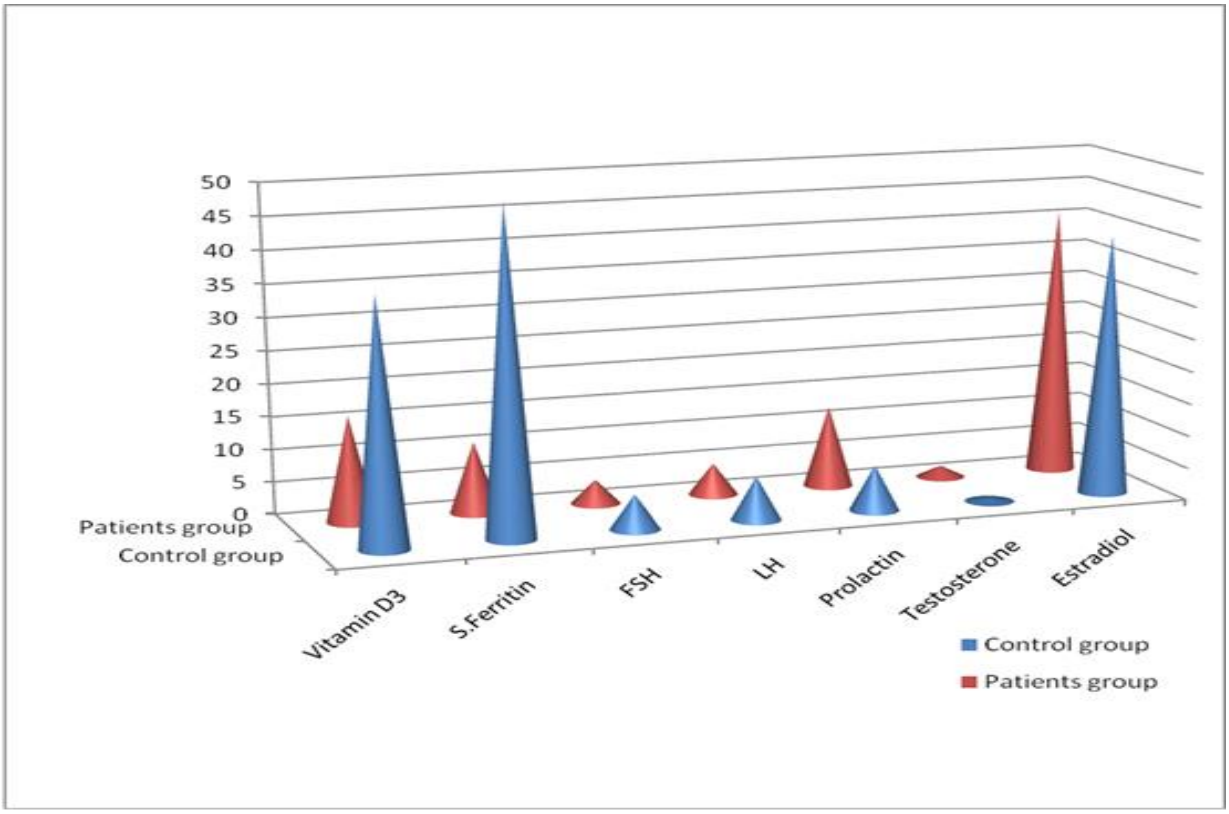

Figure (4-3):Distribution of S. Ferritin and Vit-D3 in CD Patients and control Groups.

4.2.The Pearson correlation analysis in table (4-2) showed weak to moderate relationships among the studied parameters in control group. Vitamin D3 levels were negatively correlated with FSH and testosterone, suggesting a possible inverse relationship, while its correlations with other hormones were weak and likely not significant. Estradiol showed a moderate negative correlation with ferritin, indicating that higher estrogen levels might be associated with lower iron storage. Testosterone levels were negatively correlated with ferritin but positively correlated with FSH, reflecting some hormonal interaction. Other correlations, such as those involving prolactin, LH, and FSH, were generally weak and did not suggest strong linear relationships.

Table (4-2): correlation between concentration of FSH, LH, Prolactin, Testosterone and Estradiol and levels of ferritin and Vit-D3 in control groups.

	S.Ferritin	FSH	LH	Prolactin	Testosterone	Estradiol
Vitamin D3	0.217	- 0.304	0.113	0.190	- 0.305	0.148
Estradiol	-0.353	-0.248	0.170	0.072	-0.052	
Testosterone	-0.380	0.392	0.185	0.069		

Prolactin	0.209	-0.309	-0.032			
LH	-0.267	-0.253				
FSH	-0.059					

4.3. Pearson correlation analysis for patient group revealed a moderate negative correlation between Vitamin D3 and both serum ferritin (r = -0.435) and prolactin (r = -0.433), suggesting that lower vitamin D3 levels may be associated with higher ferritin and prolactin levels. Other correlations involving vitamin D3-such as with FSH, LH, testosterone, and estradiol were weak and not likely meaningful. Estradiol showed a weak negative correlation with ferritin, and a moderate positive correlation with LH (r = 0.378), possibly indicating a hormonal link. Prolactin showed a moderate positive correlation with ferritin (r = 0.481) and weak negative correlations with FSH and LH. The remaining correlations across testosterone, FSH, and LH were weak and did not demonstrate strong linear relationships.

Table (4-3): correlation between concentration of FSH, LH, Prolactin, Testosterone and Estradiol and levels of ferritin and Vit-D3 in CD patients.

	S.Ferritin	FSH	LH	Prolactin	Testosterone	Estradiol
Vitamin D3	-0.435	-0.203	0.034	-0.433	-0.139	-0.090
Estradiol	-0.279	-0.024	0.378	-0.091	-0.090	
Testosterone	0.035	-0.114	0.100	-0.059		
Prolactin	0.481	-0.255	-0.358			
LH	-0.158	0.159				
FSH	-0.207					

Discussion

Gluten is infamous for its role in celiac disease (CD). This autoimmune conditionaffects 1% of the population and leads to a reversible inflammatory process in small bowel mucosa with acute repercussions such as diarrhea, constipation, bloating, nausea, and vomiting [81–82]. Long-term consequences of mucosal damage and inflammation include malabsorption of nutrients such as calcium, vitamin D, iron [83], vitamin B12, folic acid, and zinc [84], leading to debilitating consequences such as osteoporosis, anemia [85].

The recorded results indicated that their where Vitamin D3 levels were significantly higher in the control group (37.47 ± 10.18) compared to the (CD) patient group (16.27 ± 7.04). A strong statistical significance at P. value 0.01, suggesting that (CD) patients may have a notable deficiency in vitamin D3. This finding was in agreement with another study that suggested Vitd3 deficiency could be detected, and this could confirm the role of vitD3 in CD pathogenesis. At the same time, the evidence that vitD3 deficiency was common in patients with established CD and vitD3 administration could lead to a more favorable disease course could confirm a role of vitD3 in conditioning CD evolution [86–89].

S. Ferritin was also much higher in the control group (49.45 ± 23.47) than in (CD) patients (11.01 ± 4.36), with a strong statistical difference at P value 0.01 . This could indicate iron deficiency or altered iron storage in the (CD) patient group. This finding was in agreement with another study that recorded that

being responsible for most anemias. ID anemia (IDA) is the most common extra intestinal finding in patients with CD with a prevalence of about 7% to 81% at the time of diagnosis [90]. In contrast, approximately one in 31 patients with IDA has histologic evidence of CD [91]. Due to permanent inflammation in the small intestines, as well as villous atrophy, patients with CD typically exhibit micronutrient malabsorption and deficiencies [92]. Long-standing and untreated disease may lead to other complications, such as ulcerative jejunitis (ulcer formation of the small bowel) [93]. Malabsorption-related The changes in the bowel reduce its ability to absorb nutrients, minerals, and the fat-soluble vitamins A, D, E, and K.[94]. Anaemia may develop in several ways: iron malabsorption may cause iron deficiency anaemia, and folic acid and vitamin B12 malabsorption may give rise to megaloblastic anaemia [95] .

Vitamin D3 Deficiency and Fertility

There is increasing evidence that vitamin D plays an important role in regulating both male and female fertility [96, 97, 98, 99, 100, 101, 102, 103, 104]. The vitamin D status can influence reproductive processes throughout development. For example, it influences gametogenesis, fertilization, the preimplantation phase, and the final phases of organ development (105). It also plays a role in promoting the function of the endometrium during implantation (106).

FSH (Follicle Stimulating Hormone) and LH (Luteinizing Hormone) levels were both significantly lower in the (CD) patient group compared to controls. FSH was(5.41 ± 2.13) in controls vs. (3.74 ± 1.96) in patients, and LH was (6.71 ± 2.49) in controls vs. (4.90 ± 1.65) in patients at P. value 0.05 . These hormones are crucial for reproductive function, and their reduction might reflect hormonal imbalance. This finding was in agreement with another study that recorded Vitamin D3, a fat-soluble vitamin, is known for its crucial role in calcium metabolism. Emerging evidence suggests its involvement in various reproductive processes in both men and women[107] . Vitamin D receptors are present in reproductive tissues. Vitamin D may influence the regulation of hormones and follicular development, which are essential for ovulation [108] .

S. Ferritin Deficiency and Infertility

This finding was in agreement with another study that recorded Serum ferritin is a protein that stores iron in the body. Low levels of ferritin indicate iron deficiency [110-111] . Iron is essential for various bodily functions, including oxygen transport. This finding was in agreement with another study that suggests a link between low iron levels and an increased risk of ovulatory infertility (the inability to produce healthy eggs), Iron deficiency might negatively impact egg quality [112]. Iron deficiency can lead to anemia, which might impair oxygen delivery to reproductive organs and tissues[113].

There is some indication that low ferritin might affect the fertilization of eggs or the lining of the womb[114].

Conclusion

The current study concluded the following:

1.The Vit-D3 and S.ferritin levels decrease significantly in wheat allergy patients than control groups .

2. The FSH and LH hormones decrease significantly in (CD) patients, and increased in control groups. The testosterone and Prolactin hormones increased significantly in (CD) patients than control groups. Estradiol levels were similar between the two groups.

3.The study showed a moderate negative correlation between Vitamin D3 and both serum ferritin and prolactin, suggesting that lower vitamin D3 levels may be associated with higher ferritin and prolactin levels. Estradiol and showed a weak negative correlation with ferritin, and a moderate positive correlation with LH. Prolactin showed a moderate positive correlation with ferritin and weak negative correlations with FSH and LH.

References

[1].C, Catassi. E,F, Verdu. J,C, Bai. E, Lionetti . ''Coeliac diseas'', Lancet. 399, 2413–2426. (2022).

[2].A, Al-Toma. U, Volta. R, Auricchio. G ,Castillejo. D, S, Sanders. C ,Cellier. C,J, Mulder. K,E,A ,Lundin. '' European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorder'', United EurGastroenterol. J. 7, 583–613. (2019).

[3].T,R ,Halfdanarson . M,R ,Litzow . J,A, Murray . ''Hematologic manifestations of celiac diseas'', Blood. 2007;109:412–421. (2006).

[4].R, Martٍn-Masot . M,T, Nestares . J,Diaz-Castro . I, Lٍpez-Aliaga . M,J,M, Alférez . J, Moreno-Fernandez . J , Maldonado. '' Multifactorial Etiology of Anemia in Celiac Disease and Effect of Gluten-Free Diet: A Comprehensive Review'', Nutrients.11:2557. (2019).

[5].A ,Lopez-Vazquez. L, Rodrigo. D, Fuentes. S, Riestra. C, Bousoٍo . S, Garcia-Fernandez. J, Martinez-Borra. S ,Gonzalez. C, Lopez-Larrea.''MHC class I chain related gene A (MICA) modulates the development of coeliac disease in patients with the high risk heterodimer'', DQA1*0501/DQB1*0201. Gut. (2002).

[6]. Hershcovici T, Leshno M, Goldin E, et al: Cost-effectiveness of mass screening for celiac disease is determined by time-delay to diagnosis and quality of life on a gluten free diet. Aliment. Pharmacol. Ther. 1(8), 901–910 (2010).

[7].Stephen EH, Chandra A: Declining estimates of infertility in the United States: 1982–2002. Fertil. Steril. 86(3), 516–523 (2006).

[8]. Green PHR, Stavropoulos SN, Panagi SG, et al: Characteristics of adult celiac disese in the USA: results of a national survey. Am. J. Gastroenterol. 96(1), 126–131 (2001).

[9]. Batinic, B., Ljubic, A., Culic, S., et al. Iron status and reproductive outcome: A prospective study in women undergoing assisted reproduction. Journal of Maternal -Fetal & Neonatal Medicine, 33(1), 40–46. https://doi.org/10.1080/14767058.2018.

[10]. Schappert SM, Burt CW: Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 2001–2002. Vital Health Stat. 13. 159, 1–66 (2006).

[11].M,M ,Leonard. A,Sapone. C, Catassi. A, Fasano.''Celiac disease and nonceliac gluten sensitivity A review'', JAMA. 318. 647–656. (2017).

[12]. W, Quarpong. T,R, Card. J, West. M, Solaymani-Dodaran. R,F, Logan. M,J, Grainge. '' Mortality in people with coeliac disease: Long-term follow-up from a Scottish cohort'', United Eur. Gastroenterol. 7, 377–387.(2019).

[13].K, Lindfors. C, Ciacci. K, Kurppa. K,E,A, Lundin. G,K, Makharia. M,L, Mearin. M,J,A, urray. E,F, Verdu, K, Kaukinen.''Coeliac diseas'', Nature reviews.5, 3.(2019).

[14].P,Singh . S, Arora. A , Singh. ''Prevalence of celiac disease in Asia: a systematic review and meta-analysis'', J GastroenterolHepatol. 3: 1095–101.(2016).

[15]–E,Lionetti. C, Catassi.''New clues in celiac disease epidemiology, pathogenesis, clinical manifestations, and treatmen'', Int Rev Immunol.30(4):219–31.(2011).

[16]– R,Tortora . F, Zingone . A, Rispo. C, Bucci. P, Capone. N, Imperatore. ''Coeliac disease in the elderly in a tertiary centr'', Scand J Gastroenterol.51(10):1179–83.(2016).

[17]– A ,Fasanol, Berti. T, Gerarduzzi. T, Not. R,B, Colletti. S,Drago. ''Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study'', Arch Intern Med.163(3):286–92.(2003).

[18]- T, Dieckman. F, Koning. G, Bouma.''Celiac disease: New therapies on the horizon, Curr , Opin'', Pharmacol. 66, 102268.(2022).

[19]- B, Jabri. L,M, Sollid.''T Cells in Celiac Disease'', J. Immunology. 198, 3005–3014. (2017).

[20]- E, Alhassan. A,Yadav. C,P, Kelly. R ,Mukherjee.''Novel Nondietary Therapies for Celiac Disease'', Cell. Mol. Gastroenterol. Hepatol. 8, 335–345.(2019).

[21]- G, Goel. J,A,Tye-Din. S,W, Qiao. A,K, Russell. T, Mayassi. C ,Ciszewski. V,K, Sarna. S ,Wang. K,E, Goldstein. J,L, Dzuris.''Cytokine release and gastrointestinal symptoms after gluten challenge in celiac disease'', Sci. Adv.5, eaaw7756.(2019).

[22]. Tye-Din, J.A.; on behalf of the RESET CeD Study Group; **Daveson, A.J.M.; Goldstein, K.E.; Hand, H.L.; Neff, K.M.; Goel, G.;Williams, L.J.; Truitt, K.E.; Anderson, R.P.** Patient factors influencing acute gluten reactions and cytokine release in treated coeliacdisease. BMC Med, 18, 362. (2020).

[23]-L,A, Cecilio. M,W, Bonatto.''The Prevalence Of Hla Dq2 And Dq8 In Patients With Celiac Disease, In Family and in General Population'', Arq. Bras. Cir. Dig. 28, 183–185.(2015).

[24]-G, Mazzarella.''Effector and suppressor T cells in celiac disease'', World J. Gastroenterol. 21, 7349–7356.(2015).

[25]-R, La Scaleia. M, Barba. G, Di Nardo. M, Bonamico. S ,Oliva. R,Nenna. F, Valitutti. M, Mennini. M, Barbato. M, Montuori.''Size and dynamics of mucosal and peripheral IL-17A+ T-cell pools in pediatric age, and their disturbance in celiac disease'', Mucosal Immunology. 5, 513–523. (2012).

[26]-I, Parzanese. D, Qehajaj. F, Patrinicola. M, Aralica. M, Chiriva-Internati S, Stifter. L, Elli. F, Grizzi.''Celiac disease: From pathophysiology to treatment'', World J. Gastrointest. Pathophysiol. 8, 27–38.(2017) .

[27]-J,F, Ludvigsson. J,C, Bai. F, Biagi. T, Card. C,Ciacci. P,J, Ciclitira. P,H,R,Green. M, Hadjivassiliou. A, Holdoway. D, van Heel.''Diagnosis and management of adult coeliac disease: Guidelines from the British Society of Gastroenterology'', Gut. 63,1210–1228.(2014).

[28]-F, Cataldo. G, Montalto.''Celiac disease in the developing countries: A new and challenging public health problem'', World J.Gastroenterol. 13, 2153–2159. (2007).

[29]-S, Vivas. L, Vaquero. L, Rodrيguez-Martيn. A, Caminero.''Age-related differences in celiac disease: Specific characteristics of adult presentation'', World J. Gastrointest. Pharmacol. Their. 6, 207–212.(2015).

[30]-K,E, McGowan. D,A, Castiglione. J,D, Butzner.''The Changing Face of Childhood Celiac Disease in North America: Impact of Serological Testing'', Pediatrics. 124, 1572–1578.(2009).

[31]-S,Vivas. J,M,R, de Morales. M, Fernandez. M, Hernando. B,Herrero. J, Casqueiro. S, Gutierrez.''Age-Related Clinical,Serological, and Histopathological Features of Celiac Disease'', Am. J. Gastroenterol. 103, 2360–2365. (2008).

[32]. Volta, U.; De Giorgio, R.; Granito, A.; Stanghellini, V.; Barbara, G.; Avoni, P.; Liguori, R.; Petrolini, N.; Fiorini, E.; Montagna, P et al. Anti-ganglioside antibodies in coeliac disease with neurological disorders. Dig. Liver Dis. (2006), 38, 183–187.

[33]-Y, Sahin.''Celiac disease in children: A review of the literature'', J. Clin. Pediatric. 10, 53–71.(2021).

[34]-G, Caio. U, Volta. A, Sapone. D,A,Leffler. R, De Giorgio. C, Catassi. A, Fasano. ''Celiac disease: A comprehensive currentreview'', BMC Med. 17, 142. (2019).

[35]-J,F,Ludvigsson. D,A, Leffler. J,C, Bai. F, Biagi. A, Fasano. P,H,R, Green. M, Hadjivassiliou. K,Kaukinen. C,P, Kelly. J,N, Leonard.''The Oslo definitions for coeliac disease and related and related terms'',Gut. 62, 43–52. (2013).

[**36]-M, Khatib. R,D, Baker. E,K, Ly. R, Kozielski. S,S, Baker.**''Presenting Pattern of Pediatric Celiac Disease'', J. Pediatr. Gastroenterol Nutr.62, 60–63. (2016).

[37]-C, Gallegos. R, Merkel. ''Current Evidence in the Diagnosis and Treatment of Children With Celiac

Disease'', Gastroenterol. Nurs Off. J. Soc. Gastroenterol. Nurses Assoc. 42, 41–48. (2019).

[38]-I,D, Hill. A, Fasano. S, Guandalini. E, Hoffenberg. J, Levy. N, Reilly. R, Verma. ''NASPGHAN Clinical Report on the Diagnosisand Treatment of Gluten-related Disorders'', J. Craniofacial Surg. 63, 156–165.(2016).

[39]-S,Husby. S, Koletzko. I, Korponay-Szabó. K, Kurppa. M,L, Mearin. C ,Ribes-Koninckx. R, Shamir. R, Troncone. R, Auricchio. G,Castillejo. ''European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020'', J. Craniofacial Surg. 70, 141–156. (2020).

[40]-F, Panetta. G, Torre. F,Colistro. F,Ferretti. A, Daniele. A, Diamanti.''Clinical accuracy of anti-tissue transglutaminase asscreening test for celiac disease under 2 years'', ActaPaediatric. 100, 728–731.(2011).

[41]- D, Poddighe. D, Abdukhakimova.''Celiac Disease in Asia beyond the Middle East and Indian subcontinent: Epidemiological burden and diagnostic barriers'', World J. Gastroenterol. 27, 2251–2256.(2021).

[42]-L, Downey. R, Houten. S, Murch. D, Longson. ''Recognition, assessment, and management of coeliac disease: Summary of updated NICE guidance'', BMJ 351, h4513. (2015).

[43]-M,Fewtrell. J,Bronsky. C, Campoy. M, Domellof. N,Embleton. N,F, Mis. I, Hojsak. J,M,Hulst. F, Indrio. A, Lapillonne. ''Complementary Feeding: A Position Paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition ESPGHAN) Committee on Nutrition'', J. Pediatric. Gastroenterology Nutrition . 64, 119–132.(2017).

[44]-J,A, Silvester. A, Therrien. C,P, Kelly.''Celiac Disease: Fallacies and Facts'', Am. J. Gastroenterol. 116, 1148–1155. (2021).

[45].Wasilewski T, Łukaszewicz-Zając M, Wasilewska J, Mroczko B. Biochemistry of infertility. Clin Chim Acta. (2020);508:185–190.

[46].Datta J, Palmer MJ, Tanton C, Gibson LJ, Jones KG, Macdowall W, et al. Prevalence of infertility and help seeking among 15 000 women and men. Hum Reprod. (2016);31(9):2108–2118.

[47].WHO. Infertility is a global public health issue. Available from: https:// www.who.int/reproductivehealth/topics/infertility perspective/en/. (26 Nov 2019).

[48].Slade P, O'Neill C, Simpson AJ, Lashen H. The relationship between perceived stigma, disclosure patterns, support and distress in new attendees at an infertility clinic. Hum Reprod. (2007);22(8):2309–2317.

[49].Ajayi OO, Charles-Davies MA, Arinola OG. Progesterone, selected heavy metals and micronutrients in pregnant Nigerian women with a history of recurrent spontaneous 2.abortion. Afr Health Sci. (2012); 12(2): 153–159.

[50].Morris JS, Adjukiewicz AB, Read AE. Coeliac infertility: an indication for dietary gluten restriction? Lancet. (1970); 1(7640): 213–214.

[51].Khizroeva J, Nalli C, Bitsadze V, et al. Infertility in women with systemic autoimmune diseases. Best Pract Res Clin Endocrinol Metab.(2019); 33(6): 101369.

[52].Sharif K, Watad A, Bridgewood C, et al. Insights into the autoimmune aspect of premature ovarian insufficiency. Best Pract Res Clin Endocrinol Metab. (2019); 33(6): 101323.

[53].Sen A, Kushnir VA, Barad DH, et al. Endocrine autoimmune diseases and female infertility. Nat Rev Endocrinol. (2014); 10(1): 37–50 .

[54].Casella G, Orfanotti G, Giacomantonio L, et al. Celiac disease and obstetrical-gynecological contribution. Gastroenterol Hepatol Bed Bench. (2016); 9(4): 241–249.

[55].Kreutz JM, Adriaanse MPM, van der Ploeg EMC, et al. Narrative review: nutrient deficiencies in adults and children with treated and untreated celiac disease. Nutrients. (2020); 12 (2).

[56].Grieger JA, Grzeskowiak LE, Wilson RL, et al. Maternal selenium, copper and zinc concentrations in early pregnancy, and the association with fertility. Nutrients. (2019); 11(7).

[57].Fallah A, Mohammad-Hasani A, Colagar AH. Zinc is an essential element for male fertility: a review of Zn roles in men's health, germination, sperm quality, and fertilization. J Reprod Infertil. (2018); 19(2): 69–81.

[58].Michels KA, Wactawski-Wende J, Mills JL, et al. Folate, homocysteine and the ovarian cycle among healthy regularly menstruating women. Hum Reprod. (2017); 32(8): 1743–1750.

[59].Mahadev S, Laszkowska M, Sundström J, et al. Prevalence of celiac disease in patients with iron deficiency anemia-a systematic review with meta-analysis. Gastroenterology. (2018); 155(2): 374–382.

[60].Castaño M, Gómez-Gordo R, Cuevas D, et al. Systematic review and meta-analysis of prevalence of coeliac disease in women with infertility. Nutrients. (2019); 11(8).

[61].Grode L, Bech BH, Plana-Ripoll O, et al. Reproductive life in women with celiac disease; a nationwide, population-based matched cohort study. Hum Reprod. (2018); 33(8): 1538–1547.

[62].Gunn B, Murphy KE, Greenblatt EM. Unexplained infertility and undiagnosed celiac disease: study of a multiethnic canadian population. J Obstet Gynaecol Can. (2018); 40(3): 293–298.

[63].Grode LB, Agerholm IE, Humaidan P, et al. Unrecognised coeliac disease among men and women undergoing fertility treatment: a screening study. United European Gastroenterol J.(2018); 6(10): 1477–1484.

[64].Singh P, Arora A, Strand TA, et al. Diagnostic accuracy of point of care tests for diagnosing celiac disease: a systematic review and meta-analysis. J Clin Gastroenterol. (2019); 53(7): 535–542.

[65].Esteve M, Rosinach M, Llordés M, et al. Case-finding in primary care for coeliac disease: Accuracy and cost-effectiveness of a rapid point-of-care test. United European Gastroenterol J. (2018); 6(6): 855–865.

[66].Grode L, Møller Jensen T, Parkner T, et al. Diagnostic Accuracy of a Point-of-Care Test for Celiac Disease Antibody Screening among Infertile Patients. Inflammatory Intestinal Diseases. (2019); 4(3): 123–130.

[67].Kotze LM, Mallmann A, Miecznikowski RC, et al. Reproductive aspects in brazilian celiac women. Arq Gastroenterol. (2020); 57(1): 107–109.

[68].Cakmak E, Karakus S, Demirpence O, et al. Ovarian reserve assessment in celiac patients of reproductive age. Med Sci Monit. (2018); 24: 1152–1157.

[69].Samsami A, Ghasmpour L, Moradi Alamdarloo S, et al. Women with Autoimmune Thyroiditis have Lower Reproductive Life Span or Not? A Cross-Sectional Study. Int J Community Based Nurs Midwifery. (2020); 8(4): 305–310.

[70].Lerchbaum, E., & Obermayer-Pietsch, B. (2012). Vitamin D and fertility: A systematic review. European Journal of Endocrinology, 166(5), 765–778.

[71].Li, H. W., Brereton, R. E., Anderson, R. A., Wallace, W. H., & Ho, P. C. (2019). Vitamin D deficiency is common and associated with poor ovarian reserve in Asian infertile women. PLoS One, 14(5), e0215124.

[72].Liu, N. Q., & Hewison, M. (2012). Vitamin D, the placenta and pregnancy. Archives of Biochemistry and Biophysics, 523(1), 37–47.

[73]. Irani, M., & Merhi, Z. (2014). Role of vitamin D in ovarian physiology and its implication in reproduction: A review. Reproductive Biology and Endocrinology, 12(1), 80.

[74].Holick, M. F. (2007). Vitamin D deficiency. New England Journal of Medicine, 357(3), 266–281.

[75].Pal, L., Berry, A., Coraluzzi, L., et al. (2016). Therapeutic implications of vitamin D and calcium in overweight women with PCOS. Gynecological Endocrinology, 32(5), 340–344.

[76].Anifandis, G., Dafopoulos, K., Messini, C. I., Polyzos, N. P., & Messinis, I. E. (2018). The impact of vitamin D supplementation in women undergoing in vitro fertilization: A prospective cohort study. Gynecological Endocrinology, 34(1), 51–54.

[77].Beard, J. L., Hendricks, M. K., Perez, E. M., et al. (2005). Maternal iron deficiency anemia affects postpartum emotions and cognition. The Journal of Nutrition, 135(2), 267–272.

[78]. **Batinic, B., Ljubic, A., Culic, S., et al. (2020).** Iron status and reproductive outcome: A prospective study in women undergoing assisted reproduction. Journal of Maternal-Fetal & Neonatal Medicine, 33(1), 40–46.

[79].Gaskins, A. J., Mumford, S. L., Chavarro, J. E., et al. (2014). A prospective study of serum iron levels and fertility outcomes among women undergoing assisted reproduction. Human Reproduction, 29(3), 500–507.

[80].Schaefer, E., & Barkan, D. (2021). Iron homeostasis in the endometrium: Emerging roles in reproduction and fertility. Frontiers in Physiology, 12, 628122.

[**81]-N, Gujral. ''**Celiac disease: Prevalence, diagnosis, pathogenesis and treatment'', World J. Gastroenterol.18, 6036–6059.(2012)**.**

[82]- Stazi, A.V.; Trecca, A.; Trinti, B.''Osteoporosis in celiac disease and in endocrine and reproductive disorders'',World J. Gastroenterol.(2008), 14, 498–505.

[83]-H,M, Ndez-Bañares. H, Monzón. M, Forné. ''A short review of malabsorption and anemia'', World J. Gastroenterol.15, 4644–4652.(2009).

[84]-J,M, Kreutz. M,P,M, Adriaanse. E,M,C, Van Der Ploeg. A,C,E, Vreugdenhil.''Narrative Review: Nutrient Deficiencies in Adults and Children with Treated and Untreated Celiac Disease'', Nutrients. 12, 500.(2020).

[85]- S, Dong. T,P, Singh. X, Wei. H, Yao. H, Wang.''Protective Effect of 1,25-Dihydroxy Vitamin D3 on Pepsin-Trypsin-ResistantGliadin-Induced Tight Junction Injuries'', Dig. Dis. Sci. 63, 92–104.(2018).

[86]-N, Charoenngam. M,F, Holick.''Immunologic Effects of Vitamin D on Human Health and Disease'', Nutrients. 12, 2097.(2022).

[87]-G, Mailhot.J,H, White.''Vitamin D and Immunity in Infants and Children'', Nutrient. 12, 1233. (2021).

[88]- N,S, Akimbekov. I, Digel. D,K, Sherelkhan. Lutfor. M,S, Razzaque.''Vitamin D and the Host-Gut Microbiome: A BriefOverview'', ActaHistochem. Cytochem.53, 33–42.(2021).

[89]-M,B, Zimmermann. J, Köhrle.''The Impact of Iron and Selenium Deficiencies on Iodine and Thyroid Metabolism: Biochemistryand Relevance to Public Health'', Thyroid. 12, 867–878. (2002).

[90]-H, Gunshin. B, MacKenzie. U,V, Berger. Y, Gunshin. M,F, Romero. W,F,Boron. S,Nussberger. J,L, Gollan. M,A, Hediger.''Cloning and characterization of a mammalian proton-coupled metal-ion transporter'', Nat. Cell Biol. 388, 482–488. (1997).

[91]-M, Shayeghi. G,O, Latunde-Dada. J,S, Oakhill. A,H, Laftah. K ,Takeuchi. N, Halliday. Y, Khan. A, Warley. F,E, McCann. R,C, Hider. ''Identification of an Intestinal Heme Transporter'', Cell. 122, 789–801.(2005).

[**92]- H,J, Freeman.**''Iron deficiency anemia in celiac disease'', World J. Gastroenterol. 21, 9233–9238.(2015).

[**93]-U, Krupa-Kozak.**''Pathologic bone alterations in celiac disease: Etiology, epidemiology, and treatment'', Nutrition.30, 16–24.(2014).

[94].Tarek, M., Abdelrahman, R., & Helmy, H. (2020). Subclinical iron deficiency as a hidden cause of female infertility: A pilot study. Middle East Fertility Society Journal, 25, 10.

[95].Li J, You Y, Yue W, Jia M, Yu H, Lu T, Wu Z, Ruan Y, Wang L, Zhang D. Genetic evidence for possible involvement of the calcium channel gene CACNA1A in autism pathogenesis in Chinese Han population. PLoS One 10: e0142887, (2015).

[96].Luk J, Torrealday S, Neal Perry G, Pal L. Relevance of vitamin D in reproduction. Hum Reprod 27: 3015–3027, (2012).

[97].Mousa A, Abell S, Scragg R, de Courten B. Vitamin D in reproductive health and pregnancy. Semin Reprod Med 34: e1–e13, (2016).

[98]. Muscogiuri G, Altieri B, de Angelis C, Palomba S, Pivonello R, Colao A, Orio F. Shedding new light on female fertility: the role of vitamin D. Rev Endocr Metab Disord 18: 273–283, (2017).

[99]. Paffoni A, Ferrari S, Vigano P, Pagliardini L, Papaleo E, Candiani M, Tirelli A, Fedele L, Somigliana E. Vitamin D deficiency and infertility: insights from in vitro fertilization cycles. J Clin Endocrinol Metab 99: E2372–E2376, (2014).

[100]. Franasiak JM, Lara EE, Pellicer A. Vitamin D in human reproduction. Curr Opin Obstet Gynecol 29: 189–194, (2017).

[101].Miyazaki S, Yuzaki M, Nakada K, Shirakawa H, Nakanishi S, Nakade S, Mikoshiba K. Block of Ca2+ wave and Ca2+ oscillation by antibody to the inositol 1,4,5-trisphosphate receptor in fertilized hamster eggs. Science 257: 251–255, (1992).

[102**]**.Influence of Vitamin D supplementation on reproductive: https://pmc.ncbi.nlm.nih.gov/articles /PMC989671.

[103**]**.Vitamin D and Fertility Related? - Reproductive Health and Wellness Center: https://reproductivehealthwellness.com/vitamin-d-and-fertility .

[104**]**.Vitamin D in Reproductive Health Disorders: A Narrative Review Focusing on Infertility, Endometriosis, and Polycystic Ovarian Syndrome - MDPI: https://www.mdpi.com/1422-0067/26/5/2256 .

[105**]**.Vitamin D and Infertility: The Evidence | Fertility & Reproduction - World Scientific Publishing: https://www.worldscientific.com/doi/10.1142/S2661321821950004X

[106**]**.Effects of Vitamin D on Fertility, Pregnancy and Polycystic Ovary Syndrome—A Review: https://pmc.ncbi.nlm.nih.gov/articles/PMC9029121 .

[107**]**.How Vitamin D Affects Your Fertility: https://www.shadygrovefertility.com/article/how-vitamin-d-affects-your-fertility

[108**]**.Does Treating Iron Deficiency Improve Fertility Outcomes? - The ObG Project: https://www.obgproject.com/2025/04/17/does-treating-iron-deficiency-improve-fertility-outcomes .

[109**]**.Association between iron deficiency and fertility - PubMed: https://pubmed.ncbi.nlm.nih.gov/39817704 .

[110**]**.Ferritin And Iron Deficiency: How Low Iron Levels Affect Fertility - Lola&Lykke: https://lolalykke.com/sv/blogs/mamma-manualer/ferritin-and-iron-deficiency-fertility .

[111**]**.Do Iron Levels Affect Fertility & Conception?: https://kinfertility.com.au/blog/iron-and-fertility .

[112**]**.Can Iron Levels Impact Fertility and Conception? - Ferty9: https://www.ferty9.com/blog/iron-deficiency-impacts-fertility .

[113.Abdullah UH, Lalani S, Syed F, Arif S, Rehman R. Association of vitamin D with outcome after intra cytoplasmic sperm injection. J Matern Fetal Neonatal Med 30: 117–120, (2017).

[114**]** . Aquila S, Guido C, Middea E, Perrotta I, Bruno R, Pellegrino M, Andò S. Human male gamete endocrinology: 1alpha, 25-dihydroxyvitamin D3 (1,25(OH)2D3) regulates different aspects of human sperm biology and metabolism. Reprod Biol Endocrinol 7: 140, (2009).