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Ministry of Higher Education and
Scientific Research
University of Thi-Qar
College Of Science**



**Study of Progesterone, Testosterone, Oxidative Stress and
Lipid Profile During Two Phases of Menstrual Cycle in
Bronchial Asthma Patients in Thi-Qar Province/Iraq**

**A Thesis
Submitted to the Council of the College of Science
University of Thi-Qar
In Partial Fulfillment of the Requirements
For the Master Degree of Science in Biochemistry**

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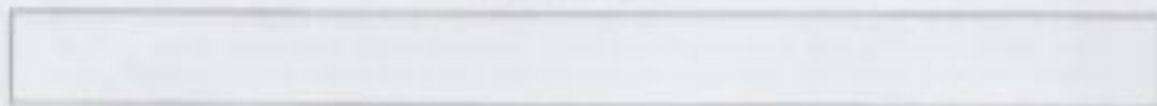
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We certify that this thesis, entitled **Clinical Study for Some Sex Hormones, Oxidative Stress and Lipid Profile During Phases Menstrual Cycle in Bronchial Asthma Patients in Thi-Qar Province/Iraq** was prepared by **Khalid Abd Edam** under your supervision at the Department of Chemistry, College of Science, University of Thi-Qar (Iraq) in partial fulfillment of the requirements for the Master degree of science in chemistry.



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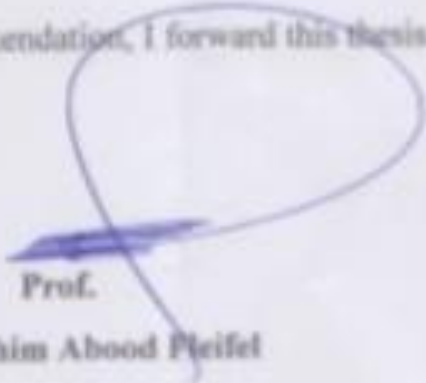
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الإهداء

إلى صاحب الإسراء والمعراج ..إلى سيد المرسلين ..إلى نبي الرحمة ونور العالمين .

سيدنا محمد ﷺ

إلى ملائكتي في الحياة ..إلى بسملة الحياة وسر الوجود ..إلى من كان دعاءها سر نجاحي وحنانها
بلسم جراحي ..

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إلى من فارقني فعز علي فراقه فكنت أتمنى وجوده معي لأعطى باستجابة دعائه ...

أبي الغالي (روحي لتراجم قبرك الفداء)

إلى من أختارها قلبي يا حلمي الذي يراودني ، أنت من تغلغل في قلبي وتهت في أرجاء
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ABBREVIATIONS

A	Absorbance
ATP	Adenosine triphosphate
α	Alpha
ALP	Alkaline phosphatase
β	Beta
BMI	Body mass index
COPD	Chronic obstructive pulmonary disease
CYP17	Cytochrome P450 17
CP	Ceruloplasmin
CM	Chylomicrons
CYP11A	Cholesterol Side Chain Cleavage Enzyme
DNA	Deoxyribonucleic acid
°C	Degree Celsius
DM	Diabetes Mellitus
D.W	Distilled water
DHEA	Dehydroepiandrosterone
DHEAS	Dehydroepiandrosterone Sulfate
dL	Deciliter
E₀	Extinction coefficient
E	Estrogen
ELFA	Enzyme Linked Fluorescent Assay
FSH	Follicle stimulating hormone

FEV1	Forced expiratory volume in one second
FENO	Fraction of exhaled nitric oxide
FRs	Free Radicals
GnRH	Gonadotropin-releasing hormone
g	Gram
GK	Glycerol kinase
GPO	Glycerol-3-phosphate oxidase
GP_x	Glutathione Peroxidase
GSHR	glutathione reductase
γ	Gamma
Δ	Greek symbol for Capital Delta
4-HNE	4-hydroxynonenal
HRV	Human rhino virus
HDL	High Density Lipoprotein
3β-HSD	3β-hydroxysteroid dehydrogenase
IDL	Intermediate density lipoprotein
IFN-γ	Interferon gamma
IHD	Ischemic heart disease
ICS	Inhaled corticosteroids
IL - 6	Interleukins – 6
IgE	Immunoglobulin E
Kg	Kilogram

KDa	Kilo Dalton
LH	Luteinizing Hormone
LABA	Long acting beta-agonists
LSD	Least Significant Difference
LPO	Lipid peroxidation
LDL	Low density lipoprotein
LPL	Lipoprotein lipase
L	Liter
LTRA	Leukotriene receptor antagonists
mol	Mole
ϵ MDA	Molar Absorption Coefficient of MDA
mg	Milligram
M	Molarity
MDA	Malondialdehyde
min	Minute
mRNA	Messenger ribonucleic acid
ml	Milliliter
μl	Microliter
μmol	Micromole
mmol	Millimole
ng	Nanogram
NADPH	Nicotinamide adenine dinucleotide phosphate
NADH	Nicotinamide adenine dinucleotide

nm	Nanometer
P	Progesterone
PRG	Progesterone
PUFA	Poly unsaturated fatty acid
P450_{scc}	Cholesterol Side Chain Cleavage Enzyme
PEFR	Peak expiratory flow rate
PEF	Peak expiratory flow
PAP	4-Amino-antipyrine
PTA	Phosphotungstic acid
POD	Peroxidase
PBR	Peripheral benzodiazepine receptor
PPD	Para-phenylene diamine
Pg	Picogram
Rpm	Rotor per minute
RSV	Respiratory syncytial virus
ROS	Reactive oxygen species
RNS	Reactive nitrogen species
SPR	Solid Phase Receptacle
SOD	Superoxide dismutase
StAR	Steroidogenic Acute Regulatory Protein
sER	Smooth endoplasmic reticulum

SHBG	Sex Hormone -Binding Globulin
SABA	Short-acting beta ₂ -agonist
SD	Standard Deviation
ϵ_{Cp}	The Extinction Coefficient of Cp
T	Testosterone
TC	Total cholesterol
Tf	Transferrin
TG	Triglyceride
TEST	Testosterone
TCA	Trichloro acetic acid
TBA	Thio barbituric acid
TIBC	Total Iron Binding Capacity
Th	T- Helper
UV	Ultra-Violate
Q10	Ubiquinone
VLDL	Very low density lipoprotein
VIS	Visible
WR	Working reagent

Summary

Asthma is a chronic inflammatory airway disorder associated with recruitment of inflammatory cells. However, the incidence, severity, and prognosis of asthma can be affected by a number of factors, including hormonal fluctuations during phases of the menstrual cycle during of asthma among women.

The present study was designed to determine the levels of hormones (**Testosterone and Progesterone**), **Oxidative Stress status (Malondialdehyde, Ceruloplasmin and Transferrin)** and **lipid profile (TC, TG, HDL-c, VLDL-c and LDL-c)** during two phases of the menstrual cycle (follicular and luteal phase) in bronchial asthma patients.

The measured parameters are studied on the basis of three variables: general comparison, age and two phases of the menstrual cycle (follicular and luteal phase).

Patients and control groups were divided, in the general comparison, into two groups:

1- Control group: includes (70) women supposed healthy volunteers without taking contraceptive pills aged (14-45 years).

2- Patient group: includes (70) women patients with bronchial asthma without taking contraceptive pills aged (14-45 years).

Patients and controls were divided according to their ages, into two age groups: A1 (14-29 years) and A2 (30-45 years).

The results of the study **showed a significant decrease in concentrations of (Testosterone, Progesterone and HDL-c)** in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

The current study showed a **significant increase in concentrations of (TC, TG, VLDL-c, LDL-c, MDA and CP)** in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

It has found that there are **no significant differences in the concentration of Tf** in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

According to age in controls and patient group, there is a significant increase in concentrations of (Testosterone, Progesterone and HDL-c) and significant decrease in concentrations of (TC, TG, VLDL-c, LDL-c, MDA and CP) in the group (A1) in follicular and luteal phase in comparison with a group (A2) in follicular and luteal phase respectively ($p \leq 0.05$).

There is **no significant difference in concentration of (Tf)** in the group (A1) in follicular and luteal phase in comparison with a group (A2) in follicular and luteal phase respectively ($p \leq 0.05$).

According to the relationship between follicular and luteal phase, the study shows a significant increase in concentrations of (Testosterone, Progesterone and HDL-c) and a significant decrease in concentrations of (TC, TG, VLDL-c and LDL-c) in all patients in the luteal phase in comparison with follicular phase.

There is **no significant difference in concentrations of (MDA, CP and Tf)** in all patients in the luteal phase in comparison with the follicular phase.

1. INTRODUCTION AND LITERATURE REVIEW

Asthma warrants a global health care awareness for an estimated 300 million people, about 8% of the world's adult population and around 250,000 annual deaths worldwide are related to asthma (Brooks, 2015). The national surveillance of asthma in the United States reported that people who were diagnosed with asthma increased from 20.3 million in 2001 to approximately 25.7 million in 2010, a yearly increase of 2.9% (Akinbami *et al.*, 2012; Moorman *et al.*, 2012). Thus, 1 in 12 adults 18 years and over had asthma, an estimated 18.7 million people, with 16.5% of adults 65 and over affected by asthma (Centers for Disease Control and Prevention [CDC], 2012; Moorman *et al.*, 2012). Asthma prevalence in older adults was estimated at 7.8% in 2012 (Blackwell *et al.*, 2014) and is expected to increase due to new incidences and as the current asthma population turns 65. Yet, many researchers believe the actual prevalence rate is higher due to asthma being underdiagnosed or misdiagnosed. This is significant because 65 and over population is estimated to reach 72.1 million people by the year 2030 (Vincent and Velkoff, 2010).

Asthma symptoms among adults are frequently considered to be the normal conditions due to aging or weight gain where asthma signs may go unnoticed by doctors because they are analogous to other comorbidities, particularly chronic obstructive pulmonary disease (Gibson *et al.*, 2010; Reed, 2010; Hanania *et al.*, 2011; Jones *et al.*, 2011). Improper identification of asthma can explain why over 50% of deaths caused by asthma occur in adults aged 65 and over (Moorman *et al.*, 2012). Asthma is considered a highly manageable disease that can be controlled with proper disease management. However, according to the CDC (2012), approximately nine adults die every day linked to improper asthma control.

1.1. Asthma

Asthma is a common chronic inflammatory disease of the respiratory which leads to a variable or even persistent airflow limitation. The main symptoms are dyspnoea (shortness of breath), wheezing, chronic cough and chest tightness. The prevalence of asthma in humans varies worldwide, affecting 1 to 18% of any investigated population (Koper *et al.*, 2017). Women are more often affected by asthma. The mechanisms underlying the gender differences in asthma prevalence are still under investigation, but refer mostly to hormonal differences and differences in lung capacity (Fuseini and Newcomb, 2017).

1.1.1. Symptoms and Signs of Asthma

They include cough, dyspnoea, wheezing, chest tightness and sputum production (Chanez and Godard, 2006).

Patients with severe airflow obstruction [asthma or chronic obstructive pulmonary disease (COPD)] often have prolonged wheezy coughing, and sometimes the sustained increase in intrathoracic pressure are sufficient to impair venous return to the heart, resulting in reduced cardiac output and cough syncope or near syncope (Graham *et al.*, 2005).

Severe acute asthma can increase the pulse rate to more than 110 beats per minute. It is common to see a hyper-expansion of the thoracic cavity and lowering of the diaphragm. Breathing can become rapid (>30 breaths /min) and shallow leading to low arterial oxygen tension with the patient becoming fatigued, cyanosed, confused and lethargic (Roger and Clive, 2003).

1.1.2. The Pathophysiology of Asthma

The pathophysiology of asthma is complex and involves three main characteristics: inflammation, bronchial hyper-responsiveness and reversible airway obstruction (Busse and Lemanske, 2001).

1-Airway inflammation

Inflammation plays the central role in the development and expression of asthma. Inflammation does not only causes the airway obstruction, but also contributes to airway hyper-responsiveness which enhances susceptibility to bronchospasm. The model that infections could trigger and aggravate asthma in already sensitized individuals has been well established (Cohn *et al.*, 2004).

2-Bronchial hyper-responsiveness

Airway inflammation also leads to bronchial hyper reactivity, described as excess airway narrowing in response to stimuli. Depending on the degree of inflammation, the airways can be closed. The more severe the asthma, the more reactive the airways. The ultimate result is the degree of airflow obstruction resulting from trigger exposure (Conboy-Ellis, 2006).

3-Airflow obstruction

Bronchospasm, edema and mucous hypersecretion lead to airflow obstruction, but it is often reversible. Variable airflow obstruction is demonstrated by measuring forced expiratory volume in the first second (FEV1) and peak expiratory flow (PEF) (Louis *et al.*, 1999). Acute bronchoconstriction is the consequence of immunoglobulin E-dependent mediator release following exposure to allergens and is the primary component of the early asthmatic response. Airway edema occurs 6-24 hours following an allergen challenge and is referred to as the late asthmatic response. Airway hyper-responsiveness involves narrowing of the airway when exposed to stimuli such as food and medicine. Airway remodelling is associated with structural changes due to long-standing inflammation and may profoundly affect airway obstruction (Holgate, 2000).

1.1.3. A etiology (Pathogenesis) of Asthma

1-Genetics

Genetics may also contribute to asthma by influencing genes involved in immunity. Airway inflammation in asthma may represent a loss of normal

balance between two populations of Th lymphocytes, Th1 and Th2. Th1 cells produce IL-2 and IFN- γ which are critical in cellular defense mechanisms in response to infection. Th2 cells, in contrast, generate a family of cytokines that can mediate allergic inflammation, and asthma is characterized by a shift toward cytokine-like disease. Therefore, this cytokine imbalance toward Th2 is caused either by overexpression of Th2-type cytokines or under expression of Th1-type cytokines (Salvi *et al.*, 2001). This genetic background will promote the production of antibody to key environmental antigens, and then increase an individual's susceptibility to asthma (Larche *et al.*, 2003).

2-Gender

Boys have a higher prevalence of allergic sensitization than girls while in adults the gender difference is reversed (Govaere *et al.*, 2007).

3-Race (Ethnicity)

Susceptibility to asthma may be higher among certain racial groups than others (Le Souëf *et al.*, 2000). Mexican Americans were less likely to report asthma when compared to non-Hispanic whites (Arif *et al.*, 2003).

4-Age

Asthma is frequent in the older adult population with the prevalence estimated to be greater than 10% (Gillman and Douglass, 2012). However, the true prevalence of asthma in older adults is suggested to be much higher due to poor perception of symptoms and misdiagnosis with other conditions such as chronic obstructive pulmonary disease and gastroesophageal reflux disease (Olivenstein and Hamid, 2011).

5-Allergens

House dust mites, animal allergens (especially cat and dog), cockroach allergens, and fungi are the most commonly reported allergens. Sensitization and frequency of exposure to allergens are important factors in the development of asthma in children (McConnell *et al.*, 2002).

1.1.4. Some Risk Factors for Asthma

1-Viral respiratory infection

Viral respiratory tract infections can have profound effects on important aspects of asthma (figure 1-1) (Buss *et al.*, 2010). In early life, many children have wheezing episodes associated with respiratory infections. There are many pathogens associated with such wheezing events, including respiratory syncytial virus (RSV), human rhino virus (HRV), metapneumovirus, parainfluenza, and coronavirus. For most infants, wheezing episodes to respiratory infections diminish with age, but for some individuals wheezing episodes in early life can mark the beginning of asthma (Buss *et al.*, 2010).

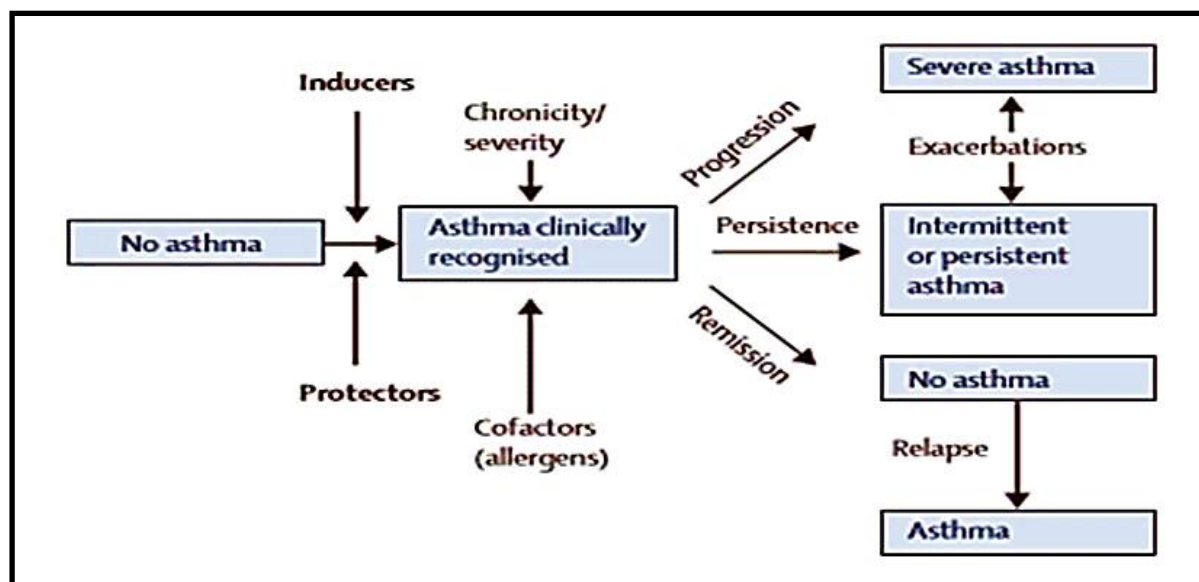


Figure (1-1): Role of Infections in Asthma (Buss *et al.*, 2010).

2-Food allergy

Children who have asthma and food allergies together have an increased risk of severe or near fatal anaphylactic reactions (Wang and Liu, 2011). In the past few decades, both conditions have been increasing in children not just in the United States but worldwide. Studies have suggested that food allergies precede asthma in children, while other studies suggest a food allergen is the risk factor for children to develop asthma (Schroeder *et al.*, 2009).

3-Early lung function abnormalities

It is found that poor airway function shortly after birth should be recognized as a risk factor for airflow obstruction in young adults (Stern *et al.*, 2007).

4-Obesity and body mass index

Innecity adults with a body mass index over 30 kg/m² are found to have more severe symptoms with increases in asthma prevalence, airflow obstruction and asthma exacerbations thus requiring long-term use of inhaled corticosteroids to help manage their symptoms (Fitzpatrick *et al.*, 2012). However Song *et al* (2012) mention that a measurement of BMI for obesity as an indicator of asthma in older adults and severity may be better determined by exploration of subcutaneous fat and sarcopenia since weight gain is a natural phase of healthy aging.

5-Antibiotic use

Certain studies that examine any antibiotic use show a greater risk of persistent wheeze and asthma in early childhood and a dose response relationship between the number of antibiotic courses and the risk of wheeze or asthma (Jedrychowski *et al.*, 2006).

6-Exposure to animals

A study performed by Almqvist *et al* showed that the exposure to cats was associated with a greater risk of allergic sensitization (Almqvist *et al.*, 2003).

1.1.5. Diagnosis of Asthma

Asthma is diagnosed through a clinical evaluation of the patient's history, physical exam, signs and symptoms, along with lung functions tests, spirometer, and airflow reversibility commonly measured by one-second forced expiratory volume (Deng *et al.*, 2010). After the age of 30 years, there are normal decreases in lung capacity (Pedone *et al.*, 2013) and elasticity of lung tissue along with the slower regeneration of cellular structures (Babb and Rodarte, 2000). There are a normal decline in muscle fibers as people age, producing a 6

to 30% decrease of muscle mass in adults over the age of 60 thereby reducing the muscle strength and power used in breathing (Kim and Sapienza, 2005). The maximal expiratory flow decreases as we age due to a decrease in the pressure exerted by the lungs (Babb and Rodarte, 2000), causing a decline in FEV1 in healthy older adults (Gibson *et al.*, 2010). The measures of airflow reversibility using FEV1 after bronchodilator can result in a false negative result in the older adult with asthma (Liu *et al.*, 2009).

Peak expiratory flow (PEF) is the maximum flow generated during expiration performed with maximal force and starting after a full inspiration. Many reports emphasize the importance of measuring peak expiratory flow rate (PEFR) in general practice to establish the diagnosis of asthma and for monitoring patients with asthma (Ghazal *et al.*, 2010).

1.1.6. Classification of Asthma

Grading takes into account the frequency and severity of past and current asthma symptoms, physical exams, and measures of lung function. Asthma is classified as either intermittent or persistent. Intermittent asthma is the least serious with symptoms of coughing and wheezing no more than two days a week. Night time flare-ups occur twice a month at the most. Mild persistent asthma is characterized as symptoms occurring more than twice a week but less than once a day. Night time flare-ups happen more than twice a month. Moderate persistent asthma symptoms occur daily and night time flare-ups occur more than once a week. Severe persistent asthma is characterized as symptoms occurring daily frequently disrupting activities and sleep (Dhar and Goshal, 2013).

1.1.7. Treatment of Asthma (Kroegel, 2017)

STEP 1: As-needed reliever inhaler

Preferred option: as-needed inhaler short-acting beta₂-agonist (SABA).

Other options: regular low dose Inhaled corticosteroids (ICS)

STEP 2: Low dose controller medication plus as-needed reliever medication

Preferred option: regular low dose ICS plus as-needed SABA.

Other options: leukotriene receptor antagonists (LTRA) are less effective than ICS.

STEP 3: One or two controllers plus as-needed reliever medication

Preferred option (adults/adolescents): combination low dose ICS/LABA as maintenance treatment plus as-needed SABA or combination low dose ICS/formoterol.

Other options: increase ICS to medium dose.

STEP4: Two or more controllers plus as-needed reliever medication.**STEP5: Higher level care and/or add-on treatment.****1.2. Menstrual Cycle**

The menstrual cycle is the regular natural change that occurs in the female reproductive system (specifically the uterus and ovaries) that makes pregnancy possible. The cycle is required for the production of oocytes and for the preparation of the uterus for pregnancy (Silverthorn and Dee Unglaub, 2013). Up to 80% of women report having some symptoms during the one to two weeks prior to menstruation. Common symptoms include acne, tender breasts, bloating, feeling tired, irritability and mood changes. These symptoms interfere with normal life and therefore qualify as premenstrual syndrome in 20 to 30% of women. In 3 to 8%, they are severe (Biggs and Demuth, 2011). Each cycle can be divided into three phases based on events in the ovary (ovarian cycle) or in the uterus (uterine cycle) (Silverthorn and Dee Unglaub, 2013). The ovarian cycle consists of the follicular phase, ovulation and luteal phase whereas the uterine cycle is divided into menstruation, proliferative phase and secretory phase.

The follicular phase is the phase of the estrous cycle (or, in humans and great apes, the menstrual cycle) during which follicles in the ovary mature. It

ends with ovulation. The main hormone controlling this stage is estradiol. There are several steps in the process of follicular development that occur in the follicular phase: initiation, recruitment and progression, pre-ovulatory maturation and ovulation. These processes occur in different areas of the body (Bagnell, 2005).

The luteal phase is the latter phase of the menstrual cycle (in humans and a few other animals) or the earlier phase of the estrous cycle (in other placental mammals). It begins with the formation of the corpus luteum and ends in either pregnancy or luteolysis. The main hormone associated with this stage is progesterone which is significantly higher during the luteal phase than other phases of the cycle (Bagnell, 2005).

The prevalence and severity of asthma are frequently associated with key moments in the reproductive life of women. Accordingly, it has been hypothesized that hormonal fluctuations during the menstrual cycle could play a crucial role in the pathophysiology of asthma, resulting in cyclic worsening of disease severity. Women seem to experience an aggravation of asthma symptoms during the premenstrual or menstrual phases of their cycle. Terms as premenstrual asthma (PMA) have been used to describe this phenomenon (Pignataro *et al.*, 2017). Showed that FEV1 decreased during the follicular phase of the menstrual cycle in about 30% of women and, precisely, it was associated with lower cAMP levels in sputum, to explain mechanistically a major bronchoconstriction in this reproductive phase. They also suggest a link between PMA and testosterone levels (Matteis *et al.*, 2014).

1.3. Hormones

The stability of the internal environment of the organism (homeostasis) depends on the full coordination between the two systems in the body which are the nervous system and endocrine system. This regulation is through secretion of glands of internal secretion of chemical messengers called hormones. These hormones affect each other by either conflict or cooperate and produce in

concentrations very low up to 1 Pg in milliliters of blood, but influential (Salem *et al.*, 2002) and the hormones are secreted within endocrine glands and from there they move into other extracellular spaces. Several hormones are distributed widely following secretion and equilibrate throughout virtually all extra-cellular spaces, including formed saliva stored in the salivary glands (Nabipour, 2003). While the nervous regulation is faster because the secretion of neurotransmitters depends on the arrival of the nervous assailant that moves very quickly in the nerve fibers (Al-Ebadi, 2006). The hormones are located under three different groups: amino hormones, peptide hormones or protein hormones and steroid hormones (Salem *et al.*, 2002).

1.3.1. Non-Steroidal Hormones

Most of the hormones in the body are polypeptides and proteins that range in size from small peptide that consist of three amino acids to proteins of 200 amino acids (Norman and Litwack, 1987). The proteins and peptides are synthesized from amino acids according to messenger ribonucleic acid (mRNA) template (Dobson, 2000), which is itself synthesized from a deoxyribonucleic acid (DNA) template inside the cell's nucleus in the same fashion as most other protein synthesis on rough endoplasmic reticulum of endocrine cells (Lodish *et al.*, 2004).

Peptide hormone precursors preprohormones (which are biologically inactive) are first synthesized and then processed in several stages in the endoplasmic reticulum (Baulieu, 1991) including removal of the N-terminal signal sequence and sometimes glycosylation, resulting in Prohormones (Griffin and Ojeda, 2000). The prohormones transferred to the Golgi apparatus to package into membrane-bound secretory vesicles which can be secreted from the cell by exocytosis in response to specific stimuli (Beato *et al.*, 1996).

1.3.2. Steroidal Hormones

These hormones are synthesized from cholesterol in the gonads and adrenal glands (Hammes, 2003) as shown in figure (1-2). These are highly lipid soluble molecules that they are simply diffuse across the cell membrane and enter the interstitial fluid and then into the blood (Feder, 1981). Steroidal hormones have an important role on reproductive system representing in hypothalamic-pituitary-gonadal axis. Gonadotropin-releasing hormone (GnRH) is secreted in an episodic fashion from the hypothalamus to activate the production of gonadotropins, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) from the anterior pituitary (Santoro *et al.*, 1988).

LH and FSH are released in a pulsatile manner to act at the gonad to control both gametogenesis (spermatogenesis or oogenesis), as well as steroid genesis (Santoro *et al.*, 1986). The major sex hormones estradiol, progesterone and testosterone are secreted in response to gonadotropins and, in turn, feedback at the level of the hypothalamus and pituitary to control normal reproductive function (Segars and Driggers, 2002).

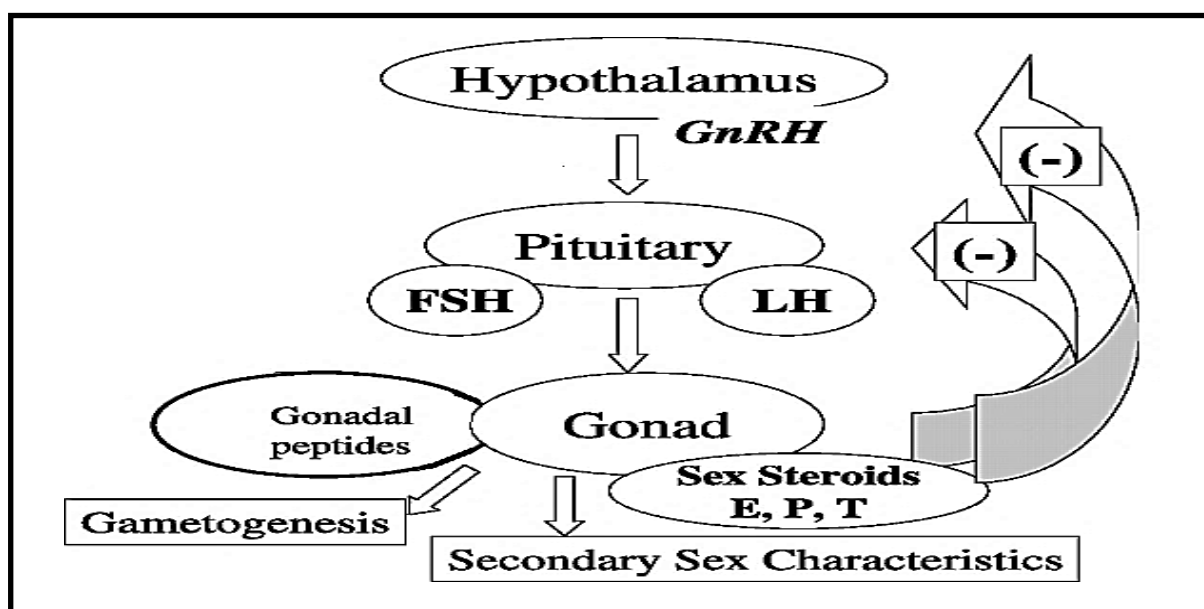
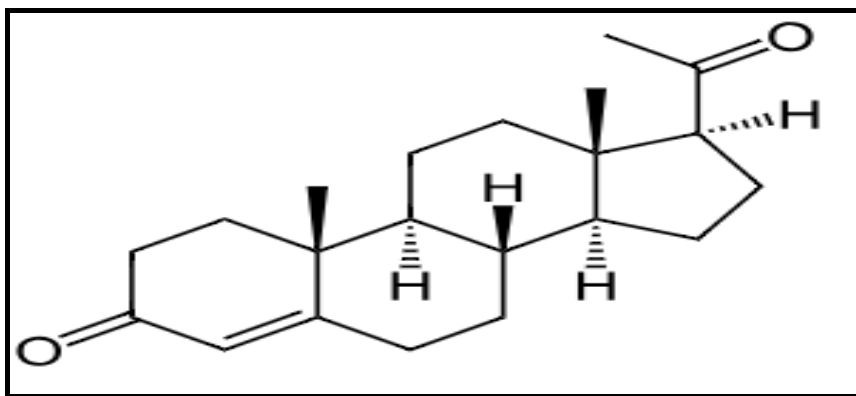


Figure (1-2): The Hypothalamic-Pituitary-Gonad alaxis, gonadotropin-Releasing Hormone, Follicle-stimulating Hormone, Luteinizing Hormone, Estrogen, Progesterone, Testosterone (Santoro *et al.*, 1988).

1.3.2.1. Progesterone

Progesterone is an endogenous steroid a progestogen sex hormone involved in the menstrual cycle, pregnancy, and embryogenesis of humans and other species. It belongs to a group of steroid hormones called the progestogen (King and Brucker, 2010) and is the major progestogen in the body. Progesterone has a variety of important functions in the body. It is also a crucial metabolic intermediate in the production of other endogenous steroids including the sex hormones and the corticosteroids it plays an important role in brain function as a neurosteroid (Baulieu and Schumacher, 2000).

Progesterone is also produced, to a lesser extent, in the adrenal glands during pregnancy and the placenta. Thus, cyclical hormone exposure beginning of menstruation and ending in menopause occurs monthly and regulates the growth and differentiation of specialized tissues within the reproductive tract and breast tissues (Graham and Clarke, 1997).



Structure of Progesterone

1.3.2.1.1. Biosynthesis of Progesterone

Progesterone synthesis requires the activity of two major enzymes: P450 side chain cleaving enzyme (P450scc) and 3 β -hydroxysteroid dehydrogenase (3 β -HSD). P450scc is found in all steroid genic tissues, including the brain. It is encoded by a single gene in both human and rat genomes (Lonsdale and Burnham, 2007). 3 β -HSD, however, has at least two human and four rat isoforms (Compagnone and Mellon, 2000). In rats, 3 β -HSD types I, II, and IV

are reported to be expressed in the brain with type I being predominant (Sanne and Krueger, 1995). In humans, it is still unclear which isoform is the predominant form in the brain (Yu *et al.*, 2002).

Figure (1-3) shows the two-step synthetic pathway for the production of progesterone from cholesterol. This takes place in the inner mitochondria membrane and in the smooth endoplasmic reticulum (sER) (Kacsoh, 2000). The first step of pregnenolone synthesis of cholesterol is the rate-limiting step. This step requires the activity of P450_{scc}, which sits in the inner mitochondrial membrane with its active site facing the mitochondrial matrix (Kacsoh, 2000). Cholesterol is very hydrophobic and must be transported from the cytoplasm to the matrix side of the inner mitochondrial membrane.

The transmembrane protein called the "peripheral benzodiazepine receptor (PBR)" facilitates this process by allowing cholesterol passage through the inner mitochondrial membrane to the active site of P450_{scc}. Once there, the P450_{scc} protein mediates three chemical reactions: 20 α -hydroxylation, 22-hydroxylation and cleaving of the C20-C22 carbon bond, to produce pregnenolone (Mellon and Griffin, 2002). The second step enzyme 3 β -HSD converts pregnenolone to progesterone through oxidation and isomerization (Compagnone and Mellon, 2000).

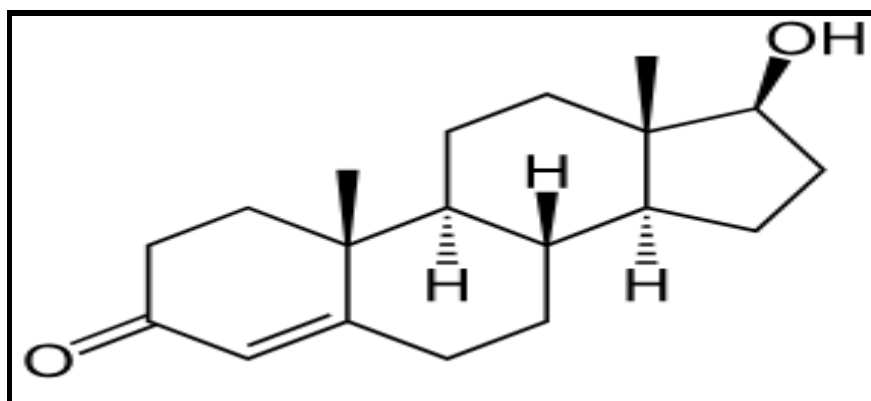
1.3.2.2. Testosterone

Testosterone is a steroidal hormone from the androgen group and is found in mammals, reptiles (Cox and John-Alder, 2005) and birds (Reed *et al.*, 2006). Testosterone production begins in the Leydig cells located in the testes of men. It is also produced, to a smaller degree, in the ovaries and the adrenal cortex in women. The central nervous system stimulates the hypothalamus to begin testosterone production which suggests a strong link between the nervous and endocrine systems (Vingren *et al.*, 2010).

It has become apparent that testosterone plays a significant role in the maintenance of bone and muscle mass, in erythropoiesis, and in mental

function. In addition, testosterone is also playing a key role in glucose homeostasis and lipid metabolism (Saad and Gooren, 2011).

In the circulation, testosterone is bound with high affinity to sex hormone-binding globulin (SHBG) and weakly to albumin with a small fraction of unbound or free testosterone (Kaufman and Vermeulen, 2005).



Structure of Testosterone

1.3.2.2.1. Biosynthesis of Testosterone

The steroid biosynthetic pathway is given in figure (1-3). Testosterone consists of (19) carbon atoms with (OH) group on 17th carbon atom (Ganong, 2005). Like other steroid hormones, testosterone is derived from cholesterol which is transferred by steroidogenic acute regulatory protein (StAR) from the outer to inner mitochondrial membrane where P450_{scc} is located (Stocco, 2007).

The mechanism of cleavage of cholesterol by cholesterol side chain cleavage enzyme (CYP11A) involves two hydroxylation steps: first on C22 and then on C20 to yield 20, 22R-dihydroxy cholesterol that is then cleaved to yield the pregnenolone and the 6-carbon isocaproic aldehyde which is then oxidized to isocaproic acid. The synthesized pregnenolone is then transferred to the smooth endoplasmic reticulum where it is a precursor for further steroid synthesis (Detlef and Peter, 2010).

The formation of testosterone from pregnenolone is via two main pathways. The first route is via a series of intermediates, each with a double bond between

C-5 and C-6 and a 3β -hydroxy group. This is commonly referred to as the Δ^5 pathway (Δ is the Greek symbol for capital delta and together with a superscripted Δ number denote the presence of the double bond in the steroid structure). The second is via a series of intermediates with a double bond between C-4 and C-5 and 3-oxogroup, this is called the Δ^4 pathways. Vitro experiments on human testicular tissue indicate that both Δ^4 and Δ^5 pathway are important, but the latter pathway is the major one for synthesis of testosterone in human (Detlef and Peter, 2010).

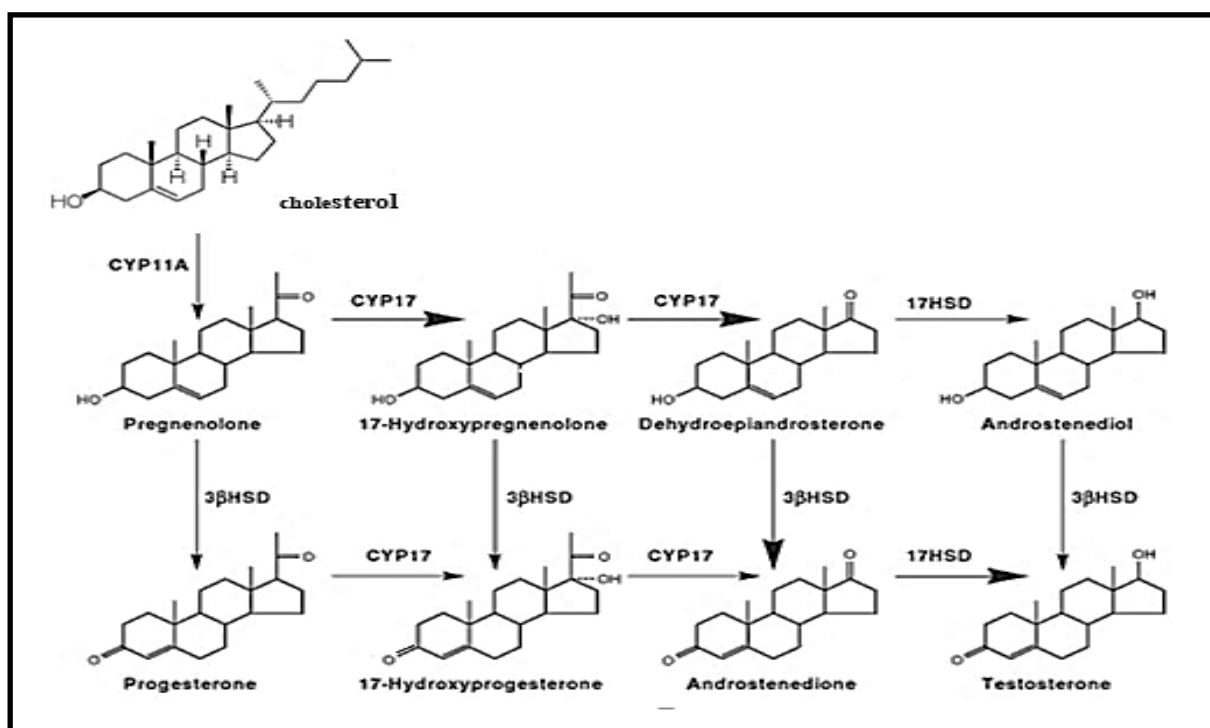


Figure (1-3): The Steroid Biochemical Anabolism Pathway from Cholesterol (Ganong, 2005).

1.4. Oxidative Stress

Oxidative stress is defined as a disorder in the equilibrium between free radicals (FR_s), reactive oxygen species (ROS), and endogenous antioxidant defense mechanisms (Tandon, 2005). More simply, it is a disturbance in the equilibrium between oxidant-antioxidant states, favoring the oxidizing environment (Chandra *et al.*, 2000).

ROS and RNS are generated from either endogenous or exogenous sources. Endogenous free radicals are generated from immune cell activation, inflammation, mental stress, excessive exercise, ischemia, infection, cancer and aging (Pham-Huy *et al.*, 2008).

ROS are involved in physiological functions in female reproduction, such as being oocyte maturation, ovarian steroid genesis, ovulation, implantation, and formation of the fluid filled cavity, blastocyst, autolysis and luteal maintenance in pregnancy. ROS act as mediators of various signalling pathways. Elevated or sustained generation of free radicals leads to imbalance in the intracellular redox homeostasis. Excess levels of free radicals and ROS can be neutralized by antioxidants (Khansaa *et al.*, 2017).

1.5. Lipid Peroxidation (LPO)

Lipid peroxidation (LPO) is the chain reaction initiated by the attack of reactive oxygen species (ROS) and reactive nitrogen species (RNS) on polyunsaturated fatty acid (PUFA) residues of phospholipids, leading to cell membrane damage and consequently to cell death (Domijan *et al.*, 2015).

The overall process of lipid peroxidation consists of three steps: initiation, propagation, and termination as shown in figure (1-4).

Step1. In Initiation, pro oxidants like hydroxyl radical abstract the allylic hydrogen forming the carbon-centered lipid radical ($L\cdot$).

Step2. In the propagation phase, ($L\cdot$) rapidly reacts with oxygen to form a lipid peroxy radical ($LOO\cdot$) which abstracts a hydrogen from another lipid molecule generating a new $L\cdot$ (that continues the chain reaction) and lipid hydro peroxide ($LOOH$).

Step3. In the termination reaction, antioxidants like vitamin E donate a hydrogen atom to the $LOO\cdot$ species and form a corresponding vitamin E radical that reacts with another $LOO\cdot$ forming non radical products.

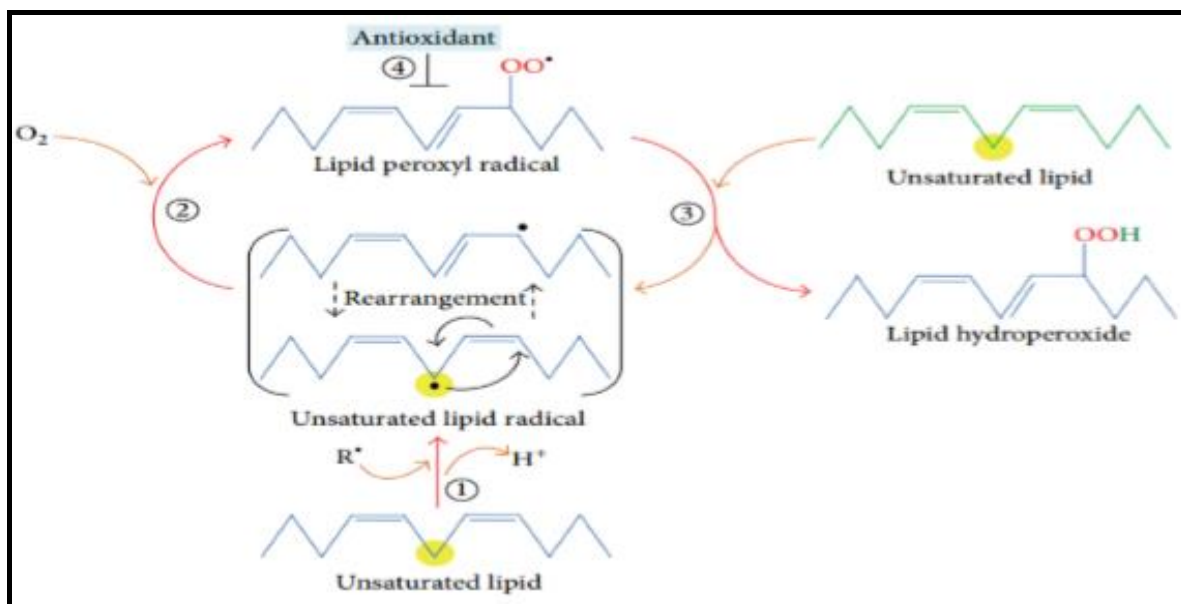


Figure (1-4): Lipid peroxidation process (Antonio *et al.*, 2014).

The primary products of the LPO are unstable hydro peroxides that decompose to various secondary products, among which are stable aldehydes, malondialdehyde (MDA) and 4-hydroxy-2-nonenal (4-HNE) acrolein (Domijan *et al.*, 2015).

The most important reactive aldehydes originated from lipid peroxidation are including malondialdehyde (MDA) and glyoxal. MDA is in many instances the most abundant individual aldehyde resulting from lipid peroxidation. It has been shown to disturb amino phospholipid organization in the membrane bilayer of erythrocytes (Thandavarayan *et al.*, 2011). Malondialdehyde is able to impair several physiological mechanisms of the human body through its ability to react with molecules such as DNA and proteins. It is therefore useful to consider this molecule as something more than a lipid peroxidation product (Del Rio *et al.*, 2013). MDA is used as a biomarker to measure the level of oxidative stress in an organism (Del Rio *et al.*, 2013).

1.6. Antioxidants System

Antioxidant molecule can prevent the oxidation of other molecule (Bjelakovic *et al.*, 2013). Oxidation reaction can produce free radicals which cause cellular damage, antioxidants which terminate this chain reaction by

removing the free radical species and inhibit other oxidation reactions by oxidizing themselves (La Monte *et al.*, 2000).

The classification of antioxidants includes endogenous antioxidants and exogenous antioxidant (Jeppsson *et al.*, 2007).

Endogenous antioxidants include Bilirubin, thiols such as glutathione, lipoic acid, N-acetyl cysteine, NADPH and NADH, ubiquinone (coenzyme Q 10), uric acid. Enzyme:- Iron-dependent catalase, selenium-dependent glutathione peroxidase, copper/zinc and manganese dependent superoxide dismutase (SOD) and metal binding proteins such transferrin (iron), ferritin (iron), myoglobin (iron), ceruloplasmin (copper) and albumin (copper). Exogenous antioxidants such as beta carotene and other carotenoids and oxycarotenoids, vitamin C, vitamin E, lipoic acid and polyphenols, such as flavonoids (Cruz *et al.*, 2015).

1.6.1. Ceruloplasmin (CP)

Ceruloplasmin (Cp) is one of the main proteins taking part in copper metabolism by distributing it in the human body. It is responsible for carrying about (65-90%) of copper in blood stream (Adamczyk-sowa *et al.*, 2016).

CP is a copper-containing alpha₂-glycoprotein with a molecular weight of approximately 151 KDa. CP is essential for iron homeostasis is involved in angiogenesis and under different conditions can act as either a pro- or anti-oxidant (Yalcin *et al.*, 2012).

The oxidase activity increases during inflammation, infection and injury which suggests that serum Cp possibly acts as an antioxidant and as an acute phase protein (Fleming *et al.*, 1991). It is implied that during exposure to oxidative stress, substantial inactivation of Cp may occur and free copper ion may be released (Choi *et al.*, 2000). Therefore, the damaged Cp may cause the augmentation of free radical-mediated damage to other macromolecules upon exposure to oxidative stress, thus, Cp is a very important component of the cellular defense mechanism against toxicity (Kang, 2006).

1.6.2. Transferrin (Tf)

Transferrin a glycosylated Fe^{3+} binding protein which is found in blood plasma, lymph, and other body fluids . It is synthesized in the liver, central nervous system, testes, ovaries, spleen, mammary glands and kidneys.

Tf has primary function the transportation of Iron to all cells. Another function of Tf is to keep free Iron at a very low concentration, approximately 10^{-18} M, avoiding the high potential risk of damage and depriving pathogens of Iron which they require for growth (Reyes-López *et al.*, 2015). Free iron is capable of stimulating produced of free radicals which cause oxidative damage such as lipid peroxidation (Ahmed *et al.*, 2012).

1.7. Lipids and Lipoproteins

1.7.1. Lipids

Lipids are a diverse and ubiquitous group of compounds which have many main biochemical functions such as acting as structural components of cell membranes and serving as energy storage sources (Fahy *et al.*, 2011). Plasma lipids consist of triacylglycerol (triglycerides) 16%, cholesterol 14%, phospholipids 30%, cholesterol esters 36% and a much smaller fraction of unesterified long-chain fatty acids or free fatty acids 4% (Murray *et al.*, 2003; Princy *et al.*, 2013).

1.7.1.1. Cholesterol

Cholesterol is a steroid commonly found in nature with a great relevance in biology, medicine and chemistry. It plays an essential role as a structural component of animal cell membranes. It is the precursor for the synthesis of many physiologically important steroids such as bile acids and steroid hormones (García *et al.*, 2012). Although a portion of the body's cholesterol is derived from dietary intake, most of it is synthesized by the liver and other tissues from simpler molecules, almost 90% of synthesis occur in the liver and gut; therefore,

peripheral cells and other organs depend largely on cholesterol delivery from the circulation (Burtis *et al.*, 1999).

1.7.1.2. Triglyceride (TG)

Triglycerides are fatty acid esters of glycerol, each containing three different fatty acids (Mayne, 2002). They are derived from three primary sources: the diet, storage depots in adipocytes and biosynthesis particularly in the liver (Mathews *et al.*, 2000). Triglyceride are hydrolysed into the glycerol and fatty acids, and after absorption, triglyceride is synthesized in the epithelial cells (Burtis and Ashwood, 1996).

1.7.2. Lipoproteins

Lipoprotein particles vary differed in composition, size, density and function (Ginsberg, 2002), Although different types of lipoprotein particles circulate in the plasma. The lipoproteins present in plasma are: chylomicrons (CM), very-low-density lipoproteins (VLDL), Intermediate density lipoprotein (IDL), low-density lipoproteins (LDL) and high-density lipoproteins (HDL) (Jonas, 2002).

1.7.2.1. Chylomicrons

It is produced in the intestinal epithelial cells from dietary fat. Then the chief carrier of exogenous triacylglycerol in the blood and appears in origin in electrophoretic field, LDL is the richest in cholesterol. When endothelial cells engulf LDL, they oxidized it to a product called oxidized LDL (Plenz and Robenek, 1998).

1.7.2.2. Very Low Density Lipoprotein (VLDL)

VLDL is made in the liver by the combination of cholesterol, triglycerides and apo protein. VLDL transports endogenous triglycerides, phospholipids, cholesterol and cholesteryl esters. It functions as the body's internal transport mechanism for lipids. VLDL levels have been correlated with accelerated rates of atherosclerosis and are elevated in a number of diseases and metabolic states.

These lipoprotein particles are smaller than chylomicrons and containless triglyceride but contain significant amounts of cholesterol (10-15% of cholesterol). As the VLDL circulates in the blood, triglycerides are deposited and the particles get smaller, eventually becoming low density lipoproteins (LDL). Serum with large masses of VLDL will be cloudy (Niu and Evans, 2011).

1.7.2.3. Intermediate Density Lipoprotein (IDL)

Small amounts of IDL are produced by the liver. The effect of lipoprotein lipase (LPL) is to hydrolyse triacylglycerol, thus reducing the size of VLDL and increasing the percentage of denser molecules (i.e., it degrades VLDL to IDL). After hydrolysis, the fatty acids are taken up by nearby cells or by serum albumin for transport to more peripheral cells. A similar process leads from IDL to LDL (August *et al.*, 2007).

1.7.2.4. Low Density Lipoprotein (LDL)

LDL is often called bad cholesterol. It is produced in the blood (remnant of IDL after triacylglycerol digestion; the end product of VLDL), it represents the primary carriers of cholesterol in the blood for delivery to all peripheral tissues and endocytosis by the liver and peripheral tissues. It contains high concentrations of cholesterol and cholesterol esters then migrate into β -globulin region (Segrest *et al.*, 2001).

1.7.2.5. High Density Lipoprotein (HDL)

HDL is often called good cholesterol. They remove excess cholesterol from tissues and vessel walls and carry it to the liver where it is removed from blood and discarded. The amount of serum HDL is inversely correlated with the incidence of cardiovascular diseases, the higher level the lower risk of atherosclerosis and vice versa. HDL carries cholesterol in the blood from other parts of the body back to the liver for excretion. So HDL helps keep cholesterol from building up in the walls of the arteries (Bandeali and Farmer, 2012).

Aim of Study

This study is designed to showed light on the following biochemical states according to two phase of phases the menstrual cycle (follicular and luteal phase) in bronchial asthma patients:

1. Assessment of serum steroidal hormones (Testosterone and Progesterone).
2. The possible disorders in serum oxidant-antioxidant balance.
3. The possible disorders in the serum lipid profile.
4. The effect of age and phases of the menstrual cycle on the mentioned above states.

2. Materials and Methods

2.1. Design of Study:

This study is conducted at AL-Hussein Teaching Hospital in Thi-Qar, especially, in respiratory counseling, Biochemistry Laboratory in the College of Science (University of Thi-Qar) at the period between 1/9/2017 to 1/6/2018.

The present study was started with (140) cases (patients and healthy) women ranging in age from (14-45) years. It is notable that the smokers women were excluded.

The controls and patients are divided into two groups:

1- Control group: includes (70) supposed healthy volunteers of women without taking contraceptive pills aged (14-45 years).

2- Patient group: includes (70) patients of women with bronchial asthma attending the private clinic or department of pulmonary in AL-Hussein Teachings Hospital without taking contraceptive pills aged (14-45 years).

The major groups are divided into subgroups according to age and menstrual phases as shown in Table (2-2).

Table (2-1): Data Patients and Controls by Age and Menstrual Phases.

Female		N	
<i>menstrual phases</i>	Age	Control	Patient
follicular phase	14-29	35	35
luteal phase	14-29	35	35
follicular phase	30-45	35	35
luteal phase	30-45	35	35

- ❖ Follicular phase of the menstrual cycle (days 12-16). (Balzano, 2001)
- ❖ Luteal phase of the menstrual cycle (days 24-28). (Balzano, 2001)

2.2. Collection of Blood Samples:

About 8mL of blood samples were taken from peripheral venous of women with bronchial asthma and controls on two phases.

The first sample was taken from the women in the follicular phase and the second sample was taken from the same women in the luteal phase. This applies to all patients and controls and allow samples to clot at room temperature in disposable tubes centrifuge to separate it in the centrifuge at 3000 rotor per minute (rpm) for 10 min. Serum samples are separated and stored at (-20°C) for later measurement both biochemical parameters, unless used immediately.

The clinical chart of this study describes experimental parameters in the following Table (2-3).

Table (2-2): The Clinical Chart of the Study

Patient Profile			
Name:			
Age:-			
Sex:-			
Occupation:-			
Cycle day:-			
Cycle length:-			
Residence	a: rural	b: city	
Habits:	a: smoking	b: alcohol	(duration)
Drugs:-			
Other diseases:-			
Marital status:-			
Biochemical Tests			
Hormones:-	Progesterone (PRG)		

	Testosterone (TEST)
Lipid peroxidation:-	Serum Malondialdehyde (MDA)
Anti-oxidants:-	Serum Ceruloplasmin (CP)
	Serum Transferrin (Tf)
Lipid profile:-	(TC, TG, HDL-c, LDL-c, VLDL-c)

2.3. Chemicals:

The chemicals used in this study with their companies are shown with suppliers in Table (2-4).

Table (2-3): Chemicals and their Suppliers

Chemicals	Suppliers
Cholesterol Kit	Biolabo, France
Glacial acetic acid	BDH, England
HDL Kit	Biolabo, France
Iron Kit	Biolabo, France
Para pheneline di amine (PPD)	BDH, England
Progesterone Hormones kit	Biomerieux, France
Sodium acetate	BDH, England
Sodium azide	Reidledchain, Germany
Testosterone hormones kit	Biomerieux, France
Thio bar bituric acid (TBA)	BDH, England
Total Iron Binding Capacity (TIBC)Kit	Biolabo, France
Tri chloro acetic acid (TCA)	BDH, England
Triglyceride Kit	Biolabo, France

2.4. Instruments:

The instruments are available in a clinical biochemistry laboratory in AL-Hussein Teaching Hospital Thi-Qar and in the laboratories of the chemistry department in the college of science (University of Thi-Qar) as shown in Table (2-5).

Table (2-4): Instruments and their Manufacturers

Instruments	Manufacturers
Centrifuge	Universal 16A, Germany
Incubator	Jard, Japan
Mini Vidas	Biomerieux, France
Sensitive balance	MO.12307078, Japan
Shacking water bath	SW23, Germany
UV/VIS spectrophotometer	T 60, PG Instruments Ltd, Germany
UV/VIS spectrophotometer	UV-7804C, Japan
Water bath	L513-0814 , French

2.5. Biochemical Parameters:

Several considerable methods are used to measure the studied parameters. It is notable that all measurements are duplicated for each sample.

2.5.1. Determination of Serum Progesterone (PRG) Hormone:

(Brugger *et al.*, 2011)

Principle:

The assay principle combines an enzyme immunoassay competition method with final fluorescent detection. The solid phase receptacle (SPR) serves as the solid phase as well as the pipetting device for the assay. The progesterone in the sample binds with the specific monoclonal antibody coating the interior of SPR. Unbound components are eliminated during the washing stages. The

conjugate is then cycled into the solid phase receptacle. The remaining free antibody sites are saturated by the conjugate. The progesterone retained is detected by the conjugate which is an alkaline phosphatase (ALP) labeled progesterone derivative. Unbound conjugate is removed by washing.

In the final step, ALP hydrolyses the substrate, 4-methylumbelliferyl phosphate, into a fluorescent product (4-methyl-umbelliferone) and the fluorescence is measured at 450 nm. The intensity of the fluorescence signal is inversely proportional to the concentration of progesterone present in the sample.

Procedure:

1. Only remove the required reagents from the refrigerator and allow them to come to room temperature for at least 30 minutes.
2. Use one "**PRG**" strip and one "**PRG**" SPR for each sample, control or calibrator to be tested. Make sure the storage pouch has been carefully resealed after the required SPRs have been removed.
3. The test is identified by the "**PRG**" code for the instrument. The calibrator must be identified by "**S1**", and tested in triplicate. If the control is to be tested, it should be identified by "**C1**".
4. Mix the calibrator, control and samples using a vortex type mixer (for serum or plasma separated from the pellet).
5. Before pipetting, ensure that samples, calibrator and control are free of bubbles.
6. For this test, the calibrator, control, and sample test portion are 200 μ L.
7. Insert the "**PRG**" SPRs and "**PRG**" strips into the instrument. Check to make sure the color labels with the assay code on the SPRs and the reagent strips match.
8. Initiate the assay as directed in the user's manual. All the assay steps are performed automatically by the instrument.

9. Reclose the vials and return them to the required temperature after pipetting.
10. The assay will be completed within approximately 45 minutes. After the assay is completed, remove the SPRs and strips from the instrument.
11. Dispose of the used SPRs and strips into an appropriate recipient.

2.5.2. Determination of Serum Testosterone (TES) Hormone:

(Yun *et al.*, 2012)

Principle:

The assay principle combines an enzyme immunoassay competition method with a final fluorescence detection (ELFA). The solid phase receptacle (SPR) serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assay steps are performed automatically by the instrument. The reaction medium is cycled in and out of the SPR several times. The sample is added to the pre-treatment solution to separate the testosterone from carrier proteins. The pre-treated sample is transferred into the well containing an alkaline phosphatase-labeled testosterone antibody (conjugate). The antigen in the sample and the testosterone antigen bound to the interior wall of the SPR compete for the anti-testosterone-specific antibody sites. Unbound components are eliminated during the washing steps.

During the final detection step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone). The fluorescence of which is measured at 450 nm. The intensity of the fluorescence is inversely proportional to the concentration of testosterone present in the sample. At the end of the assay, the results are automatically calculated by the instrument in relation to the calibration curve stored in memory, and then printed out.

Procedure:

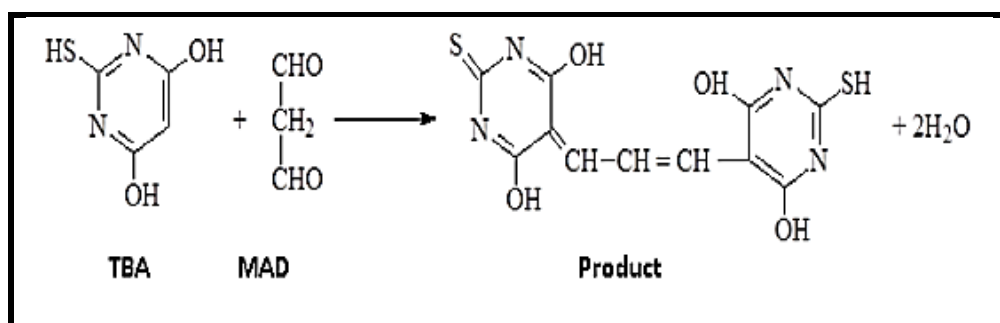
1. The required reagents remove from the refrigerator. They can be used immediately.
2. We use one "TES" strip and one "TES" SRP for each sample, control or calibrator to be tested. Make sure the storage pouch has been carefully resealed after the required SRPs have been removed.
3. The test is identified by the "TES" code for the instrument. The calibrator must be identified by "S1" and tested in duplicate. If the control needs to be tested, it should be identified by C1.
4. Mix the calibrator and/or the control and the samples using a vortex-type mixer (for serum or plasma separated from the pellet).
5. Before pipetting, ensure that samples, calibrator and control are free of bubbles.
6. For this test, the calibrator, control and sample test portion are 100 µL.
7. Insert the "TES" SPRs and "TES" strips into the instrument. Check to make sure the color labels with the assay code on the SPRs and the reagent strips match.
8. Initiate the assay as directed in the user's manual. All the assay steps are performed automatically by the instrument.
9. Reclose the vials and return them to the required temperature after pipetting.
10. The assay will be completed within approximately 40 minutes. After the assay is completed, remove the SPRs and strips from the instrument.
11. Dispose of the used SRPs and strips into an appropriate recipient.

2.5.3. Determination of Oxidative Stress Parameters:

2.5.3.1. Determination of Serum Malondialdehyde Concentration:

Principle:

Malondialdehyde (MDA) is an end-product formed during lipid peroxidation, due to degradation of cellular membrane phospholipids. MDA is released into extracellular space and finally into the blood. It has been used as an effective biomarker of lipid oxidation (Lorente *et al.*, 2015). MDA formed from the breakdown of polyunsaturated fatty acids are identified as the product of LPO that react with thiobarbituric acid (TBA), in coexisting trichloro acetic acid (TCA), to give a red chromophore absorbing at 532 nm (Fong *et al.*, 1973). MDA concentration is calculated, using the molar extinction coefficient of MDA (ϵ_{MDA}) equal to $1.56 \times 10^5 \text{ mol}^{-1} \cdot \text{cm}^{-1}$ (Wills, 1969). MDA is formed from the breakdown of polyunsaturated fatty acid, serves as a convenient index of peroxidation reaction.



Procedure:

The level of serum MDA is determined spectrophotometrically with a thiobarbituric acid (TBA) solution. In brief, to 150 μ L serum sample, the following is added: 1mL (17.5%) trichloroacetic acid (TCA) and 1ml of 0.66 % TBA, mixed, incubated in boiling water for 15 minutes, and then allowed to cool. 1 mL of 70 % TCA is added and the mixture allowed to stand at room temperature for 20 minutes, centrifuged at 2000 rpm for 15 minutes, the supernatant is taken out for scanning spectrophotometrically at (532nm) (Muslih *et al.*, 2002).

Calculation:

The concentration of MDA calculated as follows:-

$$MDA \left(\frac{\mu\text{mol}}{L} \right) = \frac{\text{absorbance at } 532\text{nm}}{L \times E_0} \times D \times 10^6$$

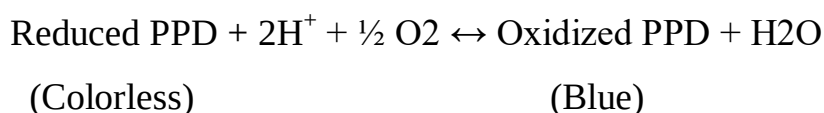
L: light path (1cm)

E_0 : Extinction coefficient $1.56 \times 10^5 \text{ M}^{-1} \cdot \text{cm}^{-1}$

D: Dilution factor = 1 mL Vol. Used in ref./0.15 = 6.7

2.5.3.2. Determination of Antioxidant Parameters:**2.5.3.2.1. Determination of Serum Ceruloplasmin Concentration:****Principle:**

Plasma Cp concentration is measured by the method of (Menden *et al.*, 1977). It is based on the Cp-catalyzed oxidation of color less para-phenylene diamine (PPD) to blue-violet oxidize form. The reaction is followed photometrically and the blank value is determined after inhibition of the enzyme with sodium azide at (0C°).



A mixture of serum, substrate and acetate buffer at pH = 6.0 is incubated at 37C° for 15 min. The reaction is stopped by the addition of sodium azide and the absorbance of the purple color formed (Oxidized PPD) in the diluted test mixture is read at 525 nm against the blank solution. The corrected absorbance is directly related to the concentration of Cp (Ravin, 1961).

Reagents:

- **Substrate solution:**

50 mg of PPD is dissolved in 5 mL (4 mL of distilled water (D.W) and 1mL of glacial acetic acid). In another container, 8.15gm sodium acetate tri hydrate is dissolved in 30 mL of D.W, then added to the first solution, mixed and

completed the volume to 50 mL with D.W. This solution is stable for three hours and it is kept refrigerated in a dark bottle (Menden *et al.*, 1977).

● **Inactivating solution:**

100 mg of sodium azide is dissolved in (500 mL) of D.W. Then it is kept cold in refrigerator prior to use. This solution must be prepared every week.

Procedure:

- 1 mL of substrate is pipetted into test tubes, incubated at 37 C° for 1 min.
- 0.1 mL of plasma is added, incubated at 37 C° for 15 min, then the tubes are removed and placed in the iced-bath for 30 min .
- 5 mL of cold inactivating solution is added, mixed and the temperature is brought to 25 C° in water bath.
- Blank is prepared by combining the substrate, inactivating solution, and 0.1mL of D.W, then the mixture is incubated as above.
- The absorbance of the test and blank is read in spectrophotometer at 525nm.
- The concentration of Cp is calculated using the extinction coefficient of Cp (ϵ_{Cp}) equal to (0.68).

$$\text{Serum Cp (g/L)} = \frac{A_{\text{test}} - A_{\text{blank}}}{\epsilon_{Cp}} \times 10 = \frac{\Delta A \times 10}{0.68}$$

2.5.3.2.2. Determination of Serum Transferrin Concentration:

2.5.3.2.2.1. Total Iron Binding Capacity (TIBC): (Burtis and Ashood, 1999)

Principle:

T.I.B.C. is determined by the addition of sufficient Fe^{3+} to saturate iron binding sites on apo transferrin. The excess Fe^{3+} were removed by adsorption with basic magnesium carbonate powder.

After centrifugation, bound iron remaining in the supernatant is measured by direct method (Ferene) or with deproteinization method.

Reagents:

Contents	Concentrations of Solutions
R1: Iron solution	Hydrochloric acid 5mmol/L.
	Ferric chloride $\geq 502 \mu\text{g/dL}$ ($\geq 90 \mu\text{mol/L}$).
R2: Precipitant	Magnesium carbonate 150 mg/capsule.

Manual Procedure

Stand reagents and specimens are let at room temperature.

The following components were pipetted in centrifuge tube	
Specimen	1mL
Iron solution (vialR1)	2mL
Mix , wait 10 minutes then add:	
Precipitant (capsule R2)	150mg (The contents of a capsule)
Mixed well by inversion. Allowed to stand at room temperature for 30 min. shaking on a rotary or swinging agitator. Centrifuge 10 min at 3000rpm	

Calculation:

1- The result is calculated as in the reagent technical data sheet used for iron determination.

2- TIBC is calculated as follows:

TIBC = Iron concentration measured in supernatant x3

(dilution 1mL specimen /2mL iron solution).

Unit conversion factor: $\mu\text{mol/L} = \mu\text{g/dL} \times 0.1792$

Calculate Transferrin Concentrations: (Vernet, 1993; Gambino *et al.*, 1997).

$$\text{Tf (g/L)} = \text{TIBC } (\mu\text{mol/L}) / 25.1$$

2.5.3.2.2.2. Iron: (Hennessy *et al.*, 1984)

Principle:

After dissociation of iron-transferrin is bound in acid medium, ascorbic acid reduces Fe^{3+} iron into Fe^{2+} iron. Fe^{2+} iron is then form a coloured complex with 3-(2-pyridyl) -5,-6 difuryl-1, -2,-4triazine-disulfonate (Ferene). The absorbance thus is measured at 600nm (580-620). It is directly proportional to the amount of iron in the specimen. There is added in the reagent to prevent the copper interference.

Reagents Composition:

Reagent	Composition
R1: Reductant	Citric acid 150 mmol/L Ascorbic acid 30mmol/L Thiourea 27mmol/ L
R2: Chromogen	Ferene 600 $\mu\text{mol/L}$
R3: Standard	Iron 200 $\mu\text{g/dL}$ (35.8 $\mu\text{mol/L}$)

Reagents Preparation:

Stand reagents and specimens are left at room temperature. Prepare 2 sets of tubes according to following boards:

Blank – Tubes	Blank	Standard	Assay
Reagent R1	1mL	1mL	1mL
Specimen	...	...	200 μL
Standard	...	200 μL	...

Distilled water	200µL	...	...
Mixed gently. Let stand for at least 3 mins at room temperature. Recorded A1 absorbances at 600 nm (580-620) against blank.			

Assay – Tubes	Blank	Standard	Assay
Working Reagent	1mL	1mL	1mL
Specimen	...	...	200µL
Standard	...	200µL	...
Distilled water	200µL	...	...
Mixed gently. Let stand for 5 mins at room temperature. Recorded A2 absorbances at 600 nm (580-620) against blank. Colour is stable for 1 hour.			

Calculation:

Calculate the result as follows:

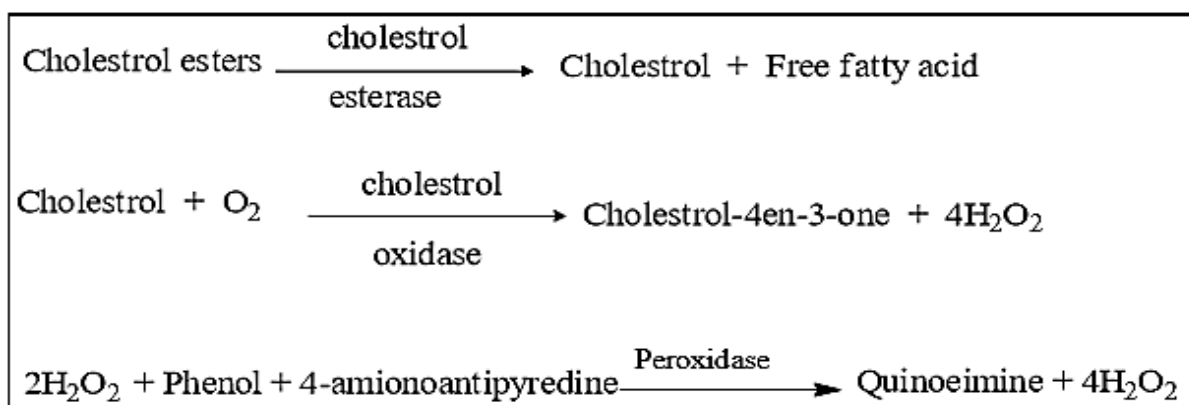
$$\text{Serum Iron conc.}(\mu\text{mol/L}) = \frac{(\text{A2}-\text{A1}) \text{ Assay}}{(\text{A2}-\text{A1}) \text{ Standard}} \times \text{Conc.of standard (35.80)}$$

2.5.4. Determination of Serum Lipid Profile:**2.5.4.1. Determination of Serum Total Cholesterol Concentration:**

(Naito and Kaplan, 1984)

Principle:

The cholesterol present in the sample originates a colored complex, according to the following reaction:



The intensity of the color formed is proportional to the cholesterol concentration in the sample.

Reagents:

R1:Buffer	Phosphate buffer	100 mmol /L
	Chloro-4-phenol	5 mmol/L
	Sodium Cholate	2.3 mmol/L
	Triton *100	1.5 mmol /L
R2:Enzymes	Cholesterol 36 eroxid (CO)	≥100IU/L
	Cholesterol esterase (CE)	≥170IU/L
	36 eroxidase (POD)	≥1200IU/L
	4-Amino-antipyrine (PAP)	0.25 mmol/L
	PFG 6000	167 μmol/L
R3: Standard	Cholesterol 200 mg/dL (5.17mmol/L)	

Preparation:

Working reagent : The contents are dissolved (→) of one vial R2 enzymes in one bottle of R1 buffer.

The contents are caped and mixed gently.

Procedure:

	Blank	Standard	Sample
Working reagent	1 mL	1 mL	1 mL
D.W	10 µL	...	...
Standard	...	10 µL	...
Specimen	...	...	10 µL

1. Mixed and incubated for 5 minutes at 37°C or 10 minutes at room temperature.
2. The absorbance (A) of the samples and standard, are read against the blank at wavelength 500 nm.

Calculation:

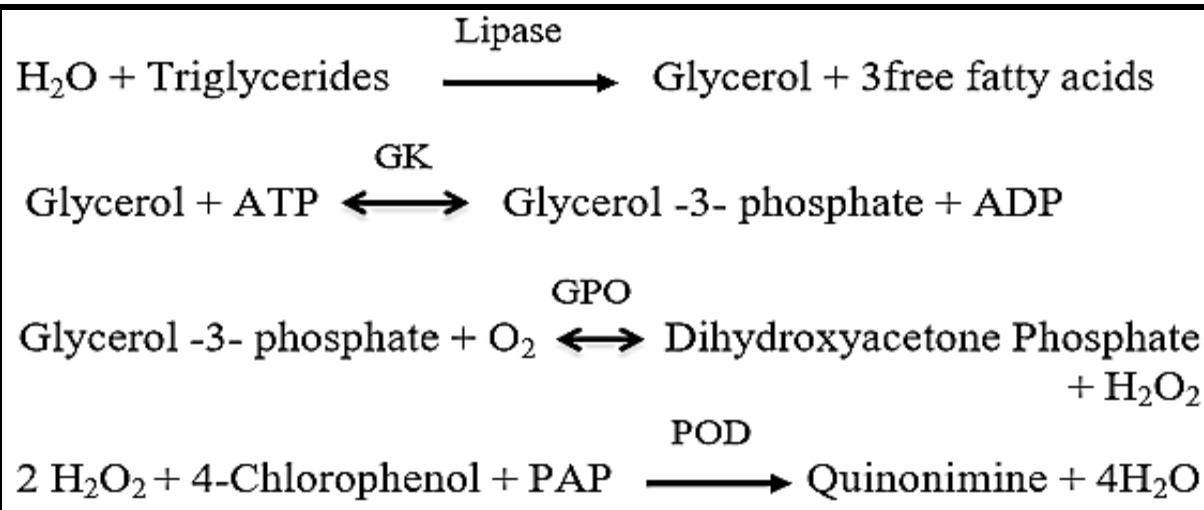
$$\text{Conce of TC (mmol/L)} = \frac{\text{Abs (Assay)}}{\text{Abs (standard)}} \times 5.17(\text{Standard Concentration})$$

2.5.4.2. Determination of Serum Triglyceride Concentration:

The used reagents are supplied via Biolabo (France), and Serum TG is measured according to (Tietz, 1999).

Principle: (Fossati and Prencipe, 1982).

Fossati and Principe method is associated with Trinder reaction.
Reaction scheme is as follows:

**Reagents composition:**

Reagent	Composition
R1: Buffer	Pipes 100 mmol/L
	Magnesium chloride 9.8 mmol/L
	Chloro-4-phrnol 3.5 mmol/L
R2: Enzymes	Lipase ≥ 1000 IU/L
	Peroxidase (POD) ≥ 1700 IU/L,
	Glycerol-3-phosphate oxidase (GPO) ≥ 3000 IU/L
	Glycerol kinase (GK) ≥ 660 IU/L
	4-aminoantipyrine (PAP) 0.5 mmol/L
R3: Standard	ATP 1.3 mmol/L
	2.28 mmol/L (200mg/dL)

Manual procedure:

- 1- R1 + R2 = Reagent
- 2- Reagent and sample are left stand at room temperature.

	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
Dematerialized water	10 µL	...	...
Standard	...	10 µL	...
Specimen	...	...	10 µL

Mixed. Let stand for 5 minutes at 37°C or 10 minutes at room temperature. Absorbance are recorded at 500 nm against the reagent blank.

Calculation:

The result is calculated as follows:

$$\text{Conce of TG (mmol/L)} = \frac{\text{Abs (Assay)}}{\text{Abs (standard)}} \times 2.28 (\text{Standard Concentration})$$

2.5.4.3. Determination of Serum HDL-c Concentration:

Principle:

Chylomicrons (CM), very low density lipoproteins (VLDL) and low density lipoproteins (LDL) contained in the specimen are precipitated by the addition of phosphotungstic acid in the presence of magnesium ions (Lopes-Virella *et al.*, 1977). The supernatant obtained after centrifugation contains high density lipoproteins (HDL). The cholesterol bound to the HDL is determined using the cholesterol RTU reagent.

Reagents composition:

R1: precipitant	Phosphotungstic acid (PTA) 1.39 mmol/L Magnesium chloride 570 mmol/L
R2: Standard	Cholesterol 100mg/dL (2.58 mmol/L)

Procedure:

- 1- Add 500 µL (0.5mL) from serum.
- 2- Add 50 µL from Precipitant.
- 3-Mixed. Wait 10 minutes in room temperature.
- 4- Centrifuge for 15 minutes at 3500 – 4000 rpm

After centrifugation, the supernatant must be clear. Where the leachate is formed is Supernatant.

	Blank	Standard	Assay
Reagent (From Cholesterol)	1 mL	1 mL	1 mL
D.W	25 µL	...	...
Standard	...	25 µL	...
Supernatant (HDL)	...	...	25 µL
Mixed. Incubated for 5 mins at 37°C or 10 mins at room temperature Record absorbance at 500 nm against reagent blank.			

Calculation:

$$\text{Conce of HDL (mmol/L)} = \frac{\text{Abs (Assay)}}{\text{Abs (standard)}} \times (\text{Standard Concentration}) \times 1.1$$

Standard Concentration = 2.58 mmol/L.

2.5.4.4. Determination of Serum VLDL-c Concentration:

VLDL-c is calculated through the following equation: (Friedwald *et al.*, 1972).

$$\text{Conce of VLDL-c (mmol/L)} = \text{Triglyceride}/2.2$$

2.5.4.5. Determination of Serum LDL-c Concentration:

LDL is calculated through the following equation: (Friedwald *et al.*, 1972).

$$\text{Conce of LDL-c (mmol/L)} = \text{Cholesterol con.} - (\text{VLDL-c}) - \text{HDLcon.}$$

2.6. Statistical Analysis:

The statistical analysis were performed with the statistical package for the social sciences SPSS for windows (version 17.0, SPSS Inc, Chicago, III) . The results were expressed as mean $\pm$ standard deviation (mean $\pm$ SD) with LSD (least significant difference). Analysis of variance (ANOVA) was used to compare parameters in different studied groups. P-values ($P \leq 0.05$) were considered statistically significant.

3. Results and Discussion

3.1. General Comparison for all Studied Parameters:

3.1.1. Serum Hormones Levels:

3.1.1.1. Serum Progesterone Levels:

The mean of serum progesterone level in the patients groups which was found to be significantly lower ($P \leq 0.05$) than that control group in both two phases as in the table (3-2) and figure (3-2). This result matches with the results of the study of (Pauli *et al.*, 1989).

Women report more pronounced symptoms which seem to change with the various life stages such as menstruation pregnancy and menopause and in association with female sex hormone levels (Fuseini and Newcomb, 2017). These hormones cause differences in the clinical manifestation of asthma. Thus, estrogen promotes bronchial hyperactivity. Both FEV1 and exhaled nitric oxide (NO) show a cycle-dependent course. Twenty to forty percent (20 – 40%) of premenopausal women suffer from pre- or peri-menstrual asthma (PMA) and experience an exacerbation in the week preceding menstruation, based on increased inflammation in the bronchi. This effect seems to be mediated by progesterone rather than by estrogen. PMA is less likely to be associated with atopy, but more frequently with aspirin sensitivity and poorer pulmonary function (Koper *et al.*, 2017).

The observed improved pulmonary function in luteal phase may be related to high progesterone levels which induces hyperventilation by direct stimulation of respiratory center and increasing oxygen consumption due to increased metabolic rate. Moreover, progesterone may potentiate prostaglandin induced relaxation of bronchial smooth muscles. This relaxation is well obvious during the luteal phase. Progesterone may also play a role in relaxation of bronchial

smooth muscle, which ultimately causes improvement of lung function (Ameen *et al.*, 2014).

Table (3-1): Serum Progesterone Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

Progesterone (ng/mL) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	0.57 $\pm$ 0.07 ^a	8.80 $\pm$ 1.11 ^a
Patient	70	0.38 $\pm$ 0.06 ^b	6.65 $\pm$ 0.77 ^b
L.S.D		0.02	0.32

Note: Each value represents mean $\pm$ S.D values with non-identical superscript (a or b), were considered significantly differences ($P \leq 0.05$).

No: Number of cases.

SD: Standard Deviation.

LSD: Least Significant Difference.

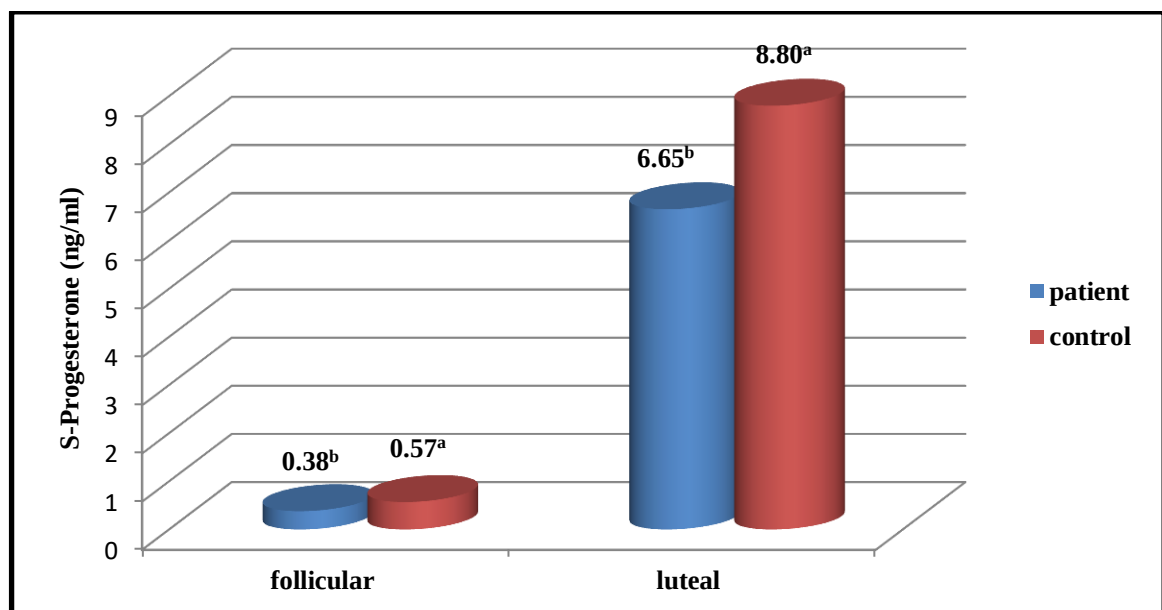


Figure (3-1): Serum Progesterone Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.1.2. Serum Testosterone Levels:

The mean of serum testosterone level in the patients groups which was found to be significantly lower ($P \leq 0.05$) than that control group in both two phases as in the table (3-2) and figure (3-2).

During the premenstrual and menstrual phase when hormonal levels are low, asthmatic patients have been found to experience increased asthma exacerbations, increased hospitalizations for asthma and decreased pulmonary function (Haggerty *et al.*, 2003). That certain systemic chronic inflammatory disorders and a few pulmonary diseases affect testosterone (T) biosynthesis (Agin and Sarvghadi, 2006).

Testosterone and its metabolites contribute to the physiological balance between autoimmunity and protective immunity by maintaining regulatory T cells. Testosterone has immunosuppressive effects and is probably also protective against immune-inflammatory processes that trigger asthma (Canguven and Albayrak, 2011).

Testosterone thus appears to have asthma-suppressive effects and the less virilising dehydroepiandrosterone (DHEA) as a sulfate (DHEAS), could be helpful in the therapy of premenstrual and severe asthma. Monitoring of DHEA serum level and substitution at deficient levels could therefore be considered for unstable asthmatic patients (Koper *et al.*, 2017).

We note a Height in the concentrations of serum progesterone and testosterone in all patients and control in the luteal phase in comparison with the follicular phase. Women of reproductive age, experience cyclic variations in serum concentrations of sex hormones where we observe in the follicular phase of the menstrual cycle, progesterone and testosterone serum levels remain low, while levels of FSH and LH peak. Finally, during the luteal phase, FSH and LH levels are low, whereas 17β -estradiol, progesterone, and testosterone are moderately high (Matteis *et al.*, 2014).

Patients who presenting premenstrual asthma worsening are frequently affected by alterations of the cyclic changes in serum levels of progesterone (Rubio *et al.*, 1988). Earlier studies indicate that an increase in progesterone secretion is a possible cause for the hyperventilation in the luteal phase (Rajesh *et al.*, 2000).

Table (3-2): Serum Testosterone Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

Testosterone (ng/mL) Mean±SD			
Group	No.	Follicular	Luteal
Control	70	0.82±0.06 ^a	0.90±0.15 ^a
Patient	70	0.50±0.09 ^b	0.71±0.10 ^b
L.S.D		0.03	0.15

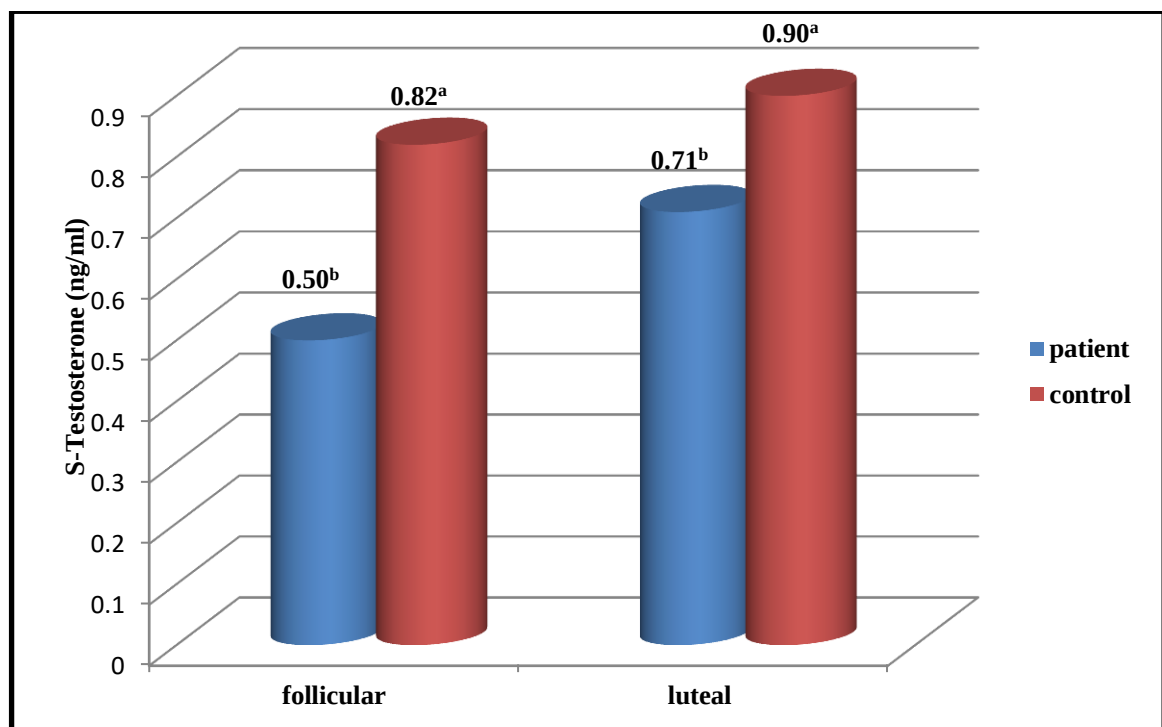


Figure (3-2): Serum Testosterone Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.2. Oxidative Stress:

3.1.2.1. Lipid Peroxidation Status (Malondialdehyde):

The results showed a significant increase in the concentrations of serum MDA in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$) as in the table (3-3) and figure (3-3). This result matches with the results of the study of (Mousa, 2015).

There is a growing number of evidence indicating the oxidative stress involvement in pathogenesis of asthma. The overproduction of reactive oxygen species (ROS) is present in allergic inflammation. Reactive oxygen species may induce symptoms characteristic of asthma: bronchospasm, bronchial hyperresponsiveness, beta-adrenergic receptor, dysfunction, mucus hypersecretion and activation of arachidonic acid cascade, increased permeability and bronchial epithelial damage (Szlagatys and Korzon, 2003).

Arachidonic acid is increased in airway inflammatory cells in bronchial asthma patients. This arachidonic acid may undergo oxidation to produce an end product of lipid peroxidation. So MDA is increased in bronchial asthma due to generation by decomposition of arachidonic acid and larger poly unsaturated fatty acid PUFA through enzymatic and nonenzymatic processes (Parhi *et al.*, 2018).

Table (3-3): Serum MDA Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

MDA ($\mu\text{mol/L}$) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	2.07 $\pm$ 0.29 ^b	2.26 $\pm$ 0.33 ^b
Patient	70	3.14 $\pm$ 0.53 ^a	3.06 $\pm$ 0.49 ^a
L.S.D		0.19	0.14

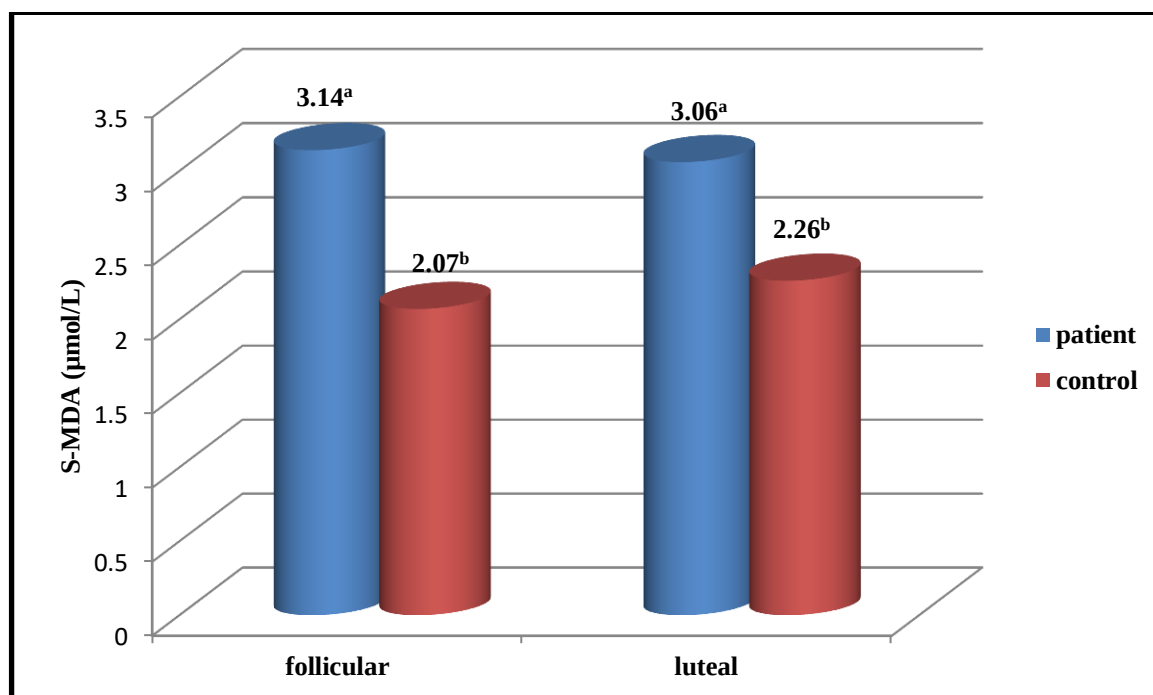


Figure (3-3): Serum MDA Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.2.2. Antioxidant System:

3.1.2.2.1. Serum Ceruloplasmin Concentration:

The results showed a significant increase in the concentration of serum CP in all patients in both follicular phase as well as in the luteal phase in comparison with a control group in the follicular phase and luteal phase

respectively ($P \leq 0.05$) as in the table (3-4) and figure (3-4). This result matches with the results of the study of (Mousa, 2015).

Levels of certain proteins in the plasma rise through acute inflammatory state or according to certain types of tissue damage. These proteins are named acute phase proteins or reactants. They are synthesized by the liver. Following stimulus through infection or injury, the macrophages liberate monocyte and interleukin-1 which induce the liver to secrete a lot of acute phase proteins (Maradi, 2012). These reactants have been shown to serve different effective roles during tissue rehabilitation of injury or inflammation in various mechanisms of host immune defense. Cp is recognized to keep the considerable peroxidase activity and capable of suppression superoxide radicals. It is responsible for restricting the damage caused by these radicals (Maradi, 2012).

The elevation of ceruloplasmin level is part of an increase in iron metabolism proteins as part of asthma and COPD, probably as an anti-inflammatory response to the airway inflammation that characterizes these conditions (Verrills *et al.*, 2011). Ceruloplasmin can be used as a non-invasive biomarkers for evaluation of chronic airway inflammation and can be useful in determining the severity of asthma (Shahin *et al.*, 2015).

Table (3-4): Serum CP Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

CP (g/L) Mean±SD			
Group	No.	Follicular	Luteal
Control	70	2.26±0.37 ^b	2.21±0.35 ^b
Patient	70	3.62±0.71 ^a	3.55±0.66 ^a
L.S.D		0.18	0.16

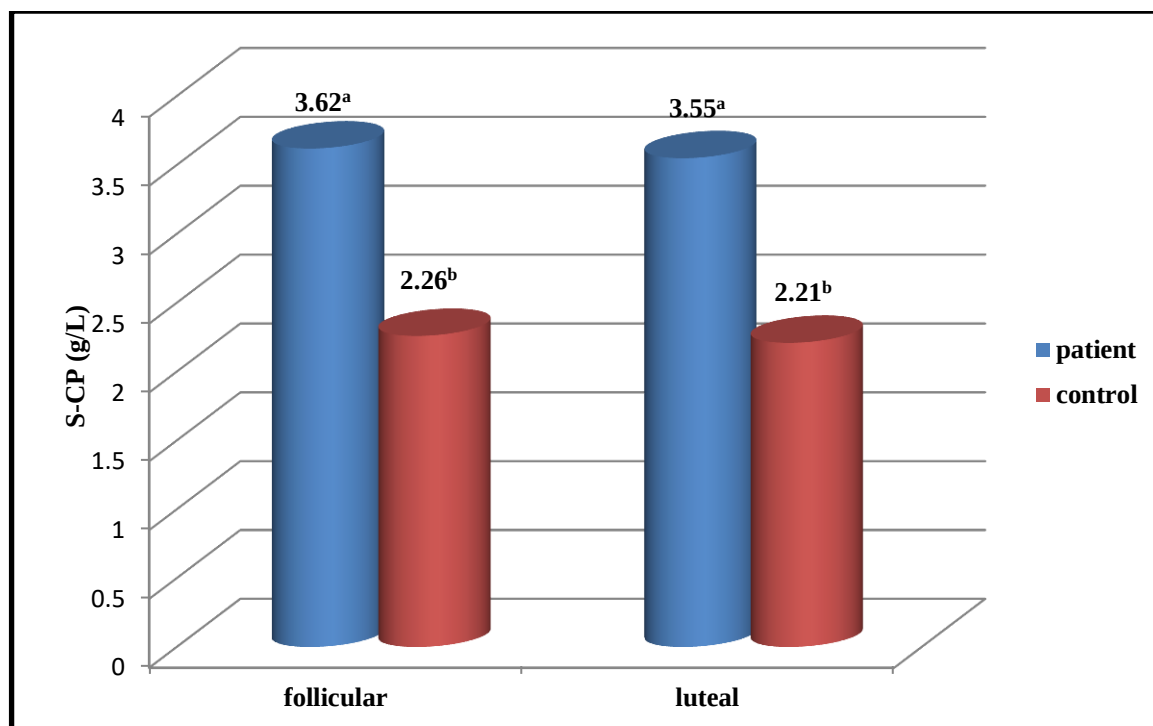


Figure (3-4): Serum CP Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.2.2.2. Serum Transferrin Concentration:

The results showed no significant difference in the concentration of serum (Tf) in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$) as in the table (3-5) and figure (3-5). This result matches with the results of the study of (Mousa, 2015).

The presence of inflammatory cells such as eosinophil, mast cells, macrophages and lymphocytes have been observed in different specimens of asthmatic patients. These inflammatory cells secrete several kinds of cytokines (Barnes, 2008). Therefore, asthma and allergic inflammation include wide cytokine network. This cytokine and their complex relationship have an important role in inflammation and immune. The acute - phase reaction is a general response to inflammation and probably triggered by interleukins, released from the site of injury or inflammation. Interleukin-2, interleukin-6 and tumor necrosis factor- α are an important mediator in the synthesis of amyloid precursor protein by the liver (Alexandrakis *et al.*, 2000).

Sex hormones lead to the production of ROS via neutrophils which have immune functions. These ROS are reported to be involved in the occurrence of ovulation in the ovaries and subsequent follicle destruction (Evans and Salamonsen, 2012). After ovulation, the corpus luteum is formed and progesterone is secreted, but if pregnancy is not established, a process of functional corpus luteum regression begins. ROS is also said to play a role in promoting this functional corpus luteum regression (Evans and Salamonsen, 2012). ROS production may be considered essential in maintaining homeostasis in ovarian function. The sex hormone estrogen is considered to have an antioxidant effect (Narumi *et al.*, 2017), and the menstrual cycle is also thought to affect the antioxidant activity in the body. Consequently, since changes in the balance of ROS production and antioxidant activity occur through the secretion of menstrual cycle-dependent sex hormones (Rink *et al.*, 2013).

Table (3-5): Serum Tf Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

Tf (g/L) Mean±SD			
Group	No.	Follicular	Luteal
Control	70	4.08±0.76 ^a	3.96±0.71 ^a
Patient	70	4.09±0.85 ^a	3.97±0.78 ^a
L.S.D		0.31	0.29

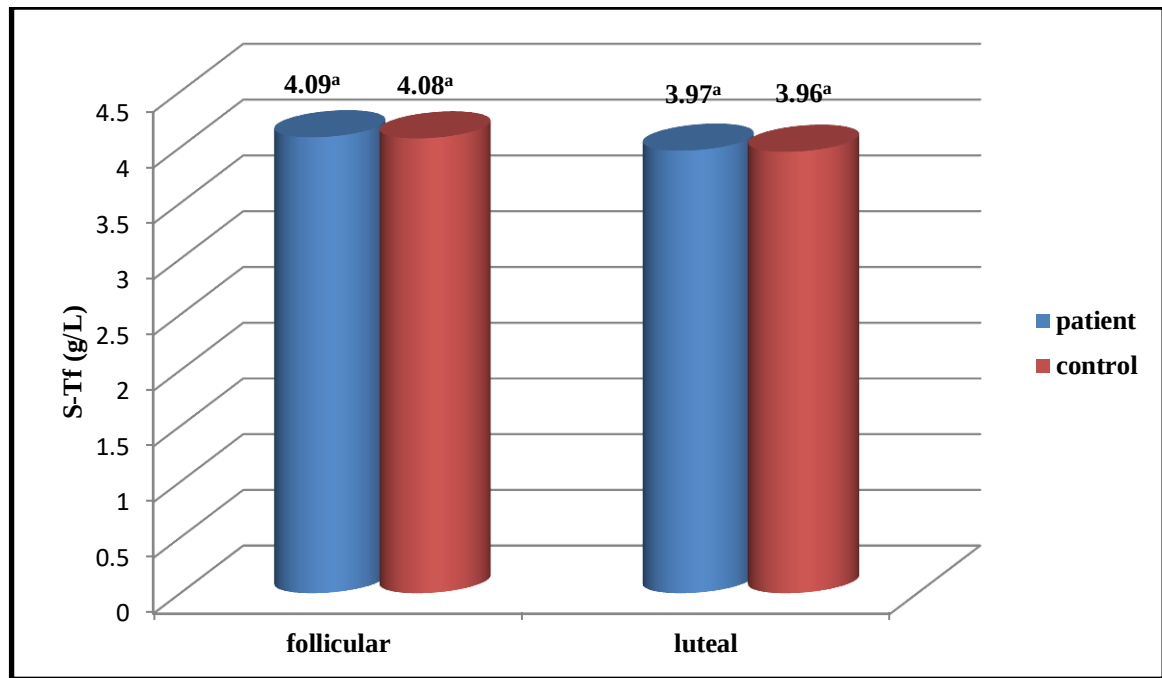


Figure (3-5): Serum Tf Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.3. Serum Lipid Profile Concentrations:

3.1.3.1. Serum Total Cholesterol (TC) Concentration:

Table (3-6) and figure (3-6) show a significant increase in the concentration of serum TC in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

Hypercholesterolemia is associated with increased frequency of asthma even when other potential confounding variables such as age, gender, and obesity is controlled (Al-Shawwa *et al.*, 2006).

Hyperlipidemia affects inflammation, and high cholesterol loading may trigger pro-inflammatory cellular responses. This indicates that low grade inflammation present in obesity augmented inflammation of asthma (synergistic interaction) on hyperlipidemia. Possible mechanisms of this synergistic interaction could be the addition of chronic inflammatory status by hypercholesterolemia in both asthma and obesity and dietary cholesterol

induced interaction of airway inflammation and systemic inflammation (Chen *et al.*, 2013).

Table (3-6): Serum TC Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

TC (mmol/L) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	4.05 $\pm$ 0.41 ^b	4.07 $\pm$ 0.65 ^b
Patient	70	5.31 $\pm$ 0.67 ^a	4.51 $\pm$ 0.79 ^a
L.S.D		0.22	0.28

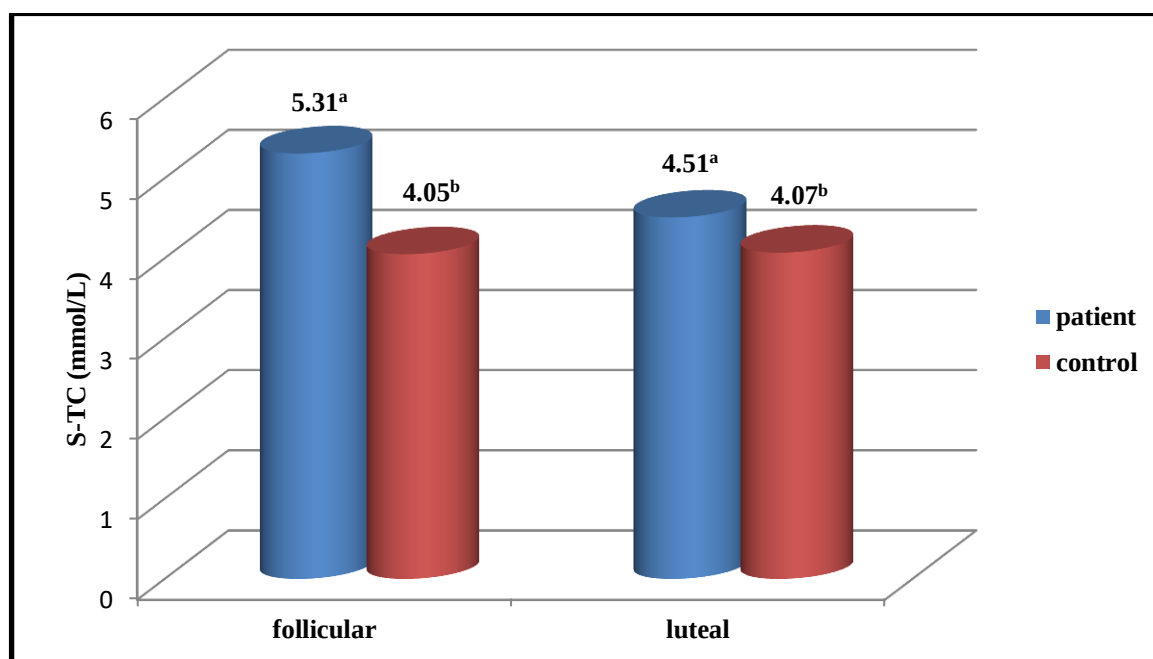


Figure (3-6): Serum TC Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.3.2. Serum Triglyceride Concentration:

Table (3-7) and figure (3-7) show a significant increase in the concentration of serum TG in all patients in both follicular phase as well in the luteal phase in

comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

Higher serum triglyceride levels are associated with increased risk of aeroallergen sensitization. Together, these findings suggest that asthma and allergy are systemic disorders with commonalities with other chronic inflammatory disorders (Vinding *et al.*, 2016).

The reason may be that increased free radicals in patients asthmatic may lead to an increase in the metabolism of triglycerides in the adipose tissue and go down into the serum, leading to a higher concentration of triglycerides (TG) in the serum (Ahmed *et al.*, 2010).

Table (3-7): Serum TG Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

TG (mmol/L) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	0.84 $\pm$ 0.16 ^b	0.89 $\pm$ 0.21 ^b
Patient	70	2.21 $\pm$ 0.46 ^a	2.04 $\pm$ 0.38 ^a
L.S.D		0.11	0.10

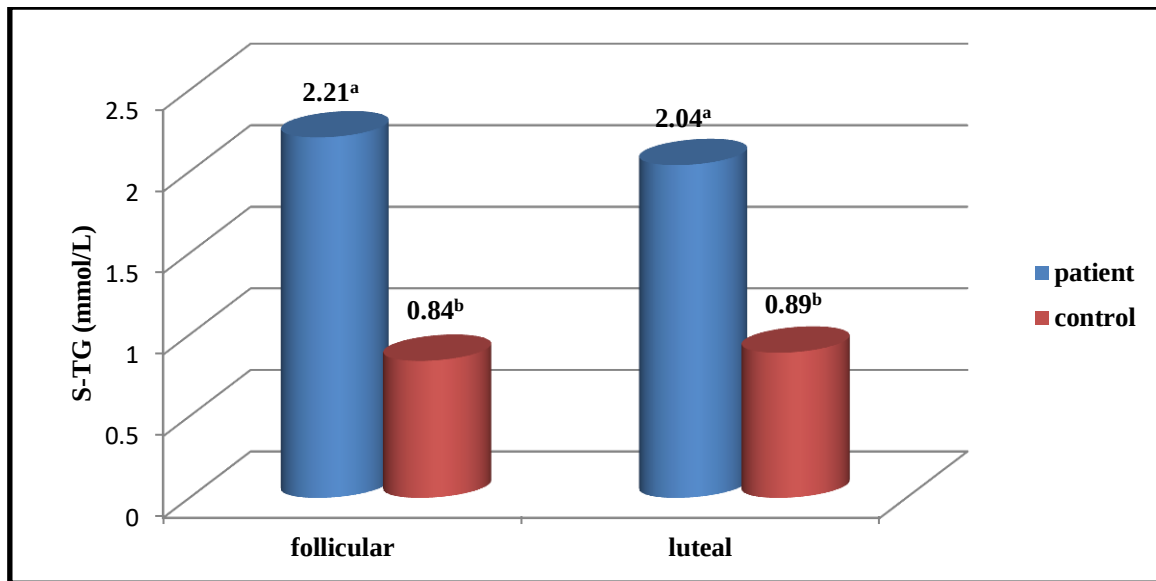


Figure (3-7): Serum TG Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.3.3. Serum HDL-c Concentration:

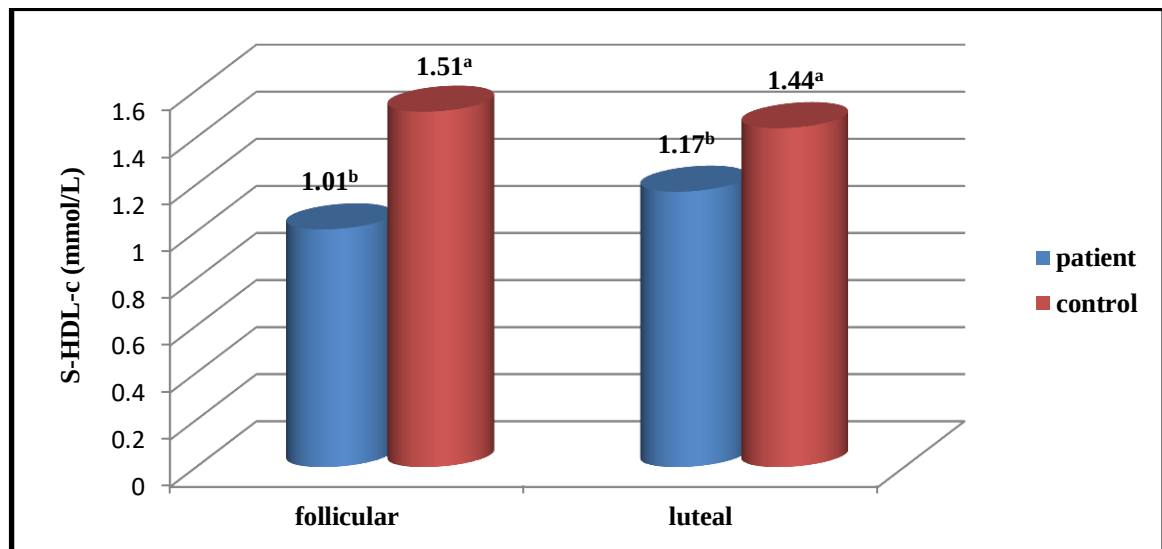
Table (3-8) and figure (3-8) show a significant decrease in the concentrations of serum HDL-c in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

Low levels of serum high density lipoproteins (HDL) have been found to be associated with an increased risk of asthma in adolescence (Su *et al.*, 2018).

This the association between asthma and low HDL-c appears particularly pronounced in IgE-positive adolescents, suggesting an enhanced role of HDL-c in asthma development in those who have a Th2- type adaptive immunity profile (Bousquet *et al.*, 2006) or in the setting of a genetic link between low HDL-c and allergic sensitization, common adverse environmental influences (e.g. unhealthy diet) can interact with both of these two determinants and have a particularly important role in asthma development (Yiallourous *et al.*, 2014).

Table (3-8): Serum HDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

HDL-c (mmol/L) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	1.51 $\pm$ 0.26 ^a	1.44 $\pm$ 0.27 ^a
Patient	70	1.01 $\pm$ 0.21 ^b	1.17 $\pm$ 0.26 ^b
L.S.D		0.09	0.12

**Figure (3-8):** Serum HDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.3.4. Serum VLDL-c Concentration:

Table (3-9) and figure (3-9) show a significant increase in the concentrations of serum VLDL-c in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

The results of the present study of this type of cholesterol (VLDL-c) are similar to the results of triglyceride level (TG). This may be due to the increased

production of VLDL-c in the liver in patients with bronchial asthma, leading to an increase in VLDL-c in the serum (Ahmed *et al.*, 2010).

Table (3-9): Serum VLDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

VLDL-c (mmol/L) Mean±SD			
Group	No.	Follicular	Luteal
Control	70	0.38±0.12 ^b	0.40±0.09 ^b
Patient	70	1.00±0.22 ^a	0.93±0.22 ^a
L.S.D		0.09	0.07

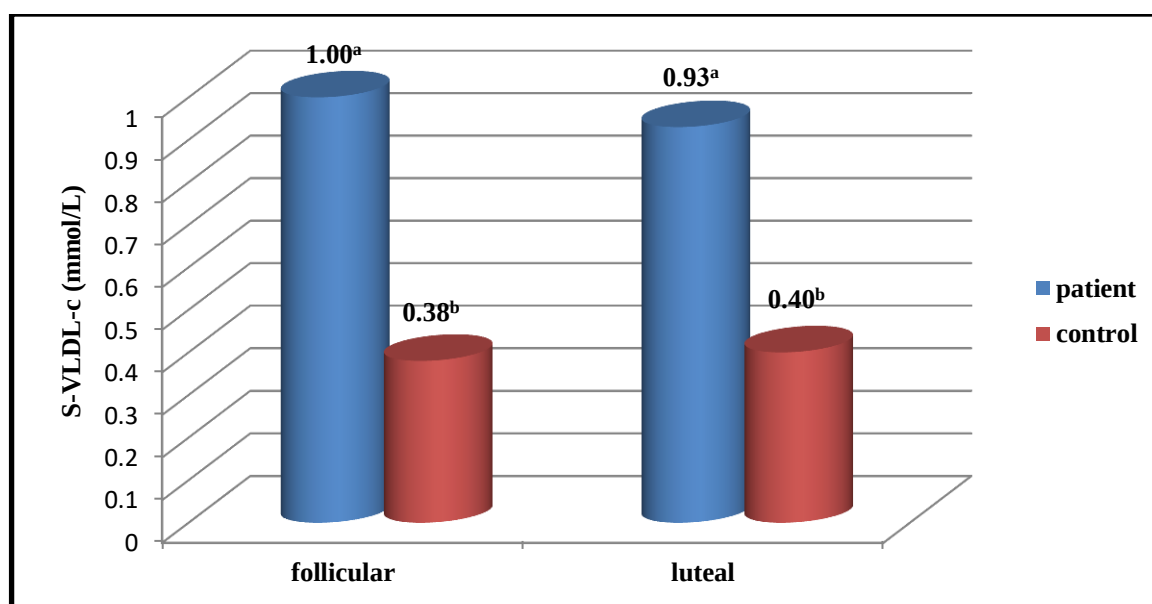


Figure (3-9): Serum VLDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.1.3.5. Serum LDL-c Concentration:

Table (3-10) and figure (3-10) show a significant increase in the concentrations of serum LDL-c in all patients in both follicular phase as well in the luteal phase in comparison with a control group in the follicular phase and luteal phase respectively ($P \leq 0.05$).

There is a positive association between increasing levels of LDL and risk of asthma (Fenger *et al.*, 2013).

Those high LDL-c levels are associated with airway obstruction, whereas high HDL-c levels are negatively associated with the fraction of exhaled nitric oxide (FENO) values (Vinding *et al.*, 2016). This finding helps explaining the mechanism to how lipoproteins take part in the pathogenesis of asthma (Peng and Huang, 2016).

The results showed a decrease in the concentrations of serum (TC, TG, VLDL-c and LDL-c) and increase in the concentrations of serum (HDL) in all patients and control in the luteal phase in comparison with all patients in the follicular phase. Previous studies have reported variable effects of cycle phase on plasma lipids and lipoproteins. These inconsistent results may have occurred because dietary intake was not controlled. There are considerable data indicating that exogenous estrogens influence plasma lipids and lipoprotein fractions (Woods *et al.*, 1987).

Exogenous estrogens have been reported to decrease TC and LDL-c and increase HDL-c (Barnett *et al.*, 2004). Estrogen increases the hepatic synthesis of LDL receptor (apolipoprotein B-100), resulting in the increased LDL uptake. In addition, estrogen treatment has been shown to increase the production of apolipoprotein A-I, a major HDL protein, in both pre- and postmenopausal women (Barnett *et al.*, 2004).

Estrogen has been shown to increase the concentration of the alpha-lipoproteins and decrease beta-lipoproteins, presumably by increased uptake of LDL by the liver. The triglyceride results would follow from decreases in the VLDL and LDL fractions, these being the primary carriers of triglycerides. During the menstrual cycle, estrogen levels peak just prior to ovulation and average higher levels during the luteal phase of the cycle compared to the follicular. These estrogen changes are consistent with the timing of the plasma

lipid responses, particularly when the half-lives of about four days for LDL and HDL are considered (Jones *et al.*, 1988).

Table (3-10): Serum LDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

LDL-c (mmol/L) Mean $\pm$ SD			
Group	No.	Follicular	Luteal
Control	70	2.26 $\pm$ 0.35 ^b	2.12 $\pm$ 0.62 ^b
Patient	70	3.30 $\pm$ 0.70 ^a	2.41 $\pm$ 0.56 ^a
L.S.D		0.22	0.23

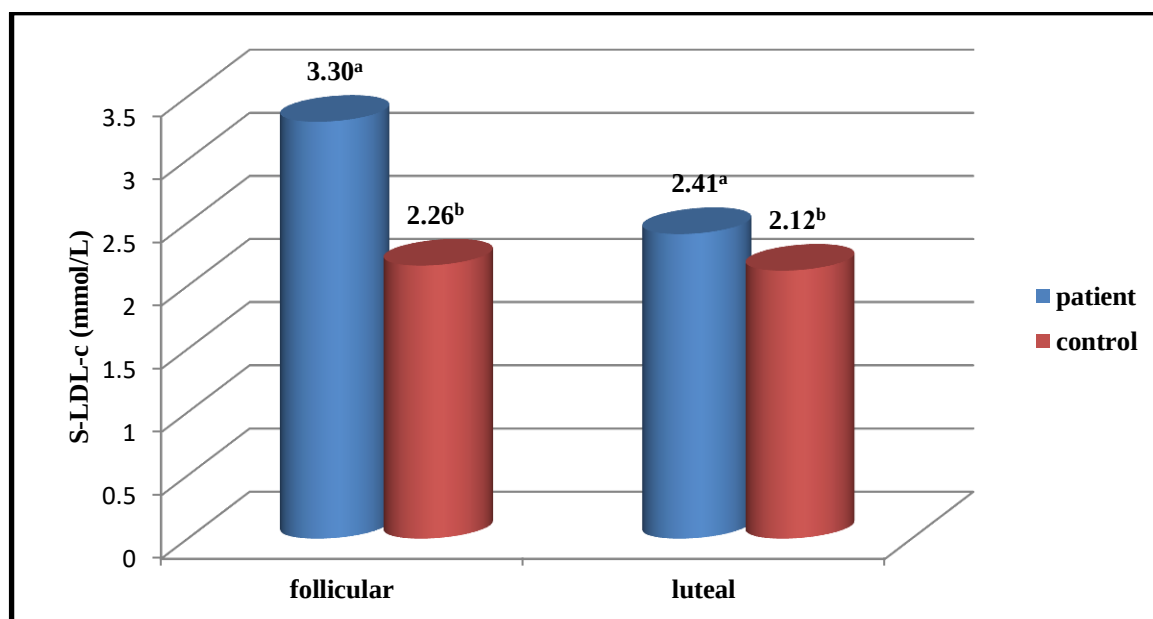


Figure (3-10): Serum LDL-c Levels in Control and Patient Groups in the Follicular and Luteal Phase of the Menstrual Cycle Phases.

3.2. The Studied Parameters According to the Age:

3.2.1. Serum Hormones Levels:

3.2.1.1. Serum Progesterone Levels:

Table (3-11) and figure (3-11) show a significant decrease in the concentration of serum progesterone in all patients' age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular phase and luteal phase respectively ($P \leq 0.05$).

There is a significant decrease in the concentration of serum progesterone in the control group (A2) in follicular and luteal phases in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

The results showed a significant decrease in the concentration of serum progesterone in the patient group (A2) in follicular and luteal phase in comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

There is an evident decline in fertility with age, clearly observed in populations in which contraception has not been employed. In such circumstances, fecundity decreases and infertility increases with age, suggesting that either the uterus, the ovary, or both are responsible for this impairment of fertility with age (Pellicer *et al.*, 1995).

Table (3-11): Serum Progesterone Concentrations for all Age Groups.

Progesterone (ng/mL) Mean $\pm$ SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	0.43 $\pm$ 0.04 ^{Ab}	0.63 $\pm$ 0.03 ^{Aa}	0.06	7.01 $\pm$ 0.61 ^{Ab}	9.31 $\pm$ 1.11 ^{Aa}	0.47
A2	35	0.34 $\pm$ 0.04 ^{Bb}	0.52 $\pm$ 0.06 ^{Ba}	0.09	6.30 $\pm$ 0.73 ^{Bb}	8.29 $\pm$ 0.86 ^{Ba}	0.42
L.S.D		0.02	0.03		0.34	0.59	

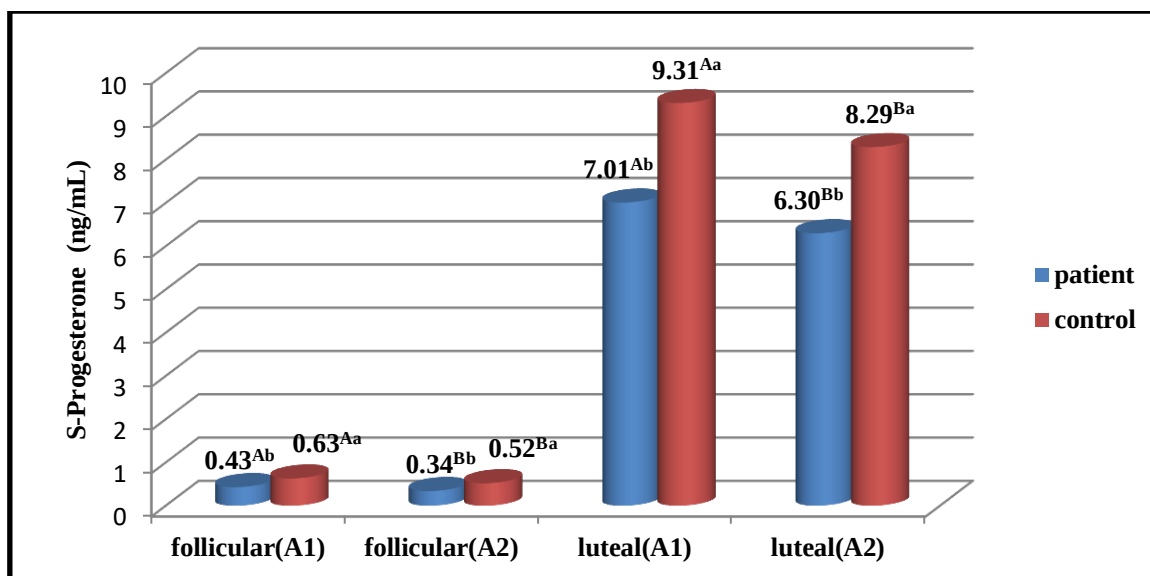


Figure (3-11): Serum Progesterone Concentrations for all Age Groups.

Note: Each value represents mean $\pm$ S.D values with non-identical superscript (a or b), are considered significantly differences ($P \leq 0.05$) to compare horizontally, and with non-identical superscript (A or B), are considered significantly differences ($P \leq 0.05$) to compare vertically.

A1: First age group range from (14-29 years).

A2: Second age group range from (30-45 years).

3.2.1.2. Serum Testosterone Levels:

Table (3-12) and figure (3-12) show a significant decrease in the concentration of serum testosterone in all patients' age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular phase and luteal phase respectively ($P \leq 0.05$).

There is a significant decrease in the concentration of serum testosterone in the control group (A2) in follicular and luteal phase in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

The results show a significant decrease in the concentration of serum testosterone in the patient group (A2) in follicular and luteal phase in

comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

There is a decline in testosterone with age in normal premenopausal women; at age 40 yr, the level is about half what it is at age 21 yr. Since the percent free testosterone does not vary significantly with age, free testosterone likewise declines steeply with age, since the great majority of circulating testosterone in normal women is derived from the metabolic transformation of the adrenal androgens dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS), and since their levels are known to decline with age (Zumoff *et al.*, 1995).

Table (3-12): Serum Testosterone Concentrations for all Age Groups.

Testosterone (ng/mL) Mean $\pm$ SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	0.53 $\pm$ 0.08 ^{Ab}	0.85 $\pm$ 0.06 ^{Aa}	0.09	0.75 $\pm$ 0.10 ^{Ab}	0.96 $\pm$ 0.16 ^{Aa}	0.07
A2	35	0.47 $\pm$ 0.08 ^{Bb}	0.79 $\pm$ 0.05 ^{Ba}	0.06	0.67 $\pm$ 0.07 ^{Bb}	0.84 $\pm$ 0.14 ^{Ba}	0.08
L.S.D		0.04	0.03		0.05	0.10	

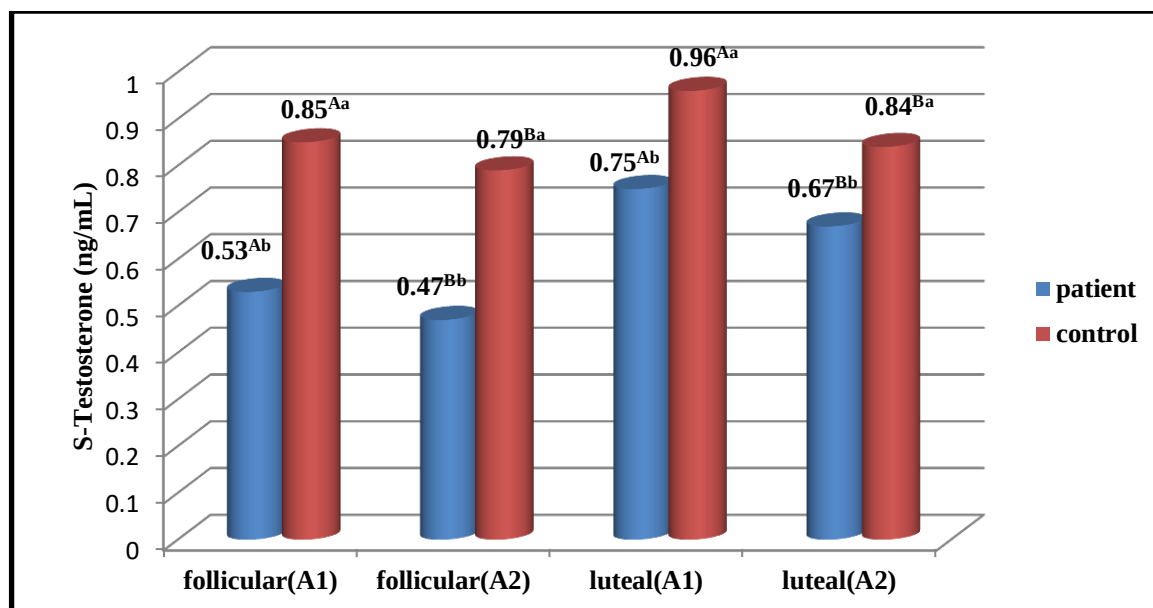


Figure (3-12): Serum Testosterone Concentrations for all Age Groups.

3.2.2. Oxidative Stress:

3.2.2.1. Lipid Peroxidation Status (Malondialdehyde):

Table (3-13) and figure (3-13) show a significant increase in the concentration of serum (MAD) in all patient age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular and luteal phase respectively ($p \leq 0.05$).

There is a significant increase in the concentration of serum (MDA) in the control group (A2) in follicular and luteal phase in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

The results show a significant increase in the concentration of serum (MDA) in the patient group (A2) in follicular and luteal phase in comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

Aging is associated with changes in physical characteristics and decline of many physiological functions. The excessive production of free radicals in the organism and the imbalance between the concentrations of these and the antioxidant defenses may be related to aging (Reddy Thavanati *et al.*, 2008).

Oxygen free radical mediated cellular damages are implicated in the aging process (Kasapoglu and Özben, 2001). Oxidative damage to DNA, proteins and lipids are induced by the overproduction of ROS accumulate with age and contributes to degenerative diseases and the aging phenomenon by disrupting cellular homeostasis (Balaban *et al.*, 2005).

Table (3-13): Serum MDA Concentrations for all Age Groups.

MDA ($\mu\text{mol/L}$) Mean $\pm$ SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	2.88 $\pm$ 0.41 ^{Ba}	1.89 $\pm$ 0.29 ^{Bb}	0.19	2.81 $\pm$ 0.50 ^{Ba}	2.10 $\pm$ 0.41 ^{Bb}	0.28
A2	35	3.40 $\pm$ 0.59 ^{Aa}	2.24 $\pm$ 0.37 ^{Ab}	0.27	3.32 $\pm$ 0.42 ^{Aa}	2.42 $\pm$ 0.42 ^{Ab}	0.22
L.S.D		0.26	0.20		0.23	0.25	

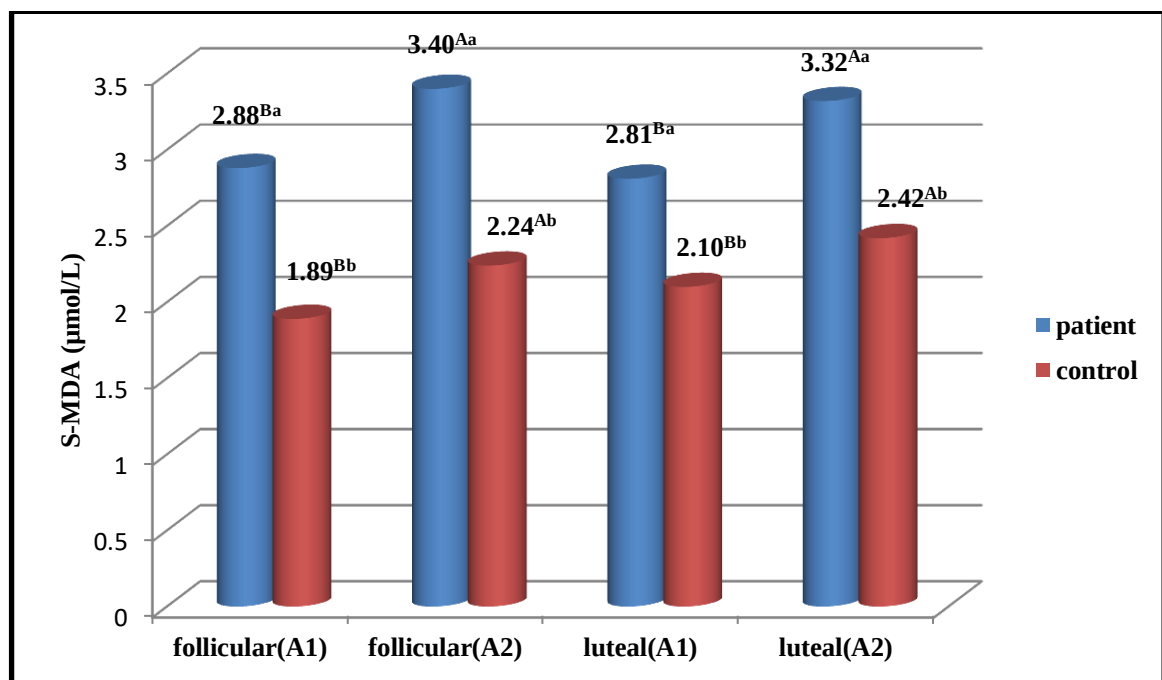


Figure (3-13): Serum MDA Concentrations for all Age Groups.

3.2.2.2. Antioxidant System:

3.2.2.2.1. Serum Ceruloplasmin Concentration:

Table (3-14) and figure (3-14) show a significant increase in the concentration of serum (CP) in all patient age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular and luteal phase respectively ($p \leq 0.05$).

There is a significant increase in the concentration of serum (CP) in the control group (A2) in follicular and luteal phase in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

The results show a significant increase in the concentration of serum (CP) in the patient group (A2) in follicular and luteal phase in comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

Changes in CP activity with age can influence the antioxidative defines system of the body; antioxidants have been proposed to be significant elements of the aging process (Nagy, 1989).

Table (3-14): Serum CP Concentrations for all Age Groups.

CP (g/L) Mean $\pm$ SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	3.41 $\pm$ 0.74 ^{Ba}	2.09 $\pm$ 0.52 ^{Bb}	0.36	3.30 $\pm$ 0.78 ^{Ba}	2.02 $\pm$ 0.43 ^{Bb}	0.38
A2	35	3.82 $\pm$ 0.80 ^{Aa}	2.43 $\pm$ 0.40 ^{Ab}	0.41	3.79 $\pm$ 0.61 ^{Aa}	2.40 $\pm$ 0.44 ^{Ab}	0.29
L.S.D		0.39	0.28		0.35	0.26	

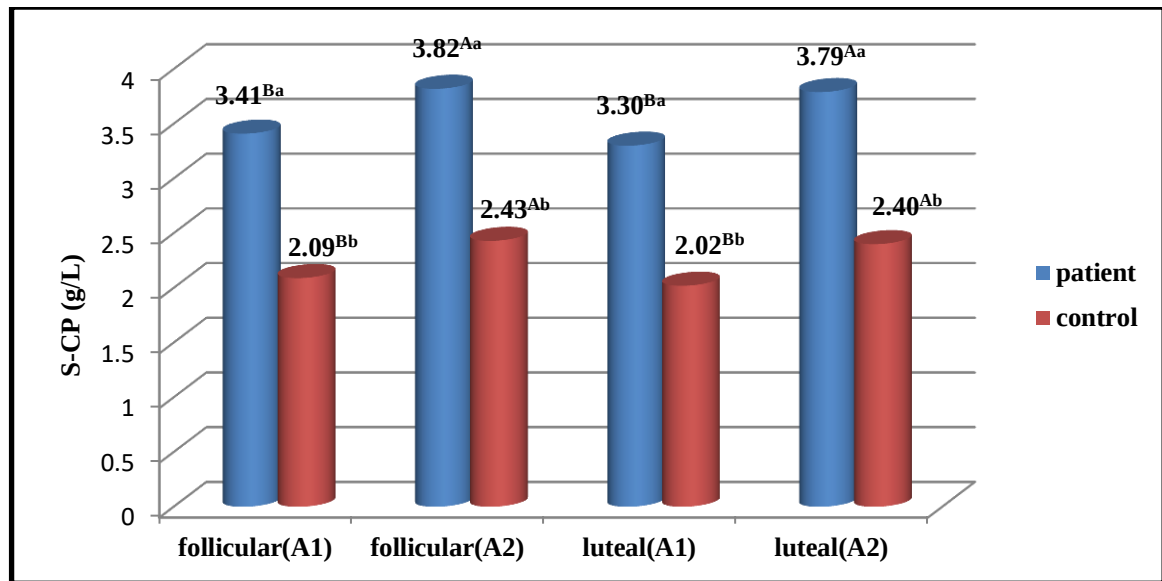


Figure (3-14): Serum CP Concentrations for all Age Groups.

3.2.2.2.2- Serum Transferrin Concentration:

Table (3-14) and figure (3-14) show no significant difference in the concentration of serum (Tf) in all patient age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular and luteal phase respectively ($p \leq 0.05$).

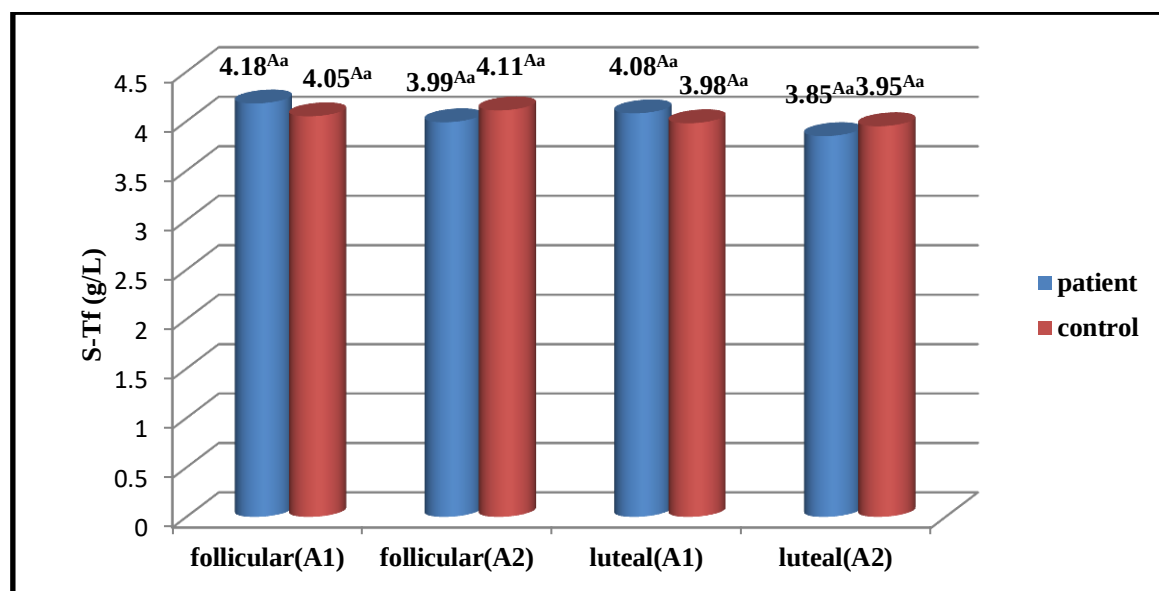
The results show no significant difference in the concentration of serum (Tf) in the control group (A2) in follicular and luteal phase in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

We also note no significant difference in the concentration of serum (Tf) in the patient group (A2) in follicular and luteal phase in comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

In women of reproductive age, the iron pool is relatively small due to physiological loss that is not compensated by adequate intake. Thus the ferritin levels are low. In postmenopausal women, decreased iron loss leads to increase in store iron and ferritin in the elderly women rise and approach those values in men (Čolak *et al.*, 2018).

Table (3-15): Serum Tf Concentrations for all Age Groups.

Tf (g/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	4.18±0.71 ^{Aa}	4.05±0.91 ^{Aa}	0.48	4.08±0.75 ^{Aa}	3.98±0.46 ^{Aa}	0.35
A2	35	3.99±0.95 ^{Aa}	4.11±0.56 ^{Aa}	0.38	3.85±0.79 ^{Aa}	3.95±0.90 ^{Aa}	0.44
L.S.D		0.40	0.46		0.41	0.43	

**Figure (3-15):** Serum Tf Concentrations for all Age Groups.

3.2.3. Serum Lipid Profile Concentrations:

Table (3-16) and figures (3-16, 3-17, 3-19 and 3-20) show a significant increase in the concentration of serum (TC, TG, LDL-c and VLDL-c) in all patient age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular and luteal phase respectively ($p \leq 0.05$).

The same table and figure (3-18) show a significant decrease in the concentration of serum (HDL-c) in all patient age groups in both follicular phase as well in the luteal phase in comparison with the controls age groups in the follicular and luteal phase respectively ($p \leq 0.05$).

There is a significant increase in the concentration of serum (TC, TG, LDL-c and VLDL-c) and a significant decrease in (HDL-c) in the control group (A2) in follicular and luteal phase in comparison with control group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

The results show a significant increase in the concentration of serum (TC, TG, LDL-c and VLDL-c) and a significant decrease in (HDL-c) in the patient group (A2) in follicular and luteal phase in comparison with patient group (A1) in follicular and luteal phase respectively ($p \leq 0.05$).

Aging is often associated with lipid metabolism disorders. Lipid metabolism disorders that are associated with the aging process constitute the early stage in the emergence of a constellation of risk factors for metabolic disorders (Gobal and Metha, 2010). With the increase of the age composition of body fat also increases which especially accumulates in the abdomen triggering the incidence of central obesity. TG composition in the muscle and liver are higher in older age compared with younger age groups (Cree *et al.*, 2004). Increased body fat composition is associated with reduced fat oxidation both at rest and inactivity (Nagy *et al.*, 1996).

Theoretically speaking, it seems that cholesterol levels increase with age until the sixties, but start to decrease beyond that age (Marhoum *et al.*, 2013).

Previous studies in the kinetics of LDL suggest that the increase in LDL with age is explained by a reduced capacity for its removal by the liver, probably secondary to reduced hepatic LDL receptor expression and/or increase in cholesterol intestinal absorption (Marhoum *et al.*, 2013).

At menopause, the HDL-c levels typically decline and LDL-c levels rise, but there is little net change in total cholesterol levels, and longitudinal lipid data for women a decade or more after menopause are scant (Wilson *et al.*, 1994).

Table (3-16): Serum Lipid Profile Concentrations for all Age Groups.

TC (mmol/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	5.10±0.55 ^{Ba}	3.89±0.44 ^{Bb}	0.27	4.13±0.56 ^{Ba}	3.75±0.63 ^{Bb}	0.33
A2	35	5.50±0.72 ^{Aa}	4.22±0.36 ^{Ab}	0.36	4.87±0.77 ^{Aa}	4.40±0.66 ^{Ab}	0.37
L.S.D		0.32	0.24		0.34	0.39	
TG (mmol/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	2.06±0.46 ^{Ba}	0.77±0.19 ^{Bb}	0.20	1.84±0.33 ^{Ba}	0.80±0.23 ^{Bb}	0.23
A2	35	2.36±0.50 ^{Aa}	0.91±0.21 ^{Ab}	0.21	2.23±0.39 ^{Aa}	0.98±0.31 ^{Ab}	0.19
L.S.D		0.24	0.12		0.18	0.16	
HDL-c (mmol/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	1.14±0.18 ^{Ab}	1.61±0.26 ^{Aa}	0.12	1.30±0.18 ^{Ab}	1.58±0.25 ^{Aa}	0.12
A2	35	0.87±0.14 ^{Bb}	1.40±0.26 ^{Ba}	0.10	1.04±0.25 ^{Bb}	1.30±0.28 ^{Ba}	0.14
L.S.D		0.08	0.15		0.11	0.16	

VLDL-c (mmol/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	0.93±0.20 ^{Ba}	0.35±0.07 ^{Bb}	0.09	0.83±0.15 ^{Ba}	0.36±0.10 ^{Bb}	0.08
A2	35	1.07±0.22 ^{Aa}	0.41±0.09 ^{Ab}	0.10	1.01±0.23 ^{Aa}	0.44±0.14 ^{Ab}	0.11
L.S.D		0.11	0.05		0.10	0.06	

LDL-c (mmol/L) Mean±SD							
Groups	No	Follicular		L.S.D	Luteal		L.S.D
		Patient	Control		Patient	Control	
A1	35	3.16±0.38 ^{Ba}	2.11±0.49 ^{Bb}	0.23	2.26±0.65 ^{Ba}	2.00±0.63 ^{Ba}	0.25
A2	35	3.44±0.61 ^{Aa}	2.40±0.45 ^{Ab}	0.29	2.56±0.57 ^{Aa}	2.25±0.60 ^{Ab}	0.27
L.S.D		0.25	0.28		0.26	0.22	

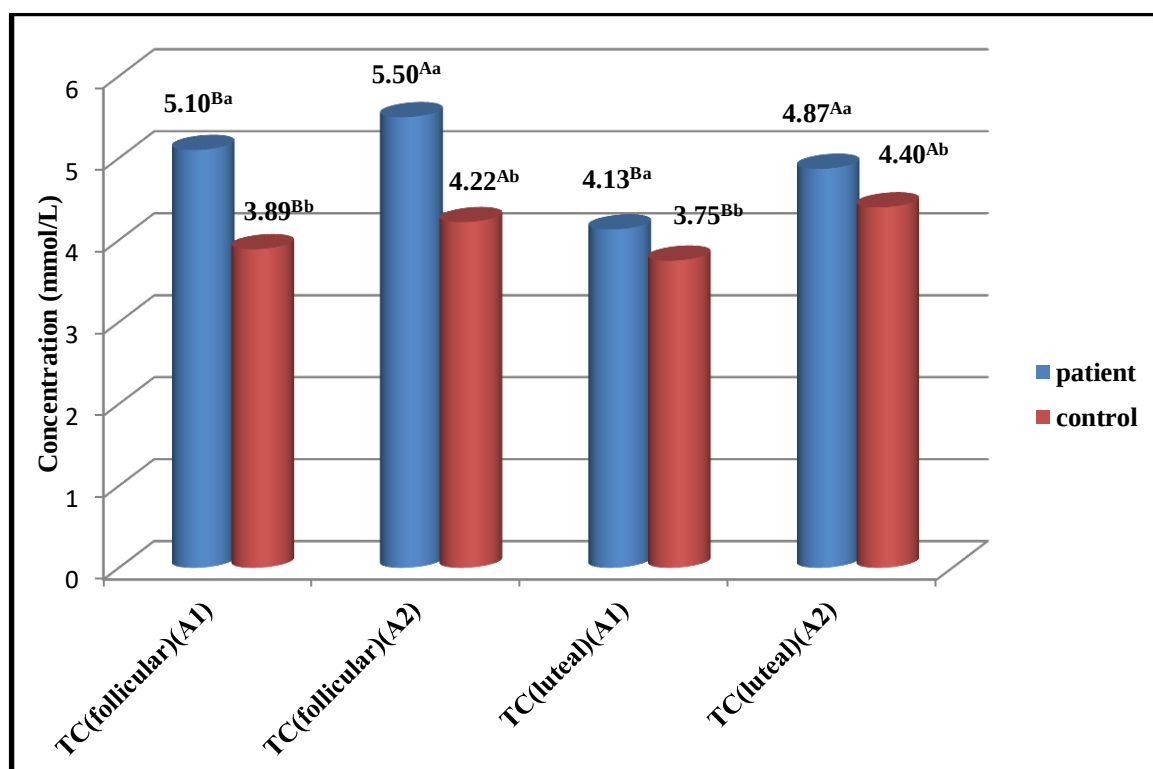


Figure (3-16): Serum TC Concentrations for all Age Groups

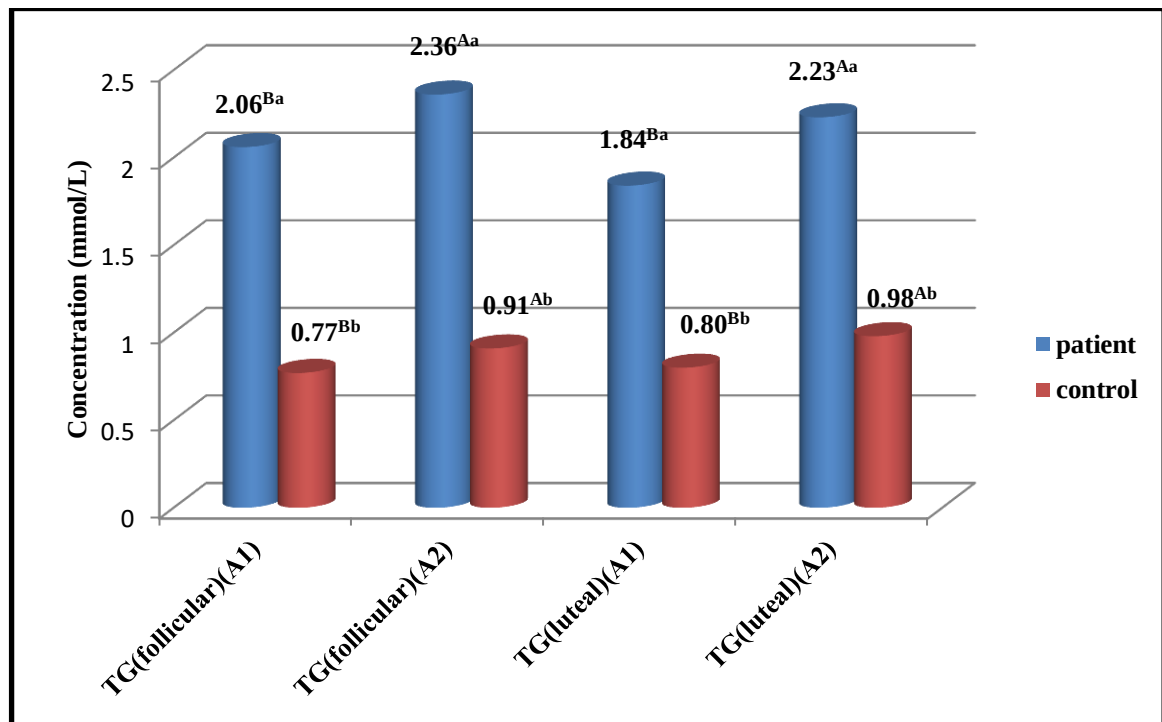


Figure (3-17): Serum TG Concentrations for all Age Groups

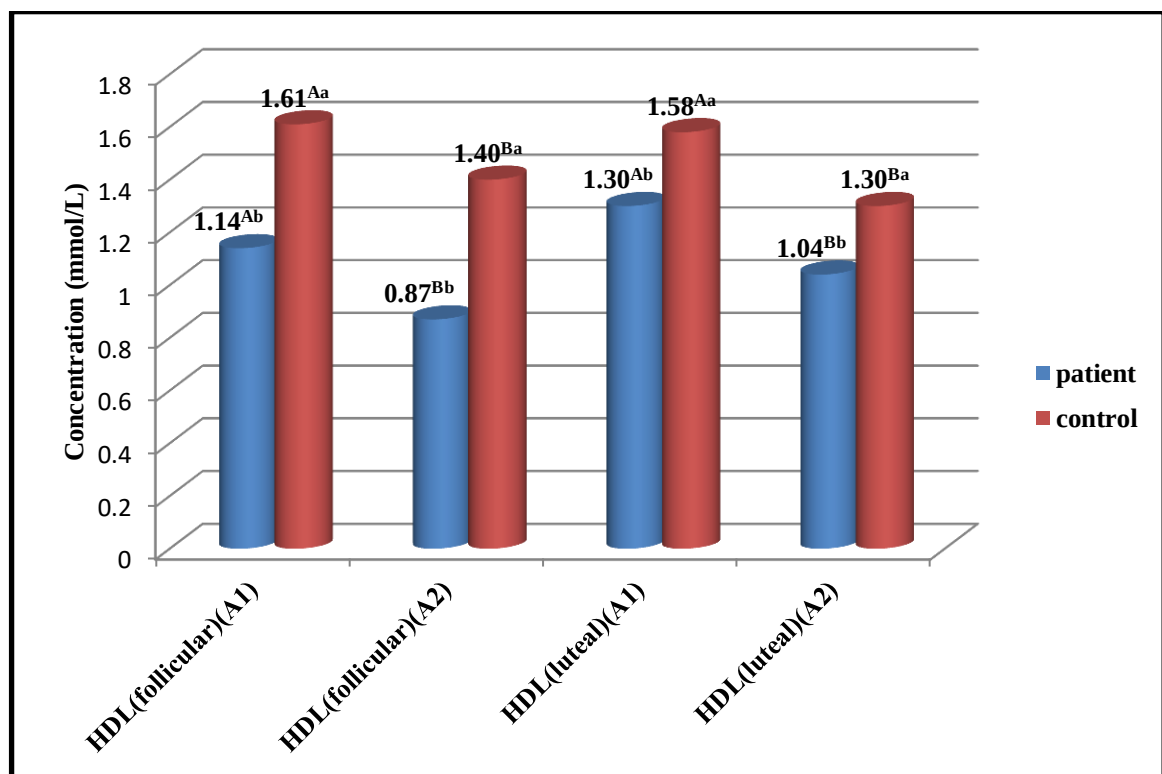


Figure (3-18): Serum HDL-c Concentrations for all Age Groups

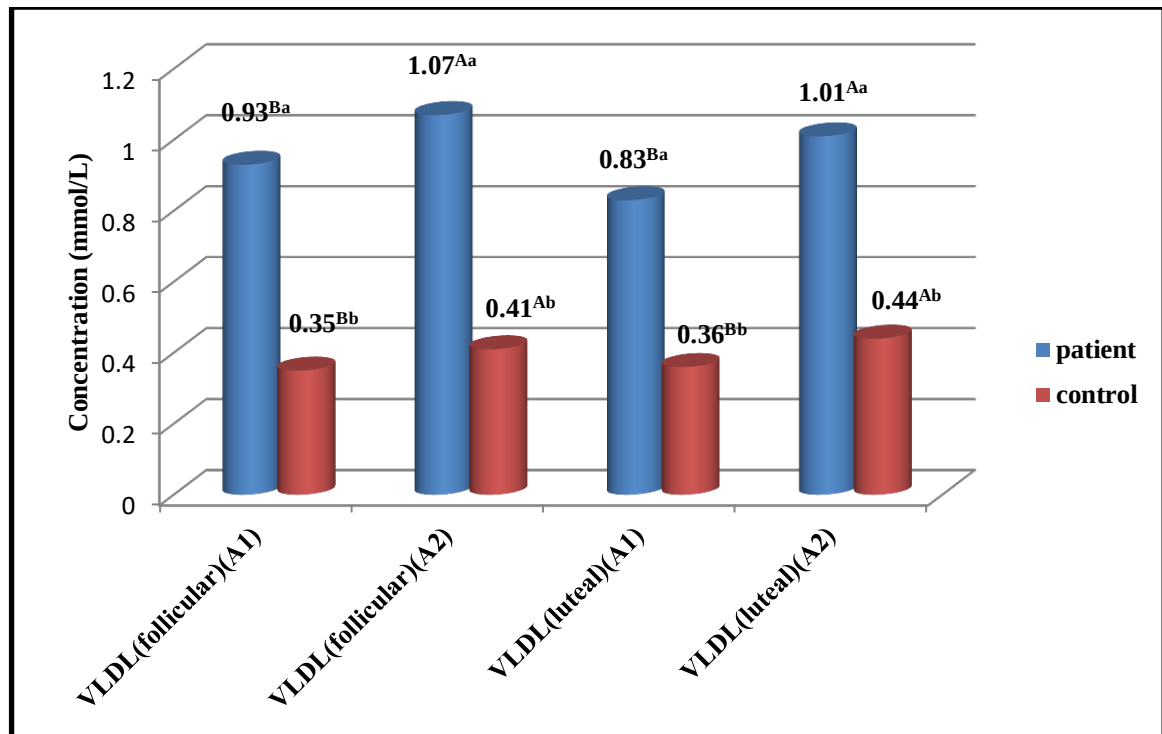


Figure (3-19): Serum VLDL-c Concentrations for all Age Groups

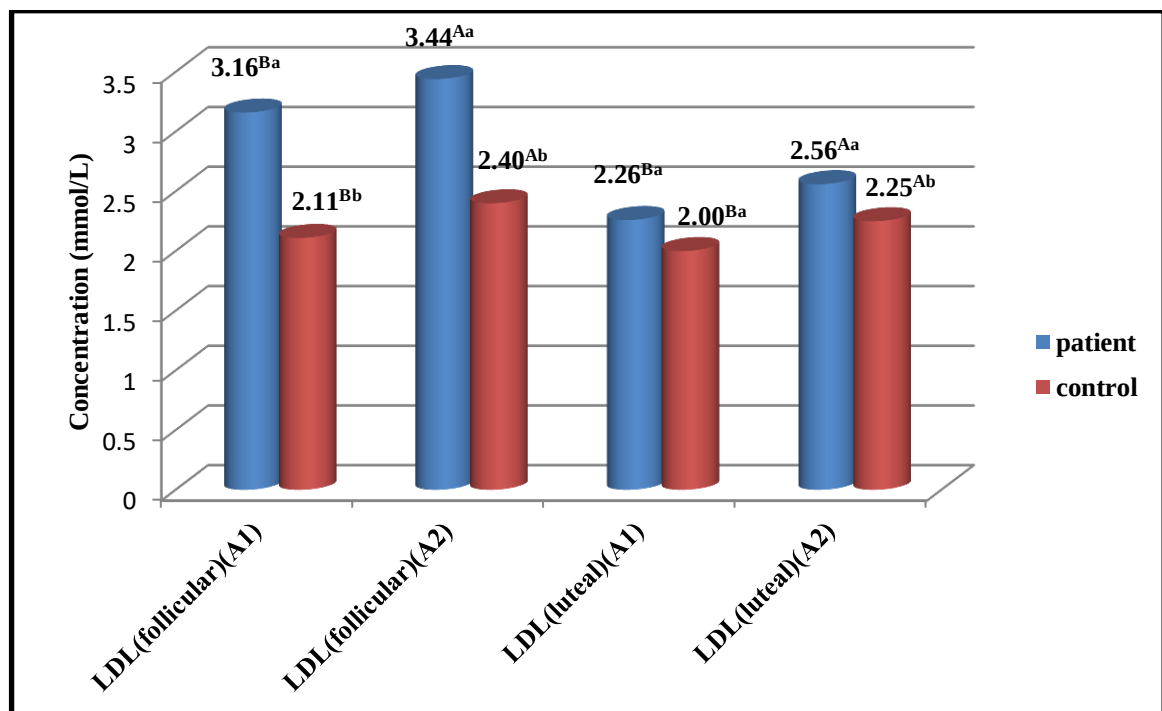


Figure (3-20): Serum LDL-c Concentrations for all Age Groups

Conclusions

From the results presented in this study, we can obtain the following conclusions during phases of the menstrual cycle (follicular and luteal phase) in women with bronchial asthma disease:

1. Bronchial asthma decreases the levels of both testosterone and progesterone.
2. Lipid peroxidation associates with bronchial asthma.
3. Disorder the antioxidant system in patients with bronchial asthma according to the levels of (Ceruloplasmin and Transferrin).
4. Dyslipidemia is present during bronchial asthma.
5. Age has an effect on the levels of (Testosterone, Progesterone, MDA, CP, TC, TG, HDL-c, VLDL-c and LDL-c) while there was no effect in (Tf) in both control and patients groups.
6. Phases of the menstrual cycle have an effect on (Testosterone, Progesterone, TC, TG, HDL-c, VLDL-c and LDL-c) while there was no effect in (MDA, CP and TF) levels.

Recommendations

It is important to design further studies relevant as indicated below:

1. Comparative study sex hormones in women with bronchial asthma in different phases of the menstrual cycle with and without contraceptive pills.
2. Study of the effects of physical activity on the levels of oxidants and anti-oxidant parameters in asthmatic athletes.
3. Effects of obesity classified according to body mass index (BMI) in women with asthmatic.

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الخلاصة

الربو هو اضطراب مزمن في التهابات مجرى الهواء المرتبطة بتجنيد الخلايا الالتهابية. ومع ذلك، يمكن أن تتأثر الإصابة، وشدة، والتنقبؤ من الربو من قبل عدد من العوامل، بما في ذلك التقلبات الهرمونية خلال مراحل الدورة الشهرية أثناء الربو في النساء.

تم تصميم هذه الدراسة لتحديد مستويات الهرمونات (التستوستيرون والبروجسترون) ، وأنماط الدهون (الكولسترول (TC)، الكليسيريدات الثلاثية (TG)، البروتينات الدهنية عالية الكثافة (HDL- c)، البروتينات الدهنية واطنة الكثافة جدا (VLDL-c) والبروتينات الدهنية واطنة الكثافة (LDL- c)) وحالة الإجهاد التأكسدي (المالونديهيد (MDA)، السيرلوبيلازمين (CP) والترانسفيرين (Tf)) خلال مرحلتين الدورة الشهرية (مرحلة الجريبي والأصفرى) في النساء المصابات بالربو.

تمت دراسة المعلمات المقاسة على أساس ثلاثة متغيرات: المقارنة العامة والعمر ومرحلتين الدورة الشهرية (مرحلة الجريبي والأصفرى).

تم تقسيم المرضى والأصحاء ، في المقارنة العامة ، إلى مجموعتين:

1- مجموعة السيطرة: ضمت (٧٠) امرأة من المفترض أن يكوناً أصحاء دون تناول حبوب منع الحمل التي تتراوح أعمارهن بين (١٤ - ٤٥) سنة.

2- مجموعة المرضى: ضمت (٧٠) مريضة مصابة بالربو القصبي دون تناول حبوب منع الحمل التي تتراوح أعمارهن بين (١٤ - ٤٥) سنة.

تم تقسيم المرضى والأصحاء وفقاً لأعمارهم ، إلى مجموعتين عمريتين: (A1) (١٤ - ٢٩) سنة و A2 (٣٠ - ٤٥) سنة.

تظهر النتائج التي تم الحصول عليها في هذه الدراسة انخفاضاً معنوياً في تراكيز (التستوستيرون ، البروجسترون و HDL-c) في جميع المرضى في كل من الطور الجريبي وكذلك في الطور الأصفرى بالمقارنة مع مجموعة السيطرة في الطور الجريبي والطور الأصفرى على التوالي ($P \leq 0.05$).

أظهرت الدراسة الحالية زيادة ملحوظة في تراكيز (TC ، TG ، VLDL-c ، LDL-c ، MDA و CP) في جميع المرضى في كل من الطور الجريبي وكذلك الطور الأصفرى بالمقارنة مع مجموعة السيطرة في الطور الجريبي والطور الأصفرى على التوالي ($P \leq 0.05$).

كما أظهرت النتائج عدم وجود فرق معنوي في تركيز (Tf) في جميع المرضى في كل من الطور الجريبي وكذلك في الطور الأصفر بالمقارنة مع مجموعة السيطرة في الطور الجريبي والطور الأصفر على التوالي ($P \leq 0.05$).

وفقاً للعمر في مجموعة السيطرة والمرضى، هناك زيادة ملحوظة في تراكيز (التستوستيرون، البروجسترون و HDL-c)، وانخفاض ملحوظ في تراكيز (LDL-c، VLDL-c، TG، TC)، MDA و CP) وعدم وجود فرق معنوي في تركيز (Tf) في المجموعة (A1) في الطور الجريبي والأصفر مقارنة مع المجموعة (A2) في طور الجريبي والأصفر على التوالي ($p \leq 0.05$).

وفقاً للعلاقة بين الطور الجريبي والأصفر، تظهر الدراسة زيادة ملحوظة في تراكيز (التستوستيرون، البروجسترون و HDL-c)، وانخفاضاً ملحوظاً في تراكيز (VLDL-C، TG، TC و LDL-c) وعدم وجود فرق في تراكيز (MDA، CP و Tf) في جميع المرضى في طور الأصفر بالمقارنة مع الطور الجريبي.



جمهورية العراق
وزارة التعليم العالي والبحث العلمي
جامعة ذي قار
كلية العلوم

دراسة البروجسترون والتستوستيرون و حالات الإجهاد التأكسدي
ونمط الدهون خلال مرحلتين من الدورة الشهرية لمرضى الربو
القصبي في محافظة ذي قار / العراق

رسالة

مقدمة إلى مجلس كلية العلوم / جامعة ذي قار
جزءاً من متطلبات نيل درجة الماجستير في الكيمياء الحياتية

من قبل

خالد عبد أيدام

بكالوريوس علوم كيمياء (جامعة ذي قار)

٢٠١١

بإشراف

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