بسم الله الرحمن الرحيم

Sudan University of Science &Technolog

College of Graduate Studies

Assessment of Prolactin level, Cholesterol and Triglyceride among Women with Polycystic Ovary Syndrome.

تقييم مستويات هرمون البرولاكتين ,الكوليسترول وثلاثي الغليسريداتلدى النساء المصابات بتكيس المبايض

A Dissertation Submitted in Partial Fulfillment for the Requirements of M.Sc. Degree in Medical Laboratory Science -Clinical chemistry

By:

Hind Ismail Abdalla Ahmad

B.Sc. in clinical-chemistry-medical laboratory

University of AL ImamAL Mahdi(2013)

Supervisor:

Dr.Abdelgadir ElmugadamPh.D. Clinicalchemistry-Medical Lab Science

Feb.2020

الآيـة

قال تعالى :

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ ۖ وَسَتُرَدُّونَ إِلَىٰ عَالِمِ الْغَيْبِ وَالشَّهَادَةِ فَيُنَبِّئُكُمْ بِمَا كُنْتُمْ تَعْمَلُونَ ﴿105﴾

صدق الله العظيم

سورة التوبة (الآية 105)

Dedication

With love and gratification I dedicate this work

To:

That person who hold my hand to teach me how

I step up on my life

My mother

Person who protect and help me all the timetolerate the

Sun burn and difficulties for us

My father

Person who stand with me and continuing to support me

My husband

My daughters I love you so much you are the reason of my happiness

keep twinkling on my sky ,godbless you

My sister,brothers,friends and relatives for their support

To all un visible hand work.

Acknowledgments

First great thanks referring to Allah for his mercies and guidance to live and achieve my goals.

Secondary it gives me apleasure and most honored to become supervised by such nice person **Dr.Abd elgadirElmugadam.**

Also special thanks to all members of Sudan university for science and technology (SUST)specially to staff members of clinical chemistry.

Great thankfulness to volunteers for their nice dealing with the research demands without any growl; as same as Dr. AL sir abo Alhassan infertility center staff.

Abstract

Background:

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinopathy characterized by both reproductive and metabolic abnormalities.This study was carried out to evaluate serum prolactin, cholesterol and triglyceride in poly cystic ovary syndrome woman in Khartoum state.

Methodology:

The study was carried on one hundred volunteer in reproductive age include 50woman as case and 50 as control at DR AL SIR Abo- Alhassan infertility center from may to November (2019),venous blood samples was collected ,processed ,and analyzed .prolactin level was estimated by Enzyme linked immune sorbent assay technique and cholesterol and triglyceride level were estimated spectrophotometer biosystem -310.Experimental case-control methodology was done. The obtained resultwere analyzed statistically by using of SPSS software program.

Result:

The level of prolactin wasincrease significant with (p-value=0.000),also cholesterol significant increase (p-value= 0.009)and triglyceride (p-value=0.001).

In poly cystic ovary syndrome patient compared to control group according to infertility ,duration of disease menstrual regulation ,family history ,cosmetic and use medication ,the study showed that prolactin increase insignificant with infertility ,therapy ,cosmetic and history with (p.value=0.124) (p.value=0.761)(p.value =0.611)(p.value= 0.986) respectively. But cholesterol increase significant compared with infertility with (p.value=0.031) and insignificant with

therapy (p.value=0.908), cosmetic (p.value=0.786) and menstrual cycle (p.value=0.180).

Triglyceride increased insignificantly with infertility (p.value=0.430), therapy (p.value=0.084) cosmetic (p.value=0.137) and menstrual cycle (p.value =0.721).

المستخلص

خلفية:

متلازمة المبيض المتعدد الكيسات (متلازمة تكيس المبايض)هي اعتلال الغدد الصماء الغير متجانس يتميز بكل من التشوهات التناسليه واعتلال في التمثيل الغذائي ,أجريت هذه الدراسة لتقييم مصل البرولاكتين ,الكوليسترولوثلاثيالغليسريدات لدى النساء المصابات بمتلازمة المبيبض المتعدد الكيسات في ولاية الخرطوم.

منهجية:

أجريت الدراسة على مائة متطوعة في سن الأنجاب ومنهم50امرأه(حالة)و50(مريض)في مركز الدكتور أبو الحسن للأنجاب وامراض الخصوبه في الفتره من مايو إلى نوفمبر (2019) وتم جمع عينات من الدم الوريدي ومعالجتها وتحليلها .قدرت بواسطة استخدام تقنية فحص الانزيمات المناعي المرتبط لمصل البرولاكتين وقدرت مستوى الكوليسترول والدهون الثلاثية بالنظام الحيوي الطيف _310. وقد تم تحليل النتيجه التي تم الحصول عليها إحصائيا باستخدام برنامج الحزمة الأحصائية للعلوم الأجتماع

النتيجة:

كان مستوى البرولاكتين في زيادة كبيرة بقيمة(p=0.000)وكذلك زيادة كبيرة في مستوي الكوليسترول بقيمة(p=0.009)ومستوى ثلاثي الغليسريدات بقيمة(p=0.001)في مرضى متلازمة تكيس المبايض مقارنة مع النساء التي لم تنجب ,وفترة الحيض ,وتاريخ الأسرة المرضي واستخدام مستحضرات التجميل والأدوية المستخدمة ’أظهرت الدراسة ان هرمون البرولاكتين يزيد عند النساء اللاتي لم ينجبن ويستخدمن .بعض العلاجات ومستحضرات التجميل ومن لديهن تاريخ مرضي بقيمة(p.value=0.986) (p.value=0.611)(p.value=0.761)(p.value=0.124)على التوالي . لكن الكوليسترول يزداد طرديا مقارنة مع اللاتي لم ينجبن ب(p.value=0.031)وليس لديه علاقة واضحة مع اللتي يستخدمن العلاج (p.value=0.908) ومستحضرات التجميل (p.value=0.786)ودورة الحيض(p.value=0.180)ويزداد ثلاثي الغليسريدات بشكل ضئيل عند النساء اللاتي لم ينجبنى (0.430)واللاتي يستخدمن العلاج (p.value=0.048)ومستحضرات التجميل (p.value=0.137)وفترة الحيض

(p.value=0.721).

الخلاصة:

وجد أن هناك زيادة في مستوى البرولاكتين , وثلاثي الغليسريدات والكوليسترول في المرضى الذين يعانون من متلازمة تكيس المبايض.

List of Contents

List of Tables

List of Figures

Abbreviations

ABBREVIATION	MEANING
BMI	Body Mass Index
FFAs	Free Fatty Acid
GnRH	Gonadotropin releasing hormone
HDL-C	High Density Lipo Protein
HL	Hepatic lipase
IR	Insulin Resistance
JACC	Journal of The American College of Cardiology
LDL-C	Low Density Lipo Protein
MS	Metabolic syndrome
PCOS	Polycystic Ovary Syndrome
T2DM	Type Tow Diabetes Mellitus
TRH	Thyroid Realizing Hormone
TSH	Thyroid Stimulating Hormone
VLDL	Very Low Density Lipo Protein

Chapter One

Introduction

1.1 Introduction:

Polycystic ovary syndrome (PCOS), characterized by hormonal imbalance and ovarian dysfunction, often starts during adolescence. Inconsistent diagnostic

criteria, variable provider knowledge, and lack of consensus pose specific challenges for the care of women with PCOS. These factors encourage inaccurate diagnosis with both under and overdiagnosis.This unfavorable diagnostic experience exasperates affected women and limits timely opportunities for intervention to minimize associated comorbidities, especially during the transition from pediatric to adult care. Recognition of these issues in the care of adolescents and women with PCOS inspired the development of the International Evidence-Based PCOS Guidelines, which emphasize the prevention, screening, and treatment of PCOS across the reproductive lifespan. The Guidelines and accompanying meta-analyses focus on three major categories of associated comorbidities: reproductive; metabolic and psychological. With the exception of infertility, this article considers common manifestations and comorbidities associated with PCOS throughout the lifecycle. The world wise prevalence of PCOS is estimated to be 5-10%. (kovanci, 2015).

Healthy lifestyle interventions with prevention of excess weight gain comprise the primary intervention for all comorbidities. Hence, early identification of girls "at risk" for PCOS and those with PCOS is a priority. Extensive guidelines for provider and patient education aim to decrease the medical, psychosocial, and economic burdens attributable to PCOS and its associated comorbidities**.(Selma et al., 2019**).

PCOS is not the only condition that can cause these types of menstrual irregularities or infertility but it is the most prevalent along with high prolactin

levels.High prolactin levels have many of the same symptoms as PCOS and needs to be ruled out using a blood test to be certain of a PCOS diagnosis.Prolactin is a hormone whose primary function is to initiate lactation. It is released by the pituitary gland, a small organ located at the base of the brain that influences the entire body. The pituitary gland produces prolactin and a number of other key hormones including growth hormone, luteinizing hormone, thyroid stimulating hormone, and adrenocorticotropin hormone.Excessive prolactin can cause a decrease in sex hormones like estrogen. When you have excessive amounts of prolactin in your blood it is called hyperprolactinemia. This is sometimes a marker of a condition known as prolactinoma, which is a tumor of the pituitary gland (usually non-cancerous). Prolactinomas produce higher than normal levels of prolactin, which can wreak havoc on the body and produce many PCOS-like symptoms(Robert etal., 2012) several factors, such as genetics, are variables in the development of polycystic ovarian syndrome. If your sister or mother has PCOS, your risk of also having it increases. Hormone imbalance is definitely a major influencing element in PCOS, together with a condition known as Insulin Resistance.(leo et al., 2016).)

The diagnosis of PCOS is based on the Rotterdam criteria for the presence of any two of the following conditions: (i) chronic anovulation, (ii) clinical/biochemical parameters for hyperandrogenism, and (iii) polycystic ovaries on ultrasonography.Insulin resistance, hyperandrogenism, and dyslipidemia are presumed to be the major risk factors for CVD in women with PCOS.(wang, 2017).

Insulin resistance and dyslipidemia allegedly play a key role on the risk of cardiovascular pathology in women with PCOS.The extent to which dyslipidemia leads to this risk is still not well understood. Dyslipidemia is the

most common abnormality in PCOS, with elevated levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol (LDL-C) and with low levels of high-density lipoprotein cholesterol (HDL-C). Talbott et al. reported increased level of LDL-C in patients with PCOS, and Conway et al. reported that the most characteristic lipid alteration is decreased levels of HDL-C. There are few studies done to know the alteration in serum lipid profile in PCOS patients; thus, this study was done to know the lipid profile variation in women with PCOS. (Gobal et al., 2016)

1.2.Rationale:

Polycystic ovary syndrome(PCOS) is the most series problem in woman worldwide and has public health importance as it is very common, affecting up to one in five woman of reproductive age and there is the most reason of infertility and abortion for many woman in last years which to be a target for research to find out the reason of thisdisease .Therefor,my objective is to examine the prolactin level ,cholesterol and triglyceride in polycystic ovary syndrome woman.

1.3Objectives:

General objective:

To evaluate serum prolactin level, cholesterol and triglyceridein polycystic ovary syndrome woman in Khartoum state.

Specific objective:

1. To measure serum prolactin level, cholesterol and triglyceride in patient with PCOS compared with control group.
2. To correlate between prolactin level, cholesterol and triglyceride.
3. To calculate body mass index(BMI).

4. Tocorrelate the biochemical parameter of the study with the variable age, BMI ,history of disease , use of cosmetic and regulation of menstrual cycle.

Chapter Two

Literature Review

2.Literature review

2.1 Definition:

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrinopathy characterized by both reproductive and metabolic abnormalities. In 2003,the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine redefined PCOS as the presence of two or more of the following features: oligo- or anovulation, signs of clinical or biochemical hyper androgen and ultrasonographic evidence of polycystic ovaries once other related endocrine and gynecological disorders are excluded.(R. Azzizetal., 2016)

Recent studies have shown an early onset of abnormal cardiovascular risk profile in women with PCOS. Many of these women develop abnormal glucose and lipid metabolism, hypertension, obesity, insulin resistance and other features suggestive of systemic inflammatory response. Because of the higher rates of prevalence of these risk factors, the symptoms of majority of the women with PCOS also fit into metabolic syndrome, which is a known risk factor for cardiovascular disorders.

A close correlation was observed between adiposity and the severity of symptoms in women with PCOS. The android type of body fat distribution, which is more commonly associated with metabolic disturbances, was found to be more common in women with PCOS.(Ghaffarzad etal., 2014)

In fact, studies that emphasized on anthropometric parameters in women with PCOS have revealed higher body mass index (BMI) and increased waist circumferenceinwomen with PCOS.(Patel et al., 2018) (Broughton et al., 2017).

2.2Symptoms:

Signs and symptoms of PCOSoften develop around the time of the first menstrual period during puberty. Sometimes PCOSdevelops later, for example, in response to substantial weight gain. A diagnosis of PCOSis made when you experience at leasttwoofthesesigns:Irregular periods. Infrequent, irregular or prolonged menstrual cycles are the most common sign of PCOS. For example, you might have fewer than nine periods a year, more than 35 daysbetween periods and abnormallyheavyperiods, Excess androgen, Elevated levels of male hormone may result in physical signs, such as excess facial and body hair (hirsutism), and occasionally severe acne and male-pattern baldness.Polycystic ovaries Your ovaries might be enlarged and contain follicles that surround the eggs. As a result, the ovaries might fail to functionregularly.PCOSsigns and symptoms are typically more severe if you're obese.(fahimeh et al., 2015).

2.3 Causes:

The exact cause of PCOSisn't known. Factors that might play a role include:

2.3.1 Excess insulin.

Insulin is the hormone produced in the pancreas that allows cells to use sugar, your body's primary energy supply. If your cells become resistant to the action of insulin, thenyour blood sugar levels can rise and your body might produce more insulin. Excess insulin might increase androgen production, causing difficulty with ovulation. (John et al.,2013)

2.3.2 Low-grade inflammation.

This term is used to describe white blood cells' production of substances to fight infection. Research has shown that women with PCOShave a type of low-

gradeinflammation that stimulates polycystic ovaries to produce androgens, which can lead to heart and blood vessel problems. (Milica et al.,2019)

2.3.3 Heredity.

Research suggests that certain genes might be linked to PCOS.(Jones et al., 2016)

2.3.4 Excess androgen.

The ovaries produce abnormally high levels of androgen, resulting in hirsutism and acne.(Jameson et al., 2017).

2.3.5Complications

Complications of PCOScan include:

Infertility

Gestational diabetes or pregnancy-induced high blood pressure Miscarriage or premature birthNonalcoholic steatohepatitis —a severe liver inflammation caused by fat accumulation in the liverMetabolic syndrome —a cluster of conditions including high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels that significantly increase your risk ofcardiovascular disease

Type 2 diabetes or prediabetes ,Sleep apnea, Depression, anxiety and eating disorders ,Abnormal uterine bleedingCancer of the uterine lining (endometrial cancer).Obesity is associated with PCOSand can worsen complications of the disorder.

(Lobo et al., 2017)

Studies have revealed that there are different degrees of obesity, dyslipidemia, insulin resistance (IR), oxidative stress and other metabolicabnormalities(Tehrani etal., 2014), and among these abnormalities,

dyslipidemia is one of the most common phenomena observed in women with(PCOS). (Macut etal., 2013).

Lipid abnormalities are found in women affected by PCOS. A recent study showed that mild hypercholesterolemia is frequently encountered in women with PCOS (Pergialiotisetal.,2018) .

Different lipidpatterns are present in PCOS, including low levels of high-density lipoprotein cholesterol (HDL-C), high triglyceride (TG), total cholesterol (TC) and low-density lipoprotein cholesterol(LDL-C) and significantly higher lipoprotein concentrations.A recent animal study found that the implementation of a high-fat diet in prepubertal rats induced metabolic andovarian alterations that were frequently present in PCOS, thus suggesting a potential impact of hyperlipidemia on the hormonal profile (Patel, 2018).

Obesity exerts a clear effect on oocytequality and early embryo growth that is triggered by lipo toxicityinduced endoplasmic reticulumstress, mitochondrial dysfunction and apoptosis(Broughton, 2017).

Observedphenotype-specific differences in lipid profiles based on androgen levels suggesting that androgens play an important role in hyperlipidemia.

(Spalkowska et al., 2018).

However, some studies have shownthat hypomethylated genes related to the synthesis of lipids and steroids may promote the synthesis of steroid hormones, including androgen, which could partially explain themechanisms of hyperandrogenismin PCOS(Panetal., 2018). These studies suggest that hyperandrogenismis an important cause of lipid abnormalities; in contrast, changes in genes related tolipids promote the development of hyperandrogenism. Women with mild hypercholesterolemia have a 11higher body mass index (BMI)

and higher fasting insulin and IRlevels than wo-menwith PCOSand normal cholesterol levels (Pergialiotis etal., 2018)

Experimental model rats exhibited ovarian changes, such as an increase in the number of cystic follicles and an increase in follicular wallthickness, in a high-fat diet-induced model of PCOS(Patel etal., 2018) suggesting that infertility is associated with dyslipidemia in PCOS. In conclusion, abnormal lipid metabolismcan promote thepathophysiology of hyperandrogenism, IR, oxidative stress, and infertility in PCOS.The waist-to-hip ratio, which is higher in PCOSwomen, is more sensitive to dyslipidemia because centrally located adipocytes appear to exert a detrimental effect on blood lipids;centrally distributed adipose tissue can also secrete a range of adipokines into circulation to increase inflammation (Spritzer etal., 2015)suggesting that adipokines are associated withinflammation in PCOS.(Mannera etal., 2011)

In addition, a high level of circulating free fatty acids (FFAs), which contribute to the development of PCOS, is most common among obese PCOSpatients(Mlinaretal., 2011).

A study found low levels of HDL and high levels of TGs in women with PCOS(Zhangetal., 2018) and HDLs are predictive for the occurrence of metabolic syndrome (MS) in PCOS(Shaman etal.,2017).

A clearincrease in LDL has been observed in PCOS, and LDL levels decrease after treatment with statinsTherefore, an abnormal lipid profile affects the pathological development of PCOS. FFAs, HDL and LDL related to lipidabnormalities play an important role in PCOS. Obesity, IRand hyperandrogenemia exert independent and interrelated effects on circulating lipid profiles, but the effect of lipid profileson IR, hyperandrogenemia, oxidative stress and anovulation remain under exploration. (Seyametal., 2017).

2.3.6 Diagnosis of poly cystic ovary syndrome:

Diagnosis can generally be accomplished with a careful history, physical examination, and basic laboratory testing, without the need for ultrasonography or other imaging. Hyperandrogenism can be diagnosed clinically by the presence of excessive acne, androgenic alopecia, or hirsutism (terminal hair in a male-pattern distribution)or chemically, by elevated serum levels of total, bioavailable, or free testosterone or dehydroepiandrosterone sulfatemeasurement of androgen levels is helpful in the rare occasion that an androgen-secreting tumor is suspected (e.g., when a patient has marked virilization or rapid onset of symptoms associated with PCOS)(Gibson et al., 2016).

Ovulatory dysfunction refers to oligomenorrhea (cycles more than 35 days apart but less than six months apart) or amenorrhea (absence of menstruation for six to 12 months after a cyclic pattern has been established (Dewailly et al., 2014).

2.4Prolactin:

Prolactin is a hormone that affects many different hormones in the body. Present in both men and women, it rarely causes problems, but those who are serious about their health should understand what it is and how it impacts the body’s overall health and well-being .Prolactin, as its name implies, is a hormone that promotes lactation (breast milk production) in mammals and is responsible for a number of other functions and systems. Prolactin is created in the front portion of the pituitary gland in your brain, as well as in the uterus, brain, breasts, prostate, adipose tissue, skin, and immune cells. (Bernard V et al., 2019).

Prolactin is released when a newborn baby suckles at his/her mother's breast, causing the production of milk. However, this is just the primary and most well-known purpose of prolactin. (Jinet al., 2019)

2.4.1 Production of prolactin:

Production of prolactin is controlled by two main hormones: dopamine and estrogen. These hormones send a message to the pituitary gland primarily indicating whether to begin or cease the production of prolactin. Dopamine restrains the production of prolactin, while estrogen increases it. (Li etal., 2019)

2.4.2 clinical manifestation:

For most people, prolactin does its job without a problem, and few are aware of the impact it has on their health. Yet some people can struggle with prolactin levels, which can cause a variety of problems.(Bernardetal., 2019) Too much prolactin in the blood causes hyperprolactinemia, a condition that can lead to menstrual disturbances, estrogen deficiency and testosterone deficiency. High prolactin levels also can cause unwanted lactation. This often occurs during pregnancy or when the thyroid is not functioning properly. Pituitary tumors, known as prolactinomas, and medications that reduce dopamine can also lead to increased prolactin levels. High levels of prolactin are linked to sexual problems. Some of these conditions can be treated with medications that mimic the action of dopamine.It's also possible to have too little prolactin, a condition known as hypoprolactinaemia. This is extremely rare, but it can occur if people have under-active pituitary glands. This is commonly noticed in women after pregnancy who are not able to produce sufficient milk. No other proven health effects of low prolactin levels have been noted. Research is underway to determine if those with low prolactin levels suffer from a reduction in immune system responses.

(Vilaretal., 2019).

Prolactin has a major role in the physiology of the breast, especially in females. Both a lack of prolactin secretion and excessive prolactin secretion result in

clinical presentations. The level of prolactin hormone is detrimental to the female's ability to lactate. Thus, imbalances in the prolactin level can compromise this ability. Furthermore, disruption in the prolactin balance can have significant effects on the menstrual cycle. In females, too much prolactin leads to amenorrhea (absence of menstruation). The physiological reason for this is related to the prolactin role in the hypothalamus-pituitary reproductive axis which will be discussed in detail later. In males, however, prolactin level imbalances have different clinical manifestations. Too much prolactin in males' results in headaches and decreased libido. The decreased libido in males is associated with decreased spermatogenesis as a result of elevated prolactin affecting hypothalamus pituitary reproductive axis.(Matalliotakis etal., 2019)

(Auriemma etal., 2019)

2.4.3 Syntheses of prolactin:

Prolactin is synthesized by lactotrophs in the anterior pituitary gland. The number of lactotrophs will increase during pregnancy in response to the physiological need to develop breast tissues and to prepare for milk production. Prolactin production is regulated at the gene transcription level. Factors that stimulate prolactin secretion to upregulate prolactin gene transcription while factors that inhibit prolactin secretion downregulate prolactin gene transcription.(Auriemmaetal., 2019).

The most important factors that regulate prolactin secretion are: thyrotropin-releasing hormone (TRH) and dopamine both secreted by the hypothalamus. TRH has a stimulatory effect on thyroid-stimulating hormone (TSH) as well as prolactin; whereas, dopamine has an inhibitory effect on prolactin. In the absence of pregnancy (i.e., high estrogen) or lactation, prolactin is tonic ally inhibited by dopamine and the effect of dopamine trumpets the effect of TRH. Prolactin has a

negative feedback on its own production by stimulating the release of dopamine in the hypothalamus. Medications that antagonize dopamine production, for example, an antipsychotic block, the tonic inhibition of dopamine result in symptoms of excessive prolactin. Conversely, medications that are dopamine agonists such as bromocriptine or cabergoline inhibit prolactin secretion. Thus, these medications are used in the treatment of prolactinoma. Estrogen in high levels, as the case with pregnancy, stimulate prolactin release directly from the anterior pituitary. Interestingly, suckling stimulates sensory nerves in the nipple that carries the signal via the spinal cord to arcuate nucleus which inhibits dopamine release by removing the inhibitory action of dopamine on prolactin. At the same time, the afferent signal from the nipple activates supraoptic and paraventricular nuclei to increase the production of oxytocin which allows for milk ejection. Prolactin also has an inhibitory effect on the release of gonadotropin-releasing hormone (GnRH) produced by the hypothalamus-inhibiting FSH and LH release from the anterior pituitary. This leads to inhibition of the ovulatory cycle in females which explains the lactational amenorrhea. This mechanism serves as a natural contraceptive and may play a role in spacing out pregnancies. Similarly, prolactin in males inhibits GnRH release resulting in decreased spermatogenesis and infertility.(Raut etal., 2019)(Kumar, 2019) (Štelcletal., 2018).

2.4.4 Function:

Prolactin function is still being studied, but research seems to show a variety of purposes for this hormone. For instance, it also regulates behavior, the immune system, metabolism, reproductive systems, and many different bodily fluids.

This makes it a crucial hormone for overall health and well-being, for both men and women(Kumar, 2019).

The main tow functions of prolactin are to stimulate milk production and to develop breast tissues. Prolactin plays a role in breast development with estrogen and progesterone by stimulating further breast growth and enlargement of the alveoli in preparation for lactation. In addition to breast tissues development, prolactin is an essential player in milk production. Prolactin stimulates milk production by inducing the enzyme that synthesizes the constituents of milk, such as lactose (the carbohydrate of milk), casein (the protein of milk), and lipids. Prolactin is involved in the biosynthesis of milk constituents by binding to the cell membrane and inducing the transcription cascade to make the necessary enzymes for milk production. Lactogenesis does not occur, however; until after parturition because high estrogen and progesterone during pregnancy down regulate prolactin receptors in the breasts. After parturition, the estrogen and progesterone levels fall precipitously. Thus, the inhibitory effects on the breast are removed. As long as suckling is maintained, prolactin level stays elevated after the pregnancy with each episode of feeding producing peak prolactin levels. If the mother does not nurse her baby, prolactin levels fall to non-pregnant levels after 1 to 2 weeks.

(Auriemmaetal., 2019)

2.4.5 Reference Range:

The reference ranges for prolactin in females is as follows:
Adult female: 3-27 ng/ml

Pregnant female: 20-400 ng/mLThe reference range for prolactin in adult males is 3-13 ng/mL. (Paganaet al.,2019)

2.5.5 Interpretation:

Hyperprolactinemia is associated primarily with prolactin-secreting pituitary tumors (prolactinoma).Conditions associated with prolactin deficiency include anterior pituitary dysfunction secondary to the followingPostpartum pituitary necrosis (Sheehan syndrome)Pituitary tumor, extrapituitary tumor,Treatment ofpituitary/extra pituitary tumor,Parasailerdisease, Head injury, Infection (tuberculosis,histoplasmosis)andInfiltrativedisease(sarcoidosis,hemochromatosis)(Paganaet al.,2019).

2.5Dyslipidemia and polycystic ovary syndrome.

Dyslipidemia is common in PCOS characterized by higher triglycerides and lower highdensity lipoprotein cholesterol. The dyslipidemia occurs independent of body mass index (BMI)however there is a synergistic deleterious effect of obesity and insulin resistance in PCOS analogous to that seen in T2DM. Dyslipidemia in PCOS has multifactorial causation. Insulin resistance plays a pivotal role by stimulation of lipolysis and altered expression of lipoprotein lipase and hepatic lipase. (QilL,2019).

2.5.1 cholesterol:

Cholesterol is a lipophilic molecule that is essential for human life. It has many roles that contribute to normally functioning cells. For example, cholesterol is an important component of the cell membrane. It contributes to the structural makeup of the membrane as well as modulates its fluidity. Cholesterol functions as a precursor molecule in the synthesis of vitamin D, steroid hormones (e.g., cortisol and aldosterone and adrenal androgens), and sex hormones (e.g., testosterone, estrogens, and progesterone). Cholesterol is also a constituent of bile salt, which is used in digestion to facilitate absorption of fat-soluble vitamins A, D, E, and K.(Di Ciaulaetal., 2017).

2.5.1.1 Sources of cholesterol:

Cholesterol can be introduced into the blood through the digestion of dietary fat via chylomicrons. However, since cholesterol has an important role in cellular function, it can also be directly synthesized by each cell in the body. The synthesis of cholesterol begins from Acetyl-CoA and follows a series of complex reactions that will not be covered in this article. A primary location for this process is the liver. (Asha, 2018).

There are several types of lipoproteins that travel through the blood, and they each have different purposes. There are high-density lipoproteins (HDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), and very low-density lipoproteins (VLDL). Notably, LDL particles are thought to act as a major transporter of cholesterol, at least two-thirds of circulating cholesterol resides in LDL, to the peripheral tissues. Conversely, HDL molecules are thought to do the opposite. They take excess cholesterol and return it to the liver for excretion. Clinically, these two lipoproteins are significant since high LDL, and low HDL increase a patient's risk of atherosclerotic vascular diseases (Sacksetal., 2017). (Karneyetal., 2017)

2.5.1.2 Functions of cholesterol:

Within the cell, cholesterol has several vital functions. Some of the primary uses for cholesterol are related to the cell membrane. It is required for the normal structure of the membrane; it contributes to its fluidit. This fluidity can influence the ability of some small molecules to diffuse through the membrane which ultimately changes the internal environment of the cell.Also within the membrane, cholesterol plays a role in intracellular transportation. Beyond its place in the cell membrane, cholesterol has several other biological functions. Of note, cholesterol is known to be an important precursor molecule for the

synthesis of vitamin D, cortisol, aldosterone, progesterone, estrogen, testosterone, bile salts, among others. (Dotson etal., 2017)

2.5.1.3Causes of high cholesterol:

High cholesterol is a significant risk factor for coronary heart disease and a cause of heart attacks.A build-up of cholesterol is part of the process that narrows arteries, called atherosclerosis. In atherosclerosis, plaques formed cause restriction

of blood flow.Reducing the intake of fat in the diet helps to manage cholesterol levels. In particular, it is helpful to limit foods that containCholesterolThis is present in animal foods, meat, and cheese.Saturated fat. This occurs in some meats, dairy products, chocolate, baked goods, deep-fried, and processed foods.Trans fats: This occurs in some fried and processed foods.Excess weight or obesity can also lead to higher blood LDL levels. Genetic factors can contribute to high cholesterol.Peoplewiththeinheritedcondition familial hypercholesterolemiahaveveryhighLDLlevels.

Other conditions that can lead to high cholesterol levels, include: diabetesliver or kidney diseasepolycystic ovary syndrome pregnancy and other conditions that increase levels of female hormones underactive thyroid glanddrugs that increase LDL cholesterol and decrease HDL (Hammersley etal., 2017).

2.5.1.4 Diagnosis of cholesterol:

A blood test to check cholesterol levels -called a lipid panel or lipid profile- typically reports: Total cholesterol, LDL cholesterol and HDL cholesterol. For the most accurate measurements, don't eat or drink anything (other than water) for nine to 12 hours before the blood sample is taken. (Bethesda, Md., 2019).

According to the 2018 guidelines on the management of blood cholesterol published in the Journal of the American College of Cardiology (JACC), these are the acceptable, borderline, and high measurements for adults.

(American Academy of Pediatrics).

All values are in mg/dL (milligrams per deciliter) and are based on fasting measurement.Total cholesterol HDL cholesterol LDL cholesterol Triglycerides Good Less than 200 (but the lower the better) Ideal is 60 or higher; 40 or higher for men and 50 or higher for women is acceptable Less than 100; below 70 if coronary artery disease is present Less than 149; ideal is <100 Borderline to Moderately elevated 200–239 n/a 130–159 150–199 High 240 or higher n/a 160 or higher; 190 considered very high 200 or higher; 500 considered very high Low n/a less than 40 n/a

.(pagana et al., 2019)

2.6 triglyceride:

Triglycerides are a type of fat (lipid) found in your blood. When you eat, your body converts any calories it doesn't need to use right away into triglycerides. Thetriglycerides are stored in your fat cells. Later, hormones release triglycerides for energy between meals. If you regularly eat more calories than you burn, particularly from high-carbohydrate foods, you may have high triglycerides (hypertriglyceridemia). (Bonow et al., 2019).

2.6.2 Normal level of triglyceride:

Normal: Less than 150 milligrams per deciliter (mg/dL), or less than 1.7

millimoles per liter (mmol/L)

Borderline high: 150 to 199 mg/dL (1.8 to 2.2 mmol/L)

High: 200 to 499 mg/dL (2.3 to 5.6 mmol/L)

Very high: 500 mg/dL or above (5.7 mmol/L or above.

(Kumar p et al., 2018.)

High triglycerides may contribute to hardening of the arteries or thickening of the artery walls (arteriosclerosis)which increases the risk of stroke, heart attack and heart disease. Extremely high triglycerides can also cause acute inflammation of the pancreas (pancreatitis). High triglycerides are often a sign of other conditions that increase the risk of heart disease and stroke, including obesity and metabolic syndrome a cluster of conditions that includes too much fat around the waist, high blood pressure, high triglycerides,high blood sugar and abnormal cholesterol levels.(Mary et al., 2019).

High triglycerides can also be a sign of: Type 2 diabetes or prediabetes Metabolic syndrome a condition when high blood pressure, obesity and high blood sugar occur together, increasing your risk of heart disease Low levels of thyroid hormones (hypothyroidism) Certain rare genetic conditions that affect how your body converts fat to energy Sometimes high triglycerides are a side effect of taking certain medications, such as: Diuretics ,Estrogen and progestin, Retinoids, Steroids, Betablockers ,Some immunosuppressants and Some HIV medications.(Kumar et al.,2018).

Chapter Three

Material and Methodology

3.Material and Methodology

3.1 study design:

Case- control (Experimental) hospital base study.

3.2 study area:

This study carried in in al-Khartoum state during the period from May 2019to November 2019 in DRALSIR Abo- AlHassan Infertility Center.

3.3 study populationand sample size:

The study includevolunteer woman whom have medical report of polycystic ovary syndrome. 50 sample were obtained from patient and 50 from healthy non polycystic over syndrome (control group).

3.4 inclusion and exclusion criteria:

Samples were collectfrom woman in reproductive age that inclusion of ultrasonography evidence of poly cystic ovary syndrome as diagnostic markerbut exclude pregnant woman, infectious disease, metabolicdisease.

3.5 collection sample:

One hundred(100) Sample were collected by using sterile dry plastic syringetourniquet was used to make veins more prominent puncture site was cleaned with 70%ethanol and blood sample (5ml) was collect in plane container from each volunteer.

All blood sample were allowed to collect to clot at room temperature. Then they were centrifuged at 4000rpm to obtain the serum and stored in 20c until analysis.

3.6 Ethical approval:

The study was approved from clinical chemistry department and medical laboratory science in SudanUniversity for science and technology.

Prior to the beginning of the study, subject were informed about the protocol of the study and were asked to sign Consent form was taken regarding acceptance, the donor known that this specimen was collected for research purpose.

3.7Methodology:

The laboratory tests were performed at Khartoum University laboratory, by using enzyme linked immunosorbent assay technique designed for detecting an quantifying hormone which an antigen must be immobilized to a solid surface then complexed with an antibody that is linked to an hormone.

3.7.1 Prolactin:(immune enzymatic assay)

3.7.1.1Principle:

Theessential reagent required for animmune enzymatic assay include high affinity and specify antibodies (enzyme labelled and immobilized)with different and distinctepitopesrecognition , in excess,and native antigen.in this procedure ,the immobilization takes place during the assay at the surface of a micro plate well through the interaction of streptavidin coated on the well and exogenously added biotinylated monoclonal anti-PRL antibody .

Upon mixing monoclonal biotinylated antibody, the enzyme labeled antibody and serum containing the native antigen,reaction results between the native antigen and the antibodies,without competition or steric hindrance to form a soluble sandwich complex. |

3.7.1.2 Procedure of Measurement (appendix)

3.7.2 Cholesterol:

(Enzymatic method)

3.7.2.1 Principle of cholesterol oxidase method

serum cholesterol is measured by cholesterol ester +H2O **cholesterol oxidase** =cholesterol+ fatty acid

cholesterol+O2 **cholesterol oxidase**= 4-cholesterol-3-one +H2O2

H2O2+4 aminophenazone**peroxidase**

= quinone mine +H2O.

3.7.2.2 Procedure of measurement(appendix**)**

3.7.3 Triglyceride

3.7.3.1Principle:

Triglyceride -------lipase =**glycerol +fatty acid**

Glycerol + ATP --------glucokinase = **Glycerol 3 phosphate + ADP**

Glycerol 3 phosphate +---------Glycerol phosphate oxidase =**Dihydroxyacetone -phosphate +H2O2**

H2O2 + 4-aminoantipyrin ------peroxidase =**Quinn amine + HCL +H2O.**

3.7.3.2 Procedure of measurement (appendix)

3.8 quality control:

The precision and accuracy of all method used in this study were checked by commercially prepared pathologically control sample before the application of tests measurement.

3.9 statisticalanalysis

Data was analyzed to obtain mean,standard deviation,and correlation by using statistical package for social science (SPSS)computer programmed version 22,

Chapter Four

Results

4.Results:

The result of biochemical parameter prolactin, cholesterol and triglyceride of poly cystic ovary syndrome women are given in tables and figures.

Table (4-1):show frequency of infertile women 17(34%) and unfertile were 33(66%), frequency of therapy uptake woman were 16(32%) and 34(68%)for not therapy uptake.

Also, frequency of cosmetic use were 30(60%) and 20(40%) not use cosmetic.

The frequency of women have history of disease 19(38%) and have not history of PCOS 31(62%).

Frequency analysis of regular menstrual cycle women 28(56%) and irregular 22(44%).

Table (4-2): show mean of age 30±6.59 and the mean of year's duration was

2.281±.78.

Table (4-3):show significant increase in prolactin, cholesterol and triglyceride with

p.value (0.000),(0.009),(0.001) respectively.

Table (4-3): show mean of prolactin infertile women (34.35±25.5) and unfertile (64.592±6.53) with (p.value=0.124) and mean of cholesterol of infertile women 203.0±36.81 and unfertile (178.8±36.21) with p.value (0.031)

Triglyceride mean with infertility women (192.8±36.81) and unfertile 184.0±34.58 with p.value (0.430).

Table (4-4): mean of the prolactein level take therapy 44.13±27.79 and not take therapy 41.64±26.38 with p.value (0.761) and cholesterol mean of woman take therapy(186.1±38.89) and 187.5 ±37.94 with p.value(0.908)

Triglyceride mean of women take therapy 200.2 ±39.47 and women not take therapy 180.8±34.59 with p.value(0.084)

T**able (4-5):**prolactin mean of women use cosmetic 40.85±25.21 and not use 44.81±29.01 wiithp.(0.611) and cholesterol mean 185.9±42.54 and 188.9 ±30.42 for cholesterol in women not use cosmetic with p.value(0.786)

Triglyceride mean 193.4 ±37.12 in cosmetic women and 177.5 ±35 in not use with p.value(0.137).

Table (4-6): mean of prolactin have history of disease 42.38± and 42.38±27 for women have not history with p.value(0.986).

Cholesterol mean 191.37 ±36.11 and 184.4±39.22 with p.value(0.532)

Triglyceride 181.2±32.59 and 190.6±39.49 with p.value (0.387)

Table(4-7): mean of prolactin in regular mensterual cycle37.60 ±24.72 and irregular 48.58 ±28.15 with p.value (0.149)

Mean of triglyceride in regular180.6 ±38.69 and irregular 195.2 ±35.98 with p.value(0.180)

Mean of triglyceride in regular185.3 ±39.30 and irregular 189.13 ±34.5 with p.value(0.721).

Table(4-1):show the demographic data of the patient of polycystic ovary syndrome.

Variables	**Frequency**	**Percentage (%)**
Infertility		
Yes	17	34.0
No	33	66.0
Therapy		
Yes	16	32.0
No	34	68.0
Cosmetic		
Yes	30	60.0
No	20	40.0
History		
Yes	19	38.0
No	31	62.0
Menstrual cycle		
Regular	28	56.0
Irregular	22	44.0
Total	**50**	**100.0**

Table(4-2):Mean concentration of patient age and duration of diseases.

Variables	Minimum	Maximum	Mean ±SD
Age (Years)	19.0	45.0	30.0±6.59
Duration (Years)	1.00	10.0	2.28±1.78

Table (4-3): show the Mean ±SD of prolactin, cholesterol and triglyceride in patient with control group.

Parameters	Case (Mean±SD)	Control (Mean±SD)	*P-value*
Prolactin (ng/mI)	42.43±26.57	25.39±19.46	0.000
Cholesterol (mg/dI)	187.0±37.85	152.4±83.24	0.009
Triglyceride (mg/dI)	187.0±36.96	149.4±92.59	0.001

*Result given in mean ±SD, *p-value* <0.05 consider significant.

Table (4-4): show the Mean ±SD of prolactin, cholesterol and triglyceride in Infertile and fertile.

Parameters	Yes (Mean±SD)	No (Mean±SD)	*P-value*
Prolactin (ng/mI)	34.35±25.50	46.59±26.53	0.124
Cholesterol (mg/dI)	203.0±36.81	178.8±36.21	0.031
Triglyceride (mg/dI)	192.8±41.71	184.0±34.58	0.430

Result given in mean ±SD, *p-value* <0.05 consider significant.

Table(4-5): show the Mean ±SD of prolactin, cholesterol and triglyceride in patient use therapy and non-use.

Parameters	Yes (Mean±SD)	No (Mean±SD)	*P-value*
Prolactin (ng/mI)	44.13±27.79	41.64±26.38	0.761
Cholesterol (mg/dI)	186.1±38.89	187.5±37.94	0.908
Triglyceride (mg/dI)	200.2±39.47	180.8±34.59	0.084

Result given in mean ±SD, *p-value* <0.05 consider significant

Table (4-6) show the Mean ±SD of prolactin , cholesterol and triglyceride in patient use Cosmetic and not use.

Parameters	Yes (Mean±SD)	No (Mean±SD)	*P-value*
Prolactin (ng/mI)	40.85±25.21	44.81±29.01	0.611
Cholesterol (mg/dI)	185.8±42.54	188.9±30.42	0.786
Triglyceride (mg/dI)	193.4±37.12	177.5±35.50	0.137

Result given in mean ±SD, *p-value* <0.05 consider significant

Table (4-7): show the Mean ±SD of prolactin, cholesterol and triglyceride in patients have history of poly cystic ovary syndrome and not.

Parameters	Yes (Mean±SD)	No (Mean±SD)	*P-value*
Prolactin (ng/mI)	42.52±26.08	42.38±27.31	0.986
Cholesterol (mg/dI)	191.37±36.11	184.4±39.22	0.532
Triglyceride (mg/dI)	181.2±32.59	190.6±39.49	0.387

Result given in mean ±SD, *p-value* <0.05 consider significant

Table (4-8): show the Mean ±SD of prolactin, cholesterol and triglyceride in regular menstrual cycle and irregular menstrual cycle patient.

Parameters	R (Mean±SD)	IR (Mean±SD)	*P-value*
Prolactin (ng/mI)	37.60±24.72	48.58±28.15	0.149
Cholesterol (mg/dI)	180.6±38.69	195.2±35.98	0.180
Triglyceride (mg/dI)	185.3±39.30	189.13±34.55	0.721

Result given in mean ±SD, *p-value* <0.05 consider significant

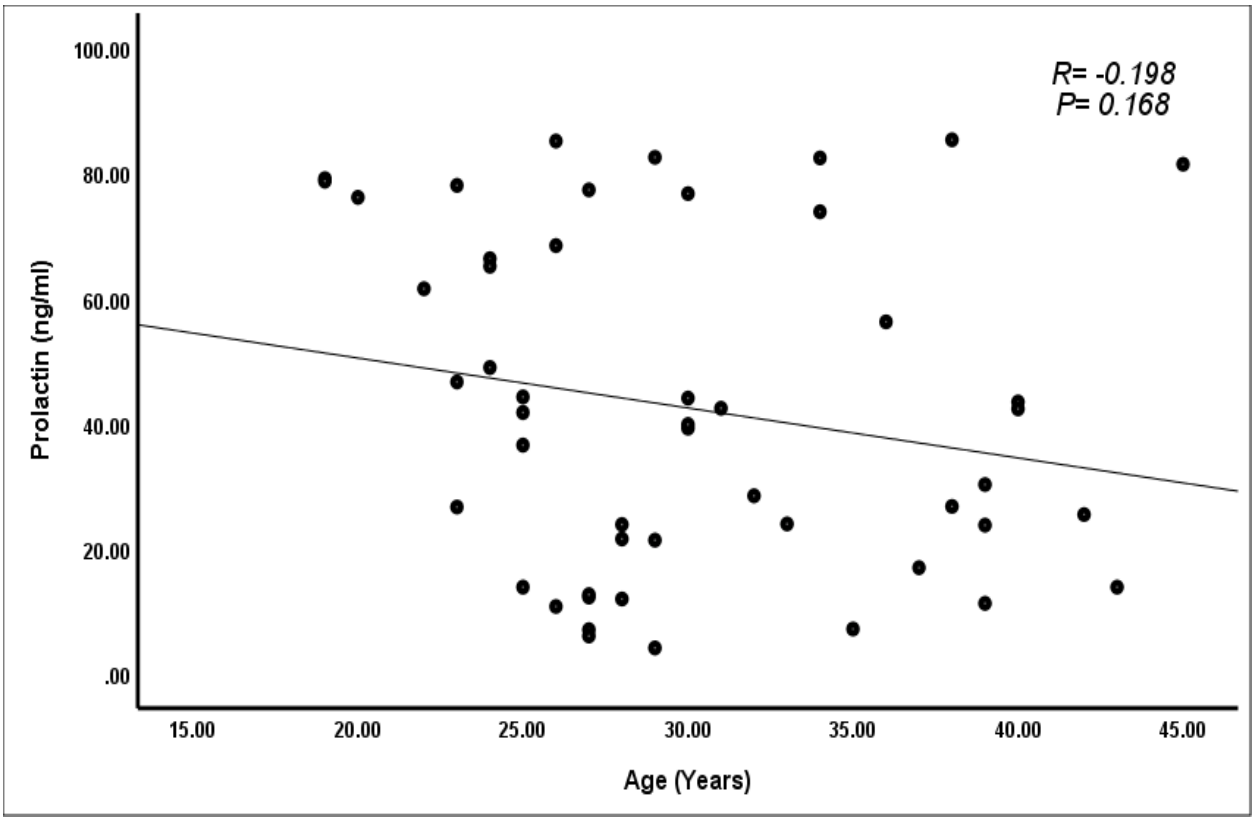


Figure (4-1):scatter plot of pearson correlation between prolactein and age of PCOS woman .

r= -0.198,p.value= 0.168.

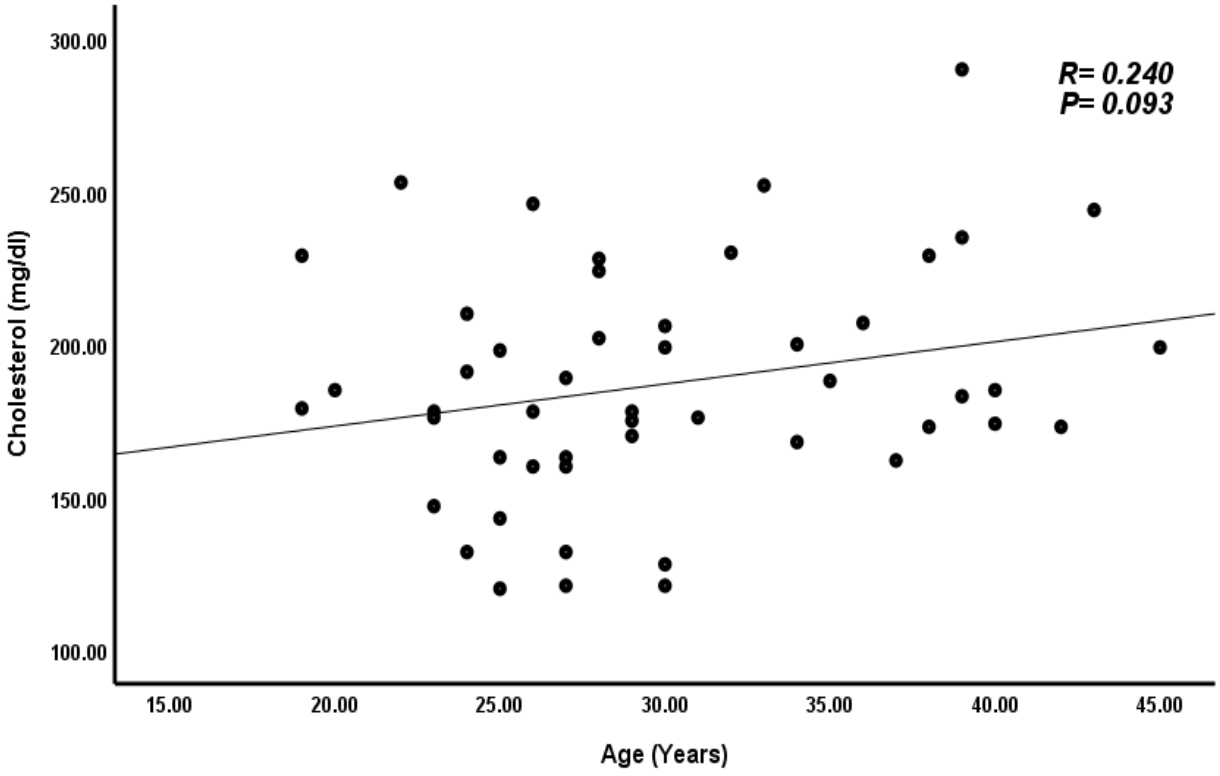


Figure (4-2):scatter plot of pearson correlation between cholesterol and age of PCOS woman .

r= 0.240,p.value= 0.093

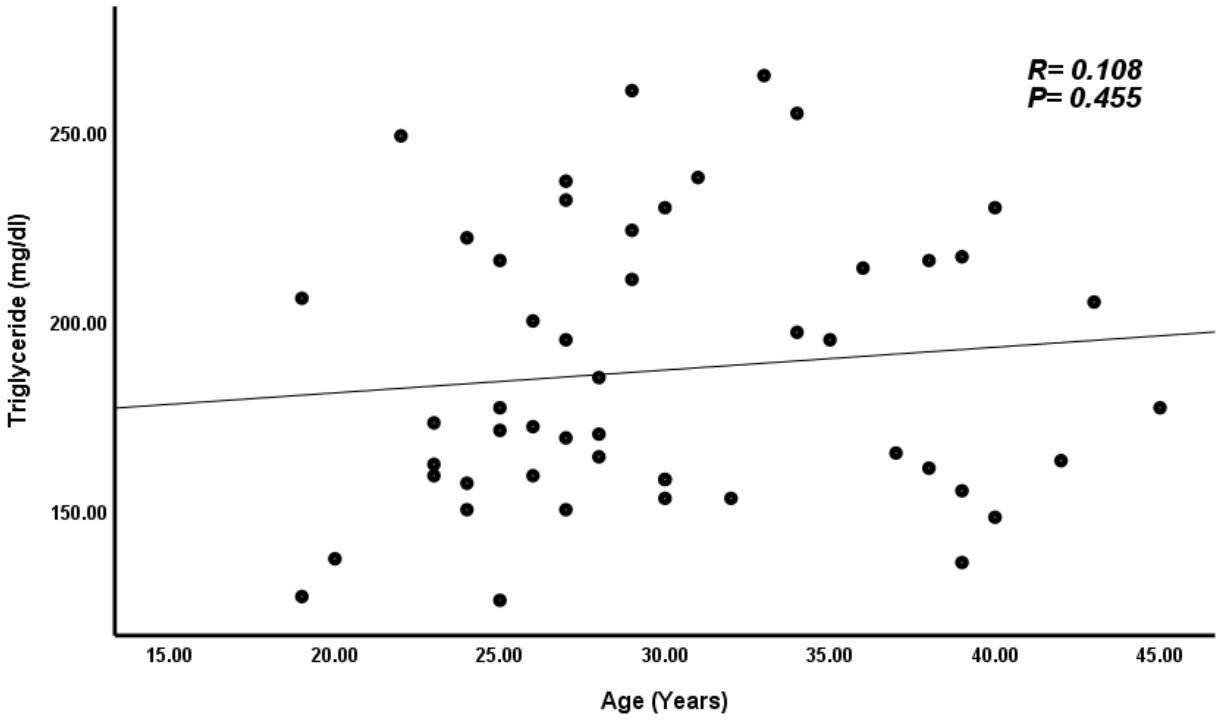


Figure (4-3):scatter plot of pearson correlation between triglyceride and age of PCOS woman .

r= 0.108,p.value= 0.455.

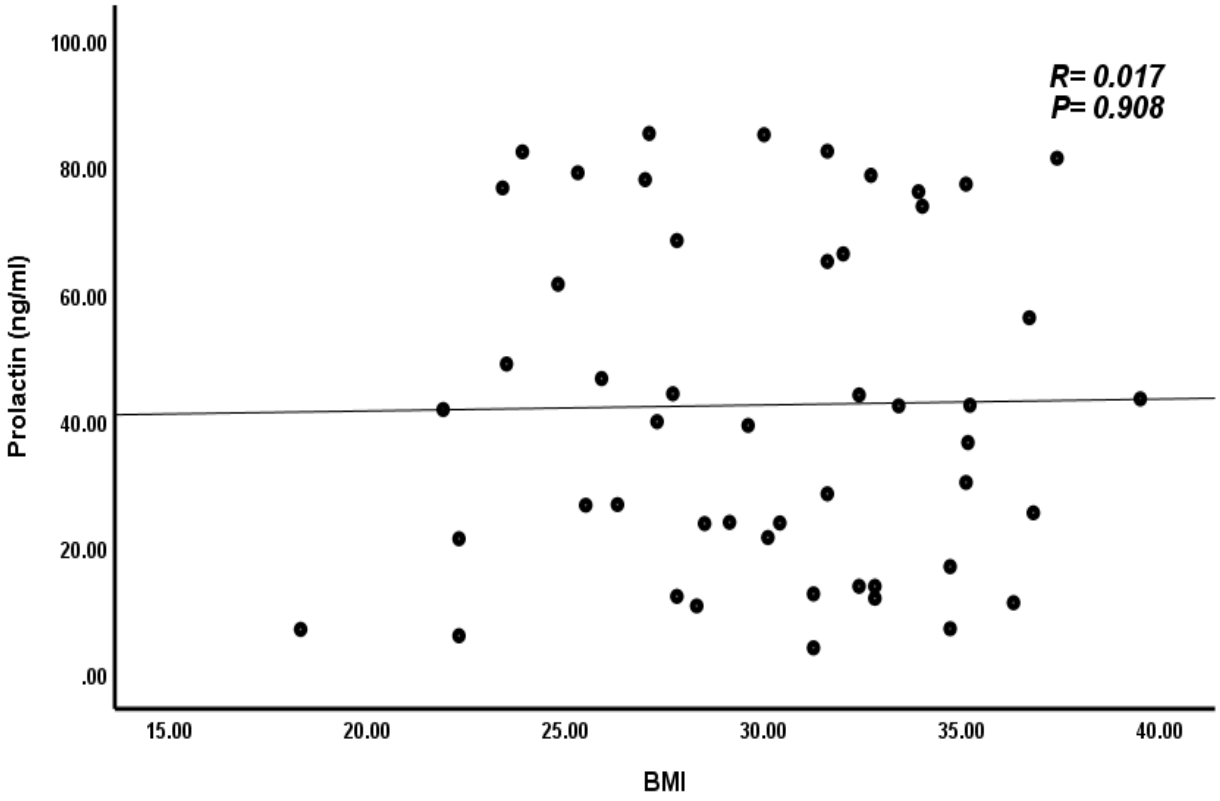


Figure (4-4):scatter plot of pearson correlation between prolactein and BMI of PCOS woman .

r= 0.017,p.value= 0.908 .

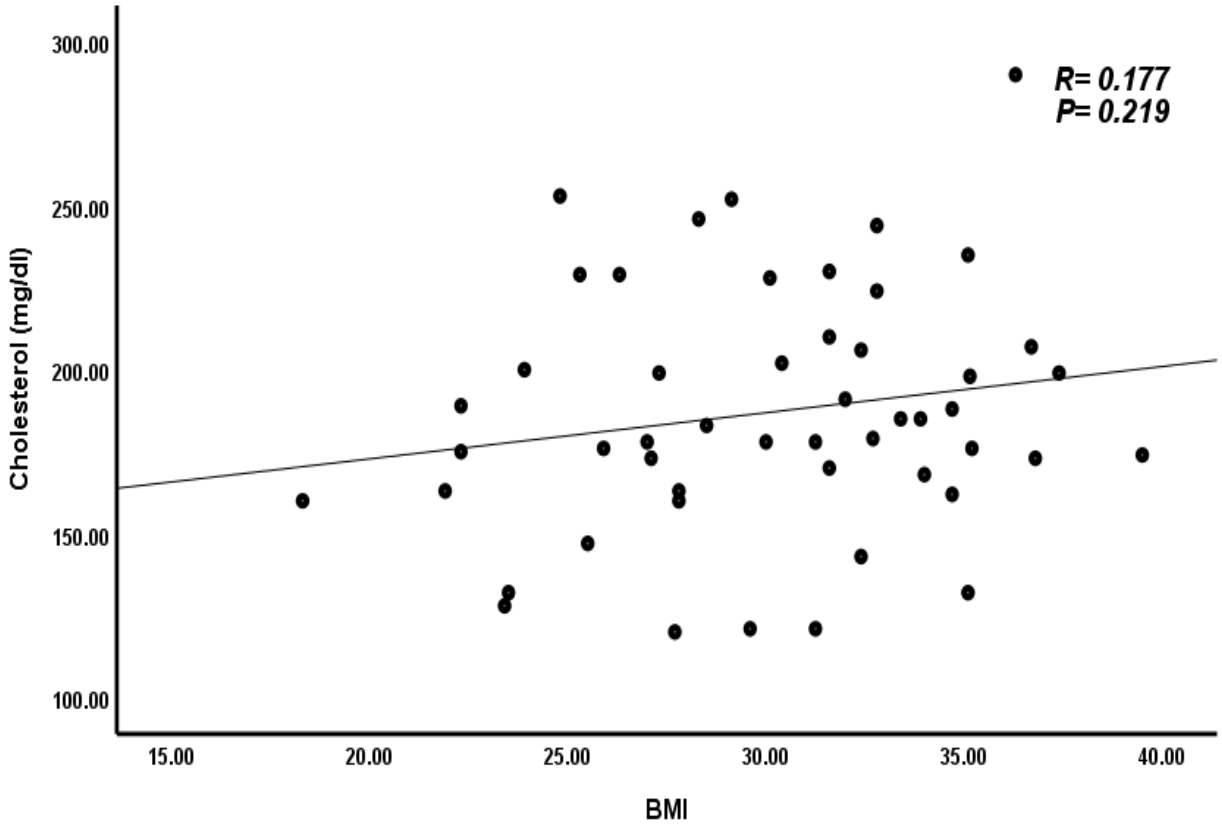


Figure (4-5):scatter plot of pearson correlation between cholesterol and BMI of PCOS woman .

r= 0.177,p.value= 0.219

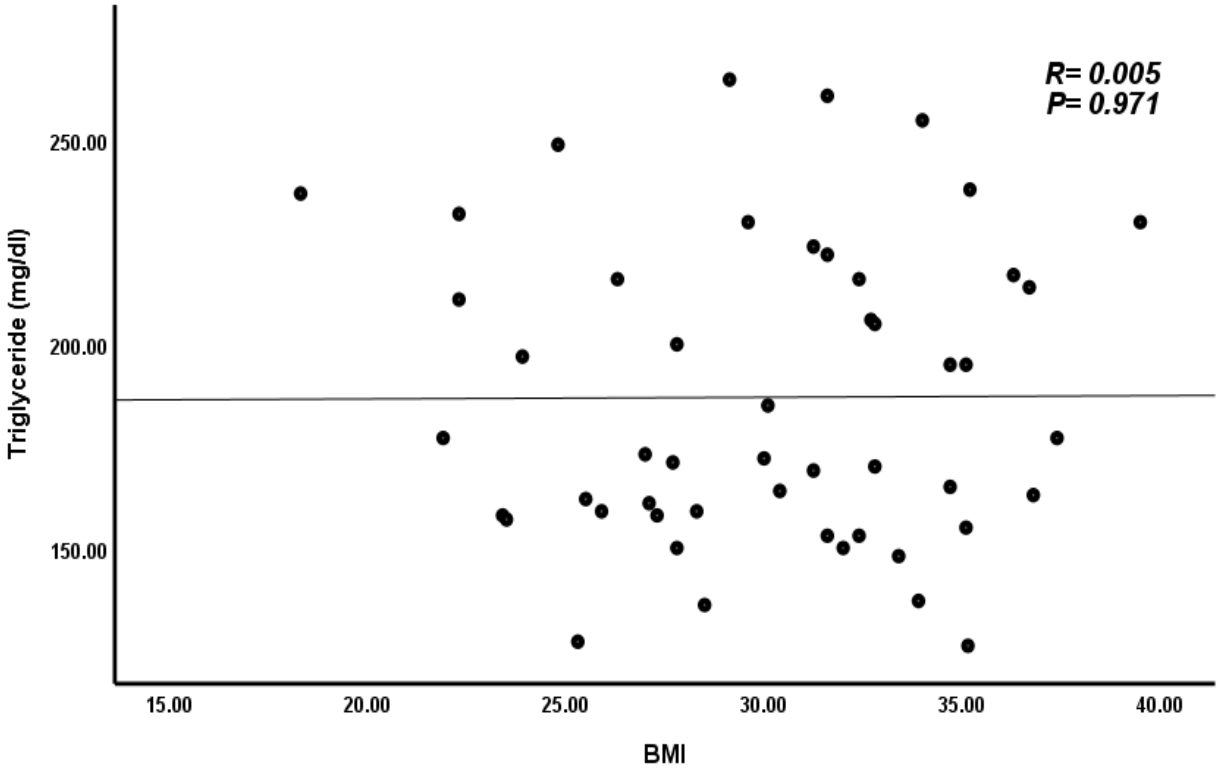


Figure (4-6):scatter plot of pearson correlation between triglyceride and BMI of PCOS woman

r= 0.005,p.value= 0.971. .

Chapter Five

Discussion, Conclusion

5.1 Discussion

Poly cystic ovary syndrome is a common disorder affecting women of reproductive age and the most common cause of under lying ovulatory problems. (Azzizet al., 2016).

In this study mean age of the females in the reproductive period was 30.0 ±6.59years.The result 50 females with PCOS, the level of prolactin increase significantly with p.value (0.000)compared with control group According to infertility ,therapy and cosmetic use ,regular of menstrual cycle and history of disease the study showed that prolactin increase insignificant with infertility ,therapy ,cosmetic and history with (p.value=0.124) (p.value=0.761)(p.value =0.611)(p.value= 0.986)

Patients with PCOS can have mildly elevated prolactin; the exact mechanism of hyperprolactinemia in PCOS is unknown. One theory is that constant high levels of estrogen experienced in PCOS would stimulate prolactin production. It is important to rule out other causes of hyperprolactinemia before making the diagnosis of PCOS(Ji Hyun, 2014)

The present study confirms the presence of a more atherogenic lipid profile in woman with PCOS. Results of studies by (Roa et al.,2009) are generally consistent with the results of my study ,cholesterol increase significant compared with infertility with (p.value=0.031) and insignificant with therapy (p.value=0.908), cosmetic (p.value=0.786) and menstrual cycle (p.value=0.180).

Triglyceride increased insignificantly with infertility (p.value=0.430), therapy (p.value=0.084) cosmetic (p.value=0.137) and menstrual cycle (p.value =0.721).

that in all, the levels of serum lipids (total cholesterol and triglyceridesin patients with polycystic ovary were higher than healthy persons. However, there

was aweak increase in cholesterol indicates the presence of primary alteration in lipid metabolism in patient with PCOS. The significant increase in triglyceride may be due to increase accumulation of triacylglycerol could as result of increased lipogenesis,decrease clearance or reduced fatty acid oxidation.

Addition, lipid metabolism in women with PCOS may also be affected by ovarian and/or adrenal secretion of sex steroids and obesity. Androgens affect lipids not only directly, but also by affecting obesity, catecholamines, and insulin. (patel, et al 2018).

Hyperandrogenism has been associated with increased hepatic lipase (HL) activity. HL hydrolyses phospholipids on the surface of HDL mediating the conversion of HDL-2 to the smaller denser HDL-3. This being a better substrate for the liver, increases the clearance of HDL. Androgens, through interaction with the androgen receptor, also decrease the catabolic removal of LDL by attenuating estrogen receptor mediated induction of LDL receptor activity.(Gobal et al., 2016)

The present study reveal negative correlation between prolactin level with age

(r= -0.198,p.value= 0.168.)and weakly increase correlation with cholesterol and triglyceride (r= 0.240,p.value= 0.093)and posative correlation between triglyceride and age(r= 0.108,p.value= 0.455).

The present studyshowno correlation between prolactin and BMI(r=0.017,p.value= 0.908) but cholesterol positive correlation (r= 0.177,p.value=0.219) and no correlation between triglceride and BMI (0.005, p.value=0.971).

5.2 Conclusion:

From the result and finding of the study,it is concluded that the serum level of prolactin is high in PCOS females patient,also increased in triglyceride and no observed change in cholesterol level .

5.3 Recommendation:

1. Prolactin hormone must be measurement with other androgenic hormone to exclude misdiagnosis with other disease.
2. Woman with PCOS showed be screened for lipid profile to help in decrease risk of atherosclerosis.
3. Woman must be modified dietary and life .

References:

A.A. Shaman, H.B. Mukhtar, H.O. Mirghani.(2017). Risk factors associated with metabolic syndrome and cardiovascular disease among women with polycystic ovary syndeome Electron Physician, volume 9, pp. 5697-5704 Cros

Asha Kumari (2018) cholesterol synthesis ,sweet Bio chemisssstery.

Auriemma RS, Pirchio R, De Alcubierre D, Pivonello R, Colao A.(2019). Dopamine Agonists. Neuroendocrinology. Volume 109 issue (1)pp34-41.

B. Mlinar, J. Marc, M. Jensterle, E.V. Bokal, A. Jerin, M.Pfeifer (2011) Expression of 11beta-hydroxysteroid dehydrogenase type 1 in visceral and subcutaneous adipose tissues of patients with polycystic ovary syndrome is associated with adiposity , Steroid Biochemistery and Molecular Biology, volume 123, pp. 127-132

Bernard V, Young J, Binart N. Prolactin (2019)a pleiotropic factor in health and disease. Nature Reviews Endocrinology. Volume 15 issue(6):356-365.

Bonow RO, et al.,(2019) Risk markers and the primary prevention of cardiovascular disease. Cardiovascular Medicine. 11th ed.

D. Macut, J. Bjekic-Macut, A.Savic-Radojevic (2013) Dyslipidemia and oxidative stress in PCOS, Frontiers of Hormone Research, volume 40, pp. 51-63.

D.E. Broughton, K.H. Moley(2017), Obesity and female infertility. Fertility and Sterility,volume107 pp.840-847.

Debbie Bridges, MD. (2012), infertility and Reproduction.

Dewailly D, Lujan ME, Carmina E, et al(2014). Definition and significance of polycystic ovarian morphology. Human Reproduction.volume20 issue(3):334–352 .

Di Ciaula A, Garruti G, Lunardi Baccetto R, Molina-Molina E, Bonfrate L, Wang DQ, Portincasa P (2017) Bile Acid Physiology. Annals of Hepatology. volume16(Suppl. 1: s3-105.):s4-s14.

Dotson RJ, Smith CR, Bueche K, Angles G, Pias SC. (2017) Influence of Cholesterol on the Oxygen Permeability of Membranes: Biophysical volume 112 issue (11):2336-2347.

E. Seyam, G.S. Al, A.G.A. Abd, M. Mohamed, A.M. Youseff, E.M. Ibrahim, et al (2017). Evaluation of prolonged use of statins on the clinical and biochemical abnormalities and ovulation dysfunction in single young women with polycystic ovary syndrome Gynecological Endocrinology. volume 34 issue(7)pp.1-8.

F.R. Tehrani, H. Rashidi, M.B. Khomami, M. Tohidi, F. Azizi(2014) The prevalence of metabolic disorders in various phenotypes of polycystic ovary syndrome. Biology Endocrinology, volume 12 , p.89 .

FahimehRamezani ,Tehrani ,samiraBehboudi -gandevani(2015)poly cystic ovary syndrome ,contemporary Gynecologic practice ,chapter 3454.

G.S. Gobl, Ott,L. Bozkurt, M.feichtinger, V.Rehmann, A.cserjan, et al,(2016).The association between glucose metabolism and ectopic lipid content in different clinical classification of PCOS. Plose One, 11,Article e 16057.

Ghaffarzad, R. Amani, S.M. Mehrzad, M. Darabi, B. Cheraghian, (2014) Correlation of serum lipoprotein ratios with insulin resistance in infertile women with polycystic ovarian syndrome. Fertility and Sterility, volume10 , pp. 29-35.

Hammersley, D., & Signy, M. (2017) Ezetimibe. Therapeutic Advances in Chronic Diseases, volume 8 issue (1):p 4–11 .

J. Zhang, J. Hu, C. Zhang, Y. Jiao, X. Kong, W. Wang, (2018) Analyses of risk factors for polycystic ovary syndrome complicated with non alcoholic fatty liver disease. Experimental and Therapeutic Medicine, volume 15,pp.4259-4264.

J.X. Pan, Y.J. Tan, F.F. Wang, N.N. Hou, Y.Q. Xiang, J.Y. Zhang, et a(2018)l. Aberrant expression and DNA methylation of lipid metabolism genes in PCOS., clinical Epigenetics. volume10,p.6.

Jameson JL ,et al .(2017)Hyperandrogenism, hirsutism, and poly cystic ovary syndrome ,Endocrinology 7th edition.

Ji Hyun Chun,PA-c,MPAS,BC-ADM, (2014), Syndrome .Clinician Reviews volum 24 issue(2):p26-27 .

Jin Y, Fan M. (2019) Treatment of gynecomastia with prednisone. International Medical Research.volume 47 issue (5)p2288-2295.

Joanna Goldberg ,Timjewell (2016) prolactin level test ,Health care.

John C. Marshall .MD et al , (2012)ALL Women with PCOS should be treated for insulin resistance. Fertility and sterility. volum79 , issue(1) pp18-22.

Jones MR, et al ,(2016)genetic determinants of poly cystic ovary synderome ,fertility and sterility volum 106 issue (25).

Karney A, Brągoszewska H, Soluch L, OłtarzewskiM.(2017) [Risk factors for atherosclerosis in obese children aged 6-12 years. Developmental Period Medicine. volume 21 issue (3)p259-265.

KovanciE,buster JE. (2015) polycysticovary syndrome. Clinical gynecology .second edition.

Kumar MS. (2019) Peptides and Peptidomimetics as Potential Antiobesity Agents, Front Nutrition .volume(6)issue 11.

Kumar P, et al. (2017) Lipid and metabolic disorders. Clinical Medicine 9th

Li H, Huang Y, Li Y, Zheng B, Cui J, Liu M.(2019) Endocrine Manifestations in POEMS syndromes BMC Endocrine Discordes .volume;19 issue (1)p:33.

Lobo RA, et al. (2017) Polycystic ovary syndrome., Comprehensive Gynecology. 7th ed.

M Gibson-Helm et al (2016) Delayed diagnosis and lack of information associated with dissatisfaction in woman with polycystic ovary syndrome. Clinical Endocrinology and metabolism.

M. Spalkowska, S. Mrozinska, A. Galuszka-Bednarczyk, K. Gosztyla, A. Przywara, J. Guzik, et al.(2018) The PCOS patients differ in lipid profile According to their phenotypes. Expermental and Clinical Endocrinology and Diabetes, volume126 pp.437-444.

Mary EllenT ,Sweeney, MD et al (2019) Hypertriglyceridemia, Endocrinology

Matalliotakis M, Koliarakis I, Matalliotaki C, Trivli A, HatzidakiE.(2019) Clinical manifestations, evaluation and management of hyperprolactinemia in adolescent and young girls: a brief review. Acta Biomed .volume 90 issue (1):p149-159.

Milica Popovic Gideon sartorius ,mirjam Christ crain (2019),polycystic ovary syndrome : is there apathophsyological role for interleukin -1?.Seminars in immunopathology volum 41,447-459 .

P.M. Spritzer, S.B. Lecke, F. Satler, D.M. Morsch (2015) Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic

ovary syndrome Society for Reproduction, volume 149 issue (5), pp. R219-R227.

Pagana KD, Pagana TJ, Pagana TN. Mosby's (2019) Diagnostic & Laboratory Test Reference. 14th ed.

paganaKD,paganaTJ,paganaTN(2019) Diagnostic and laboratory Test Refrence. 14th

QiLiu .et al, (2019) Dyslipidemia involvement in development of poly cystic ovary syndrome. obstetrics and Gynecology, volume 58. issue (4) p 447-453.

R. Azziz, E. Carmina, Z. Chen, A. Dunaif, J.S. Laven, R.S. Legro, et al.(2016) Polycystic ovary syndrome. Nature Reviews Disease Primers,volume 2, p. 16057.

R. Patel, G. Shah,(2018) High-fat diet exposure from pre-pubertal age induces polycystic ovary syndrome (PCOS) in rats, Reproduction, volume 155 , pp. 141-151.

R.wang,(2017), The Rotterdam criteria for poly cystic ovary syndrome .Hum Reprod .volume32 issue (2) p 261-264.

Raut S, Deshpande S, BalasinorNH.(2019) Unveiling the Role of Prolactin and

Receptor in Male Reproduction. Hormone and. Metabolic. Research volume 51 issue (4): p215-219.

Roa BM, Arata-Bellabarba G, Valeri L, et al. (2009) [Relationship between the triglyceride/high-density lipoprotein-cholesterol ratio, insulin resistance index and cardiometabolic risk factors in women with polycystic ovary syndrome. Endocrinology Y Nutrition. volume 56 issue (2) p59–65.

Robert Ferry jr, MD.(2012) prolactinoma. Medicine Net

S.L. Mannera, H. Leonhardt, J. Kullberg, E. Jennische, N.A. Ode, G.R. Holm, et al (2011) Adipose tissue has aberrant morphology and function in PCOS: Endocrinology, volume 152, p. 332.

Sacks FM, Lichtenstein AH, Wu JHY, Appel LJ, Creager MA, Kris-Etherton et al (2017) Dietary Fats and Cardiovascular Disease. Circulation. volume 136 issue (3)p23.

Selma Feldman, Helena Teede, Alexia s pena (2019) curtailing PCOS,pediatric research volume 87.

Štelcl M, Vrublovský P, Machač Š (2018). Prolactin and alteration of fertility. CeskaGynekol.

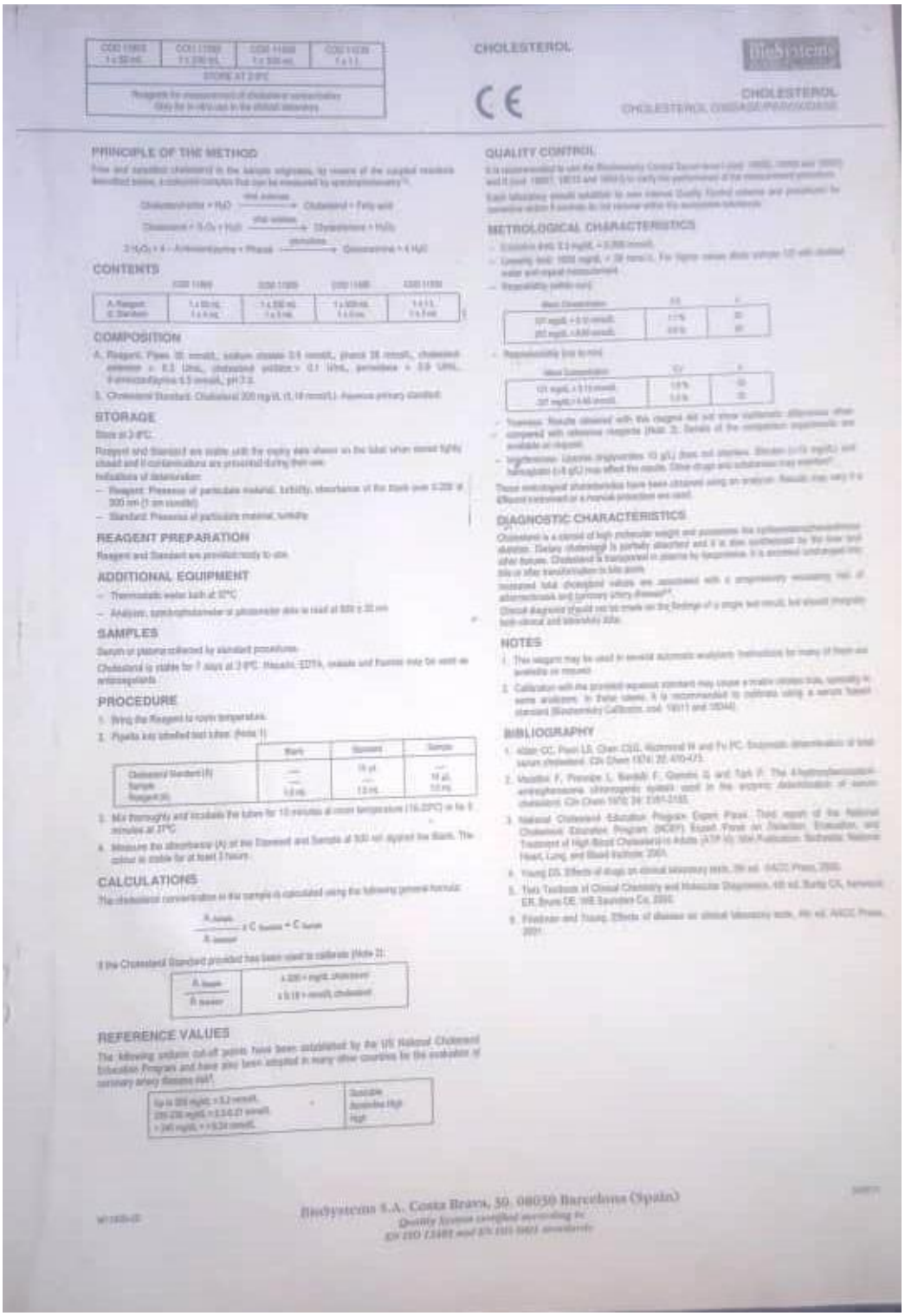
V. Pergialiotis, E. Trakakis, C. Chrelias, N. Papantoniou, E. Hatziagelaki,(2018)
The impact of mild hypercholesterolemia on glycemic and hormonal profiles, Hormone Molecular Biology Clinical Investigation , volume 10.

V.de leo , M.C. musacchio, (2016), genetic ,hormonal and metabolic ascpect of pcos .Reproductive Biology and Endocrinology ,article number 38 .

Vilar L, Vilar CF, Lyra R, Freitas MDC,(2019) Pit falls in the Diagnostic Evaluation of Hyperprolactinemia. Neuroendocrinology.volume;109issue(1):p7-19.

Appendices

Appendixes



CHOLESTEROL

CHOLESTEROL

PRINCIPLE OF THE METHOD

CONTENTS

COMPOSITION

STORAGE

REAGENT PREPARATION

ADDITIONAL EQUIPMENT

SAMPLES

PROCEDURE

CALCULATIONS

REFERENCE VALUES

QUALITY CONTROL

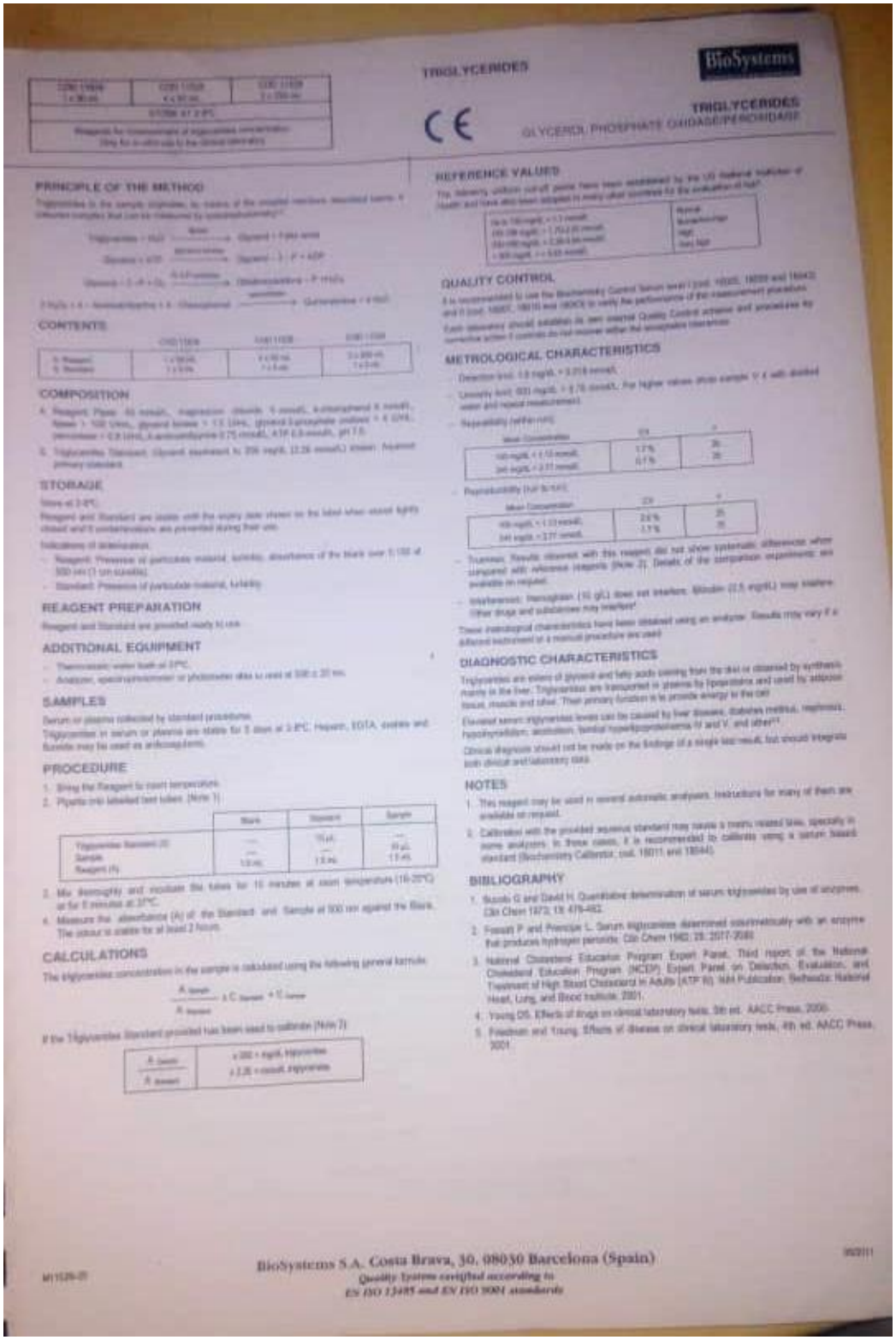
METROLOGICAL CHARACTERISTICS

DIAGNOSTIC CHARACTERISTICS

NOTES

BIBLIOGRAPHY

Biosystems S.A. Costa Brava, 30. 08030 Barcelona (Spain).



TRIGLYCERIDES

BioSystems

CE

TRIGLYCERIDES

GLYCEROL PHOSPHATE OXIDASE/PEROXIDASE

PRINCIPLE OF THE METHOD

CONTENTS

COMPOSITION

STORAGE

REAGENT PREPARATION

ADDITIONAL EQUIPMENT

SAMPLES

PROCEDURE

CALCULATIONS

REFERENCE VALUES

QUALITY CONTROL

METROLOGICAL CHARACTERISTICS

DIAGNOSTIC CHARACTERISTICS

NOTES

BIBLIOGRAPHY

BioSystems S.A. Costa Brava, 30. 08030 Barcelona (Spain)

Quality System complied according to
EN ISO 13485 and EN ISO 9001 standards