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Evaluation of Endoglin (sEng)/CD105 level in women with polycystic ovary syndrome at Al-Najaf Province

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***Abstract*---**Endoglin (sEng)/CD105 is a transmembrane auxiliary receptor for transforming growth factor beta (TGF-b) it works as a non-signaling coreceptor of the TGF-b modulating its responses. The main finding of these study that, in obese groups (PCOS and control), there were higher values of TGF-b1 and the lower values of plasma sEng. Even more importantly.

***Keywords*---**Endoglin (sEng)/CD105, polycystic ovary syndrome, women.

Introduction

Polycystic ovary syndrome (PCOS) is the most common gynecological disease in women at reproductive age, which is characterized by metabolic and endocrine abnormalities, as well as chronic inflammation (Seyyed Abootorabi *et al.*, 2018). The most common risk factors for the progress of PCOS include family history of PCOS, fast food diet habits, lack of physical exercise, body mass index and waist circumference (Begum et al., 2017).

Endoglin (CD105) is a 180-kDa homodimeric glycoprotein composed of two 95 kDa disulfide-linked subunits. It has a transmembrane structure and functions as a component of the transforming growth factor-β receptor complex. Endoglin is highly expressed on proliferating endothelial cells, A soluble form of endoglin (sEng) is found in the circulation under normal and pathologic conditions (Bock, *et al,*. 2011).

Endoglin (sEng)/CD105 is a transmembrane auxiliary receptor for transforming growth factor beta (TGF-b) it works as a non-signaling coreceptor of the TGF-b modulating its responses. There are a number of reports suggesting that soluble endoglin may be regarded as a biomarker of endothelial dysfunction, for instance,

atherosclerosis, hypercholesterolemia, type 2 diabetes mellitus (T2DM), and hypertension(Irani, *et al*,. 2015).

Transforming growth factor (TGF)-b1 is a multifunctional cytokine that is produced by a variety of cells and its level dysregulated in women with PCOS, which might play a role in the pathophysiology of this syndrome. Substantial evidences implicate that TGF-b1 activation is closely associated with endothelial dysfunction and hypertension.There is scattered evidence for the association between TGF-b1, visceral adiposity, metabolic syndrome, nonalcoholic fatty liver disease and T2DM **(**Rashad, *et al*,. 2018).

Material and Methods

The study included 128 subjects is divided into two groups: The first group is the patient group, which consists of 83 patients with PCOS, which excludede 38 sample according exclusion criteria, And remained 45 patients PCOS was identified by a specialized gynaecologists of the "Fertility Center in AL-Sadder Teaching Hospital in Najaf Governorate/ Ministry of Health/Iraq, during the period from the 1st Nov. 2021 to 1st March. 2022, according to the Rotterdam Consensus (2003), which requires the presence of at least two of the following characteristics: polycystic ovaries on ultrasound scan, menstrual irregularities and hyperandrogenism. The age group of the patients ranged from (17-49) years. The inclusion criteria for the patients are all patients with PCOS. The second group is the control group, which consists of 45 femels with no PCOS, normal testosterone, a regular menstruation period, and normal ovulation are eligible, with normal ovaries as they were observed by the gynaecologists which no take contraceptive, with no past of somewhat malady. The age group ranged from (17-50) years.

Exclusion criteria

Thirty eight samples were excluded from the initial sample of Eighty three due to these pathologies such as Diabetes mellitus, hypoplasia of ovary, white heifer disease and ovarian tumor.

Blood Collection

The blood samples of this study were obtained from female in 2nd of menstrual cycle through drag 5 ml of blood by using of medical sterile syringes from brachial vein, and placed in a gel tube. Then the gel tube were placed at room temperature for 30 minutes to coagulate the blood, and then samples were centrifuged (6000 rpm/min) for 5 minutes to separate the serum from other components of the blood. The serum was withdrawn by micro pipette and then placed in the Eppendorf tubes in two repeaters and kept frozen at -20 ◦C for the determination of Apelin, Endoglins, Inhibin B, LH, FSH, TSH, Prolactine (Lesser *et al.*, 2020).

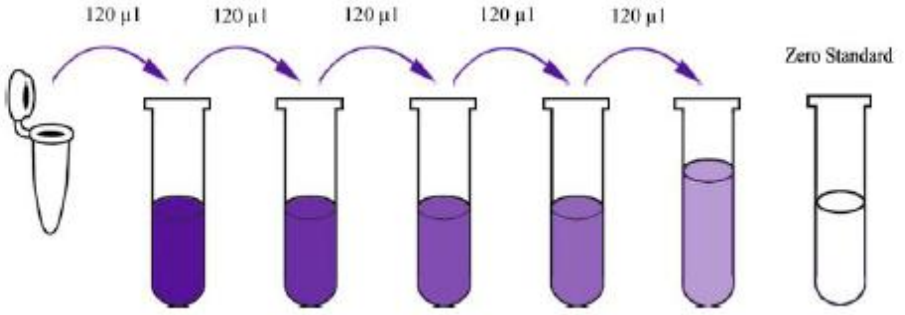
Endoglin (sEng) measurment method

Assay Principle: This kit is an Enzyme-Linked Immunosorbent Assay (ELISA). The plate has been pre-coated with human sENG/sCD105 antibody.

sENG/sCD105 present in the sample is added and binds to antibodies coated on the wells. And then biotinylated human sENG/sCD105 Antibody is added and binds to sENG/sCD105 in the sample. Then Streptavidin-HRP is added and binds to the Biotinylated sENG/sCD105 antibody. After incubation unbound Streptavidin-HRP is washed away during a washing step. Substrate solution is then added and color develops in proportion to the amount of human sENG/sCD105. The reaction is terminated by addition of acidic stop solution and absorbance is measured at 450 nm.

Assay Procedure:

1. Prepared all reagents, standard solutions and samples as instructed. Brought all reagents to room temperature before used. The assay performed at room temperature.



2. Determined the number of strips required for the assay. Inserted the strips in the frames for use. The unused strips should be stored at 2-8°C.
3. Added 50µl standard to standard well. **Note**: Didn't add antibody to standard well because the standard solution contained biotinylated antibody.
4. Added 40µl sample to sample wells and then added 10µl anti-sENG/sCD105 antibody to sample wells, then added 50µl streptavidin-HRP to sample wells and standard wells (Not blank control well). Mixed well. Covered the plate with a sealer. Incubated 60 minutes at 37°C.
5. Removed the sealer and washed the plate 5 times with wash buffer. Soaked wells with at least 0.35 ml wash buffer for 30 seconds to 1 minute for each wash. For automated washing, aspirate all wells and washed 5 times with wash buffer, overfilling wells with wash buffer. Blotted the plate onto paper towels or other absorbent material.
6. Added 50µl substrate solution A to each well and then added 50µl substrate solution B to each well. Incubated plate covered with a new sealer for 10 minutes at 37°C in the dark.
7. Added 50µl Stop Solution to each well, the blue color will changed into yellow immediately.
8. Determined the optical density (OD value) of each well immediately using a microplate reader set to 450 nm within 10 minuets after adding the stop solution.

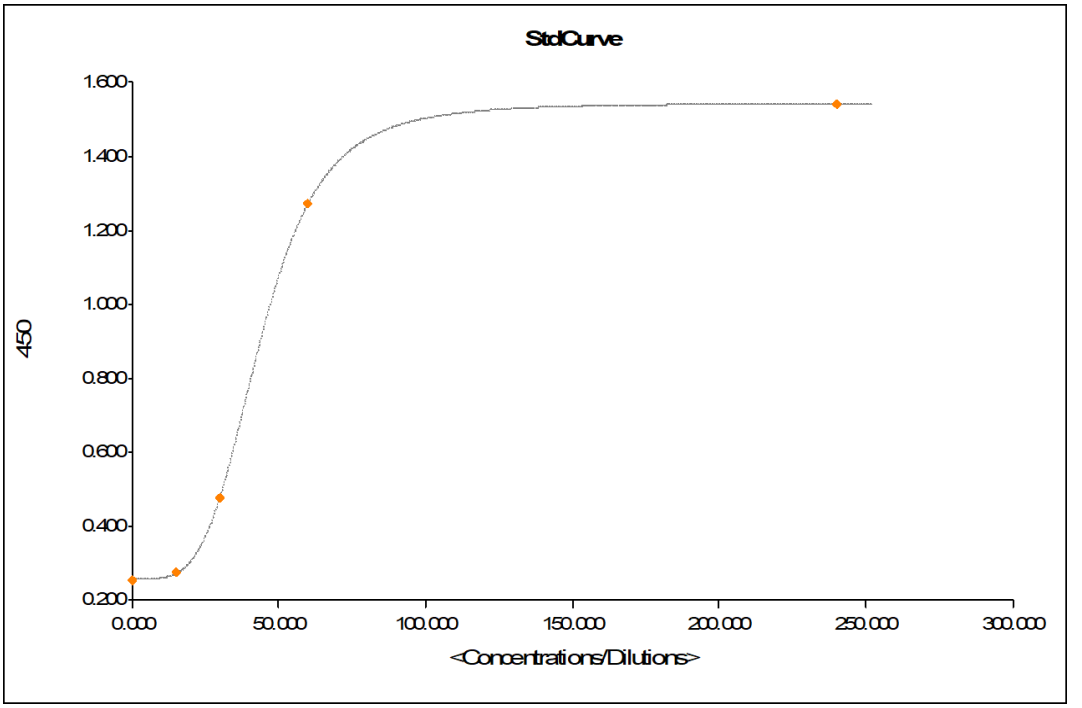


Figure (1): Standard curve of Endoglin(sENG/sCD105)

Result and Discussion

The mean level of Endoglin (sENG/sCD105) in PCOS patiens women group was (31.13 ng/ml) and was significantly lower than in control women groups (NO PCOS) that was (42.04ng/ml), as shown in table (1) and figure (2).

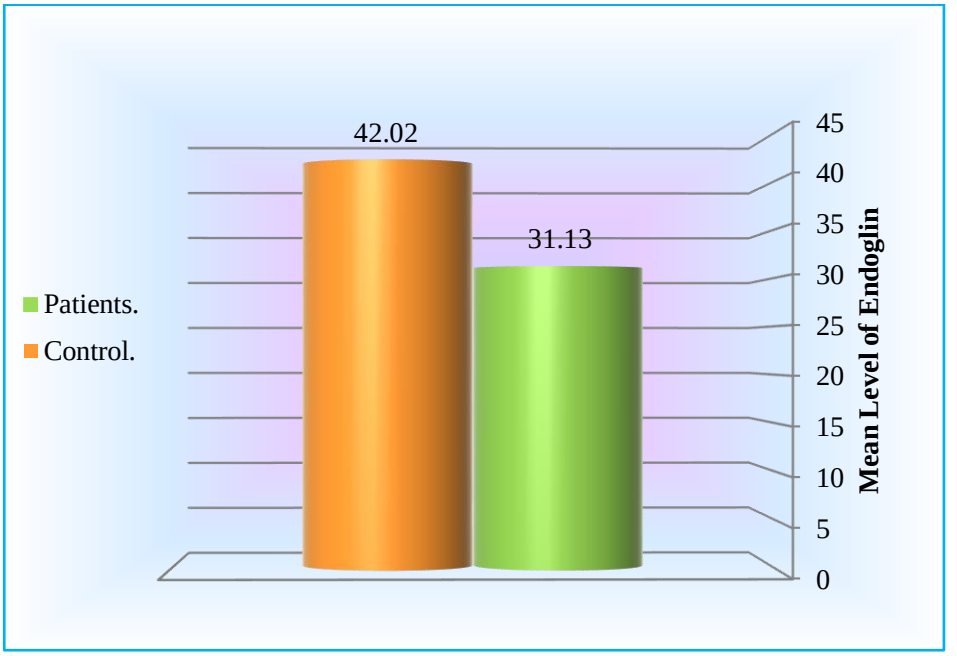


Figure (2): Comparison the mean levels of Endoglin (sENG/sCD105) in PCOS patiens women group and control women groups (NO PCOS)

Table (1)
Comparison the mean, standard error and p-value of Endoglin(sENG/sCD105) between PCOS patiens women group and control women groups (NO PCOS)

Parameter		N	Mean	Std. E	P-value
Endoglin(sENG/sCD10)	Patients	45	31.13	1.26	0.0001**
	control	45	42.04	4.89	

P > 0.05 = Non-Significant (NS)
P < 0.05 = significant (*)
P < 0.01 = Highly significant (**)

In line with our results, Tal *et al.*, 2013, found increased TGF-b1 and decreased sEng in PCOS. These data suggest that increased TGF-b1 bioavailability may contribute to the pathogenesis of PCOS and its increased risk for ovarian hyperstimulation.

By contrast, the study conducted by Irani *et al.*, 2015, found that sENG protein concentration was not different between PCOS and non-PCOS control group at baseline. By contrast, the study conducted that sENG protein concentration was not different between PCOS and non- PCOS control group at baseline.

The main finding of these study that, in obese groups (PCOS and control), there were higher values of TGF-b1 and the lower values of plasma sEng. Even more importantly. The study demonstrated that, there were higher values of TGF-b1 in PCOS. In addition, that study revealed clear evidence that plasma sEng levels

were statistically lower in PCOS patients compared to control (Rashad *et al.*, 2018).

Women with PCOS have abnormal increase in TGF-b1 bioavailability (TGF-b1/sENG) due to an increase in serum TGF-b1 and decrease in sENG levels (Ibrahim *et al.*, 2020).

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