

## Original Research Article

**Assessment of serum Prostate specific antigen (PSA) level among Sudanese women with polycystic ovarian syndrome In Khartoum state**Mohajir Hussein<sup>1</sup>, Ali Mohamed<sup>2</sup>, Elmutuz Hussein<sup>3\*</sup>, Abdelgadir Eltom<sup>4</sup><sup>1</sup>M.Sc.–clinical chemistry- Al-Zaiem Al-Azhari University, Sudan, Ministry of health Blue Nile stat -Sudan<sup>2</sup>M.Sc. - clinical chemistry - Al-Zaiem Al-Azhari University" Sudan, Albuheira Hospital - Sudan<sup>3\*</sup>PhD.–clinical chemistry- Al-Zaiem Al-Azhari University -Sudan, University of Tabuk  
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**Abstract:** PCOS is one of the commonest endocrine disorders in women of reproductive age group, cause of androgen excess in women. Prostatic specific antigen (PSA) is the most specific prostatic tumor marker in men, PSA can no longer be tumor-specific marker for only prostatic tissue, PSA may new one diagnostic tool for PCOS. Aim of study to assess the level of PSA in Sudanese women with PCOS and determine the performance of PSA in diagnosis of PCOS. Methodology cross sectional study, Blood samples of 50 Sudanese infertile women with PCOS as case, 11 infertile without PCOS and 40 health fertile as control was analyzed for TPSA. They were significant difference between the means of total prostate specific antigen (TPSA) in PCOS case (N=50) (0.025±0.013ng/ml) than normal fertile control (N=40) (0.004±0.005ng/ml) (p-value 0.001), and infertile without PCOS (N=11) (0.013±0.005) (p-value 0.004). Very weak, insignificant, negative correlation of TPSA and AMH (r =-0.132, p =0.360), ROC curve for TPSA regarding fertile control was found to be 0.924(92.4%) AUC =0.924 and 0.790(79.0%) AUC =0.790 regarding infertile without PCOS. The serum levels of TPSA are increased in PCOS than control group. The accuracy of TPSA in predicting PCOS is good when regarding fertile (health) control, but decrease with infertile without PCOS. The accuracy and consistency of TPSA weak when comparing to AMH, Very weak negative correlation between TPSA and AMH.

**Keywords:** polycystic ovary syndrome, prostate specific antigen, androgen excess, Anti-Müllerian hormone

**INTRODUCTION:**

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy of women, is combination of chronic anovulation or oligomenorrhoea and clinical or biochemical hyperandrogenism and ovarian polycystic changes observed by ultrasound [1], affect about 6–8% of the population [2]. PCOS in recent become most common problem among women in reproductive age that visit fertility center in Sudan, the diagnosis and differential diagnosis of PCOS remains confused to many clinicians because have different criteria and different phenotypes and have different manifestations in different people due to genetic and environmental background and until now have no separately lab test and clinicians depend on rule out all other cause of heperandrogenism and ultrasound so

may lead to miss diagnosis, which lead to increase infertility and other PCOS complication. Recent study conducted to assess Serum Anti-Müllerian hormone as laboratory predictor in infertile women with PCOS [3]. Prostate specific antigen (PSA) is a serine protease of human glandular kallikrein family and has historically been used as the most specific and sensitive marker for prostatic Cancer in male [4], PSA production in the prostate is under the control of steroid hormones. Androgens up-regulate the expression of the PSA gene through the androgen receptor, PSA has been detected recently in some female tissues (including breast, ovarian, and endometrial tissues) and body fluids (amniotic fluid, milk, and breast cyst fluid) [5]. The presence of PSA in these female tissues seems to be associated closely with steroid hormone regulation,

especially androgens, glucocorticoids, and progestin but not estrogen [6].previous study found that serum PSA levels were increased significantly in women with hirsutism [5] other study demonstrated that women with PCOS had significantly higher serum concentration of TPSA than healthy women and showed TPSA positively correlated with testosterone [2].

#### MATERIALS AND METHODS:

Cross sectional study was conducted in Khartoum state with a surface area 22000 Km and population of about 5 million inhabitants, Patient enrolled in this study were from (D.Alsir Abu alhassan Fertility Center) during Sep 2016 to Dec 2016.

#### Study population and Sample size:

50 Sudanese infertile women which will diagnosis as PCOS (diagnosed according to hormonal profile and ultrasound and confirm the diagnosis by Anti-mullrien Hormone above 4ng/ml considered PCOS were recruited as case and in contrast 11 infertile Sudanese women without PCOS and 40 healthy fertile women volunteers were involved as a control group. Both groups were age matched.

#### Selection criteria:

##### Inclusion criteria:

Infertile Sudanese women that well diagnosed as PCOS (age between 18 to 35), which agree to participate in this study was enrolled.

##### Exclusion criteria:

Women who (recent pregnancy, use ovulatory agents, and glucocorticoids) was excluded.

#### Ethical consideration of the study:

The study was revised and ethically approved by the ethical committee of the Faculty of Medical Laboratory sciences, Elzaeim Elazhari University and the Permission of this study was obtained from the medical lab directors of (D.Alsir Abu alhassan Fertility Center).

#### Data collection:

Standard questionnaire was used to obtain the clinical data for each participant in this study.

#### Sample collection:

Blood sample was collected from peripheral Vein from each subject ,In sterile condition and using a local antiseptic for skin, 5mls of venous blood was collected in plain blood container and centrifuged for 15 minutes at 3500rpm; and serum was separated and stored in -20 until whole sample ware collected.

#### Biochemical measurements:

##### Total prostatic specific Antigen (tPSA) measurement:

Total PSA Was measured by ultrasensitive method by sandwich Electrochemiluminescent (ECL) immunoassay method, with detection limit 0.005ng/ml (Elecsys Roche's technology 2010.)

**Anti-mullrien Hormone (AMH):** Was measured by ELISA kit.

#### STATISTICAL ANALYSIS:

Mean  $\pm$  SD for describe the data, student-t test to compare between means and ROC curve were done, all data was performed using SPSS ( Statistical Package for the Social Sciences software package), version 11.5.

#### RESULTS:

The result of present study involved (N=50) Polycystic ovarian syndrome (PCOS) case, (N=40) fertile control and (N=11) infertile control subjects.

#### Descriptive statistics:

Table (1) shows the minimum, maximum and mean  $\pm$  SD of age, AMH and tPSA for normal fertile control, infertile control and PCOS case, as shown from table that the minimum age, AMH and tPSA for fertile control subjects ware 20 year, 0.90ng/ml and 0.00ng/ml respectively, where the maximum values ware 36 yare, 4.00ng/ml and 0.02ng/ml, with mean  $\pm$  SD 29.5 $\pm$ 3.9year, 2.80 $\pm$ 0.82ng/ml and 0.004 $\pm$ 0.005ngml respectively.

On the other hand ,the infertile control subjects had minimum age, AMH and tPSA of 22 year, 0.00ng/ml and 0.00ng/ml respectively, while the maximum values ware 35 yare, 2.40ng/ml and 0.02ng/ml ,with  $\pm$  SD (30.3 $\pm$ 4.4 year, 0.78 $\pm$ 0.842ng/ml and 0.013 $\pm$ 0.005ngml) respectively. As for PCOS case table (1) indicates the minimum age was 16yaer and the max was44 year with mean  $\pm$  SD( 29.3 $\pm$  6.2year ).the minimum levels of both AMH and tPSA ware 4.10 and 0.00ng/ml, respectively, where are the max levels 44.00 and 0.05ng/ml with mean  $\pm$ SD (12.12 $\pm$ 10.83 and 0.025 $\pm$ 0.013ng/ml) respectively.

#### Table (2): Comparison between fertile control and PCOS case for the levels of AMH and tPSA:

The level of AMH in PCOS case was significant higher (12.124 $\pm$ 10.833ng/ml) than in fertile control subjects (2.801 $\pm$ 0.819ng/ml) (p-value: 0.001).

ROC for diagnostic accuracy of AMH model in predicting PCOs is given in (Figure 1) Was found to

be (100%) sensitivity and 100% specific (area under the curve 1.00, SE±0.00, Asymptotic sig.=0.00, lower bound =1 and upper bound =1). (Figure 2) shows the consistency of AMH to detect the PCOs by using split-half reliability test that was 0.60 (60%) (Area; 0.60, SE±=0.08, asymptotic sig. =0.225, lower bound =0.441 and upper bound 0.759).

**Table (2)** Also shows that the level of total prostate specific antigen (tPSA) was significant elevated in case (0.025±0.013ng/ml) than in control (0.004±0.005ng/ml) with increasing estimated by about 525.0%.

ROC curve (Figure 3) for diagnostic accuracy of the TPSA test in predicting PCOs regarding fertile control was found to be 0.924(92.4%) (Area =0.924. SE±=0.027, asymptotic sig. =0.00, lower bound 0.1 =0.871 and upper bound 0.977) 92% sensitivity and 90% specific cut off point .009ng/ml.

(Figure 4) indicate that the consistency of tPSA to diagnosis PCOs was 0.501(50.1%),(area 0.501 , SE±=0.083, asymptotic sig.=0.992, lower bound =0.338 and upper bound 0.664) which not significantly different.

**Comparison between infertile control and PCOS case for the levels of AMH and tPSA:**

**Table (3)** shows that the level of AMH in PCOs case was significant higher (12.124±10.833ng/ml) than in infertile control subjects (0.784±0.842ng/ml) by about 1446.4% (p-value: 0.000). ROC (Figure 5) for diagnostic accuracy of AMH model in predicting PCOs regarding infertile was found to be (100%) and 100% specific (area under the curve 1.00, SE±0.00, Asymptotic sig. =0.00, lower bound: 1.00 and upper bound =1.00)

**Table (3)** Also shows that the level of (tPSA) was significant higher in case PCO S (0.025±0.013ng/ml) than in infertile control (0.013±0.005ng/ml) (p-value 0.004\*\*) with increasing estimated by about 92.3.0%.

ROC curve (Figure 6) for diagnostic accuracy of the TPSA test in predicting PCOS regarding infertile control was found to be 0.790(79.0%) (Area =0.790. SE±=0.057, asymptotic sig. =0.003, lower bound 0.1 =0.679 and upper bound= 0.901).

**Comparison between AMH and tPSA tests for diagnosis of PCOS:**

ROC curve (Figure 7) for comparison between AMH and tPSA diagnostic test indicated that the accuracy of AMH (higher value) in predicting PCOs regarding to tPSA was 0.716(71.6%) Area =0.716. SE±=0.076, asymptotic sig. =0.026, lower bound =0.567 and upper bound 0.866) with significant different from 0.5(p<0.0

**Effect of age on AMH and TPSA level in PCOs case:**

Table (4) shows that AMH level in 16\_30 year age (4.090±5.091ng/ml) wasn't significant different from those who had >30 year (4.075±2.705ng/ml (p>0.05). similarly, the level of tPSA in 16\_30year (0.007±0.009ng/ml) was not significantly different as compared to >30year age (0.007±0.011ng/ml).

**Correlations between AMH and TPSA in PCOS case:**

Pearson correlation test was used to present the correlation between TPSA and AMH. There was very weak insignificant negative correlation of TPSA and AMH (r =-0.132, p =0.360) (Table 3.5)(Figure.8)

**Table 1: Descriptive statistics minimum, maximum, mean and SD for quantitative variable:**

Variable	N	Descriptive statistics		
		Minimum	Maximum	mean± SD
<b>Fertile control</b>	40			
Age (year)		20	36	29.5±3.9
AMH(ng/ml)		0.90	4.00	2.80±0.82
TPSA (ng/ml)		0.00	0.02	0.004±0.005
<b>Infertile control</b>	11			
Age (year)		22	35	30.3±4.4
AMH(ng/ml)		0.00	2.40	0.784±0.842
TPSA (ng/ml)		0.00	0.02	0.013±0.005
<b>PCOS (case):</b>	50			
Age (year)		16	44	29.3±6.2
AMH(ng/ml)		4.10	44.00	12.12±10.83
TPSA (ng/ml)		0.00	0.05	0.025±0.013

**Table 2: Comparison of AMH and TPSA in fertile control and PCOS case:**

parameter	Control( fertile)	Case (PCOS)	P-value
AMH	2.80±0.82	12.12±10.83	0.001
TPSA	0.004±0.005	0.025±0.013	0.001

t Independent t test was used to calculate P value  
 P value less than 0.05 considered significant

**Table 3: Comparison of AMH and TPSA in infertile control and PCOS case:**

parameter	Control( infertile)	Case (PCOS)	P-value
AMH	0.784±0.842	12.12±10.83	0.001
TPSA	0.013±0.005	0.025±0.013	0.004

t Independent t test was used to calculate P value  
 P value less than 0.05 considered significant

**Table 4: level of AMH and TPSA ac affected by age of PCOS:**

parameter	1__30year	>30	P-value
AMH	4.090±5.091	4.075±2.705	0.990
TPSA	0.007±0.009	0.007±0.011	0.958

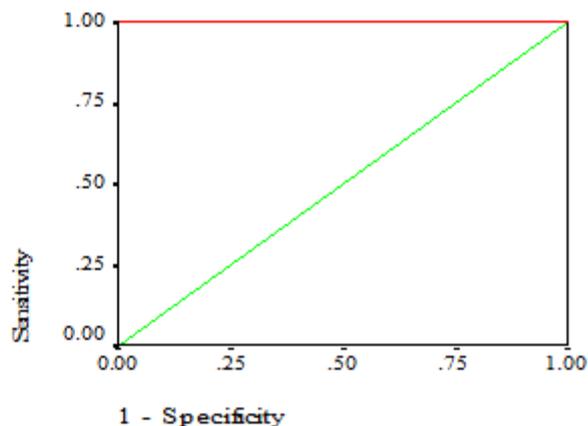
t Independent t test was used to calculate P value  
 P value less than 0.05 considered significant

**Table 5: relationship between AMH and TPSA in PCOS case**

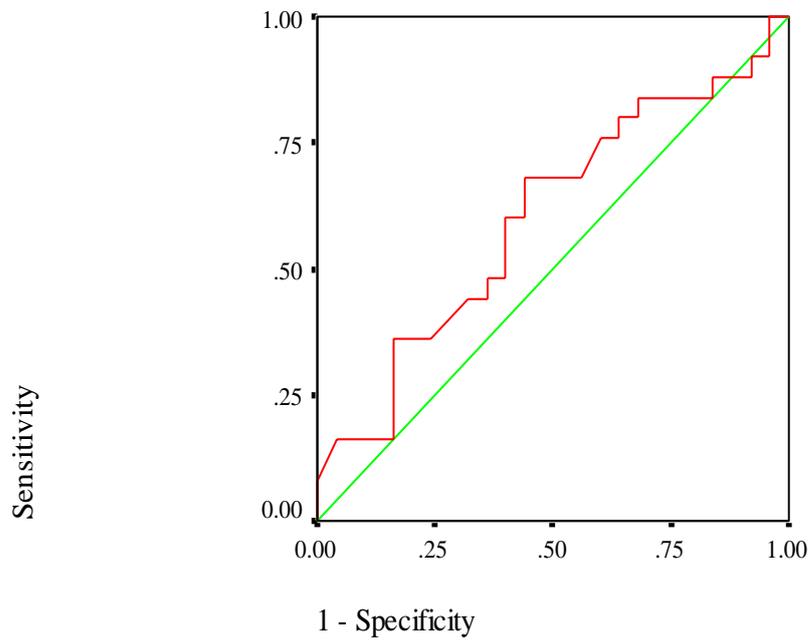
Parameter	r = Pearson	p Value	correlation coefficient
AMH	-0.132		0.360

Pearson correlations was used

value less than 0.05 considered significant



**Fig.(1): ROC curve for AMH as diagnostic tool for PCOS regarding fertile control**



Fig(2): ROC curve for consistency of AMH as diagnostic tool for PCOS

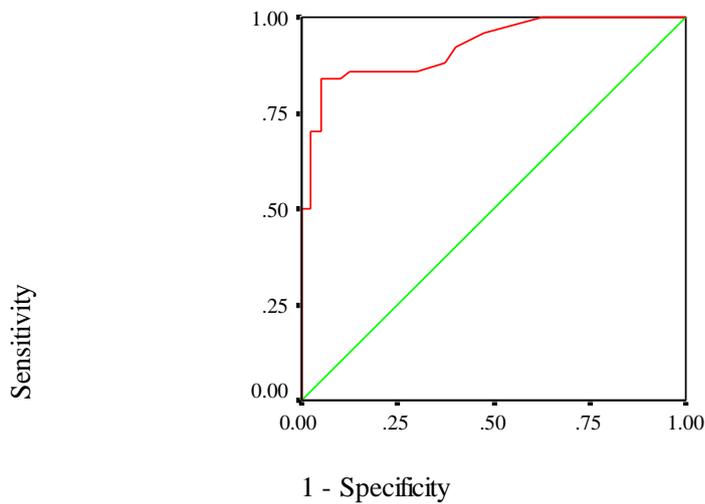


Fig.(3):ROC curve for TPSA as diagnostic tool for PCOS regarding fertile control

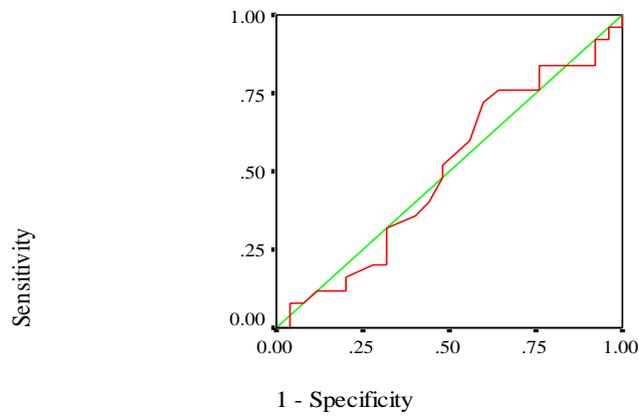


Fig.(4): RCO curve for consistency of TPSA as a diagnostic tool for PCOS.

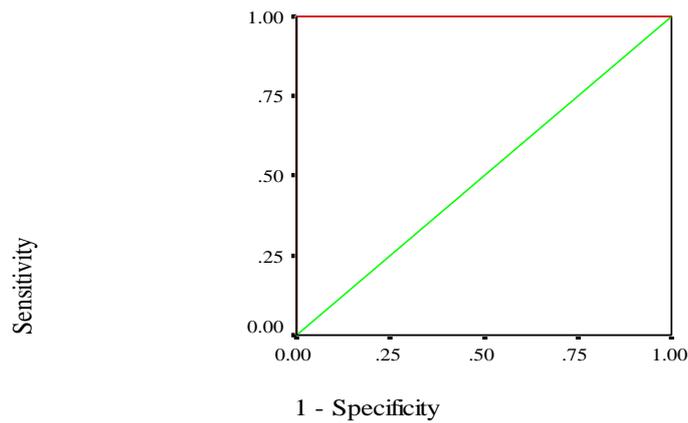


Fig.(5): RCO curve for AMH as a diagnostic tool for PCOS regarding infertile control.

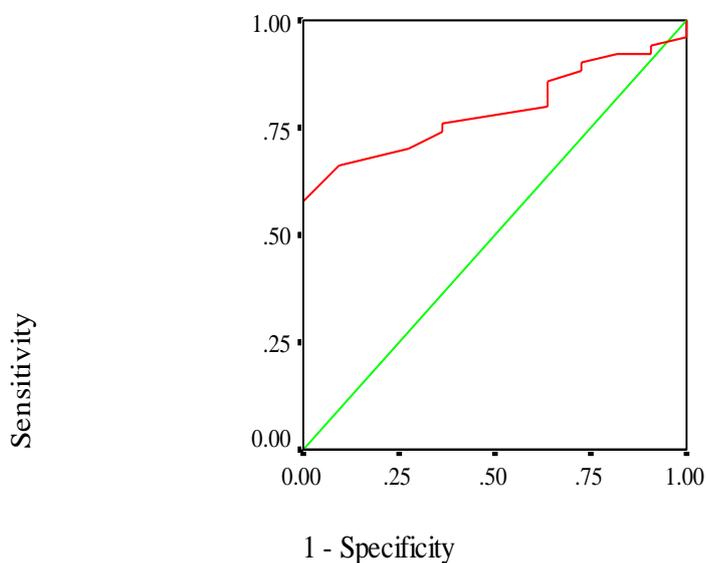


Fig.(6): ROC curve for TPSA as adignostic tool for PCOS regarding infertile control.

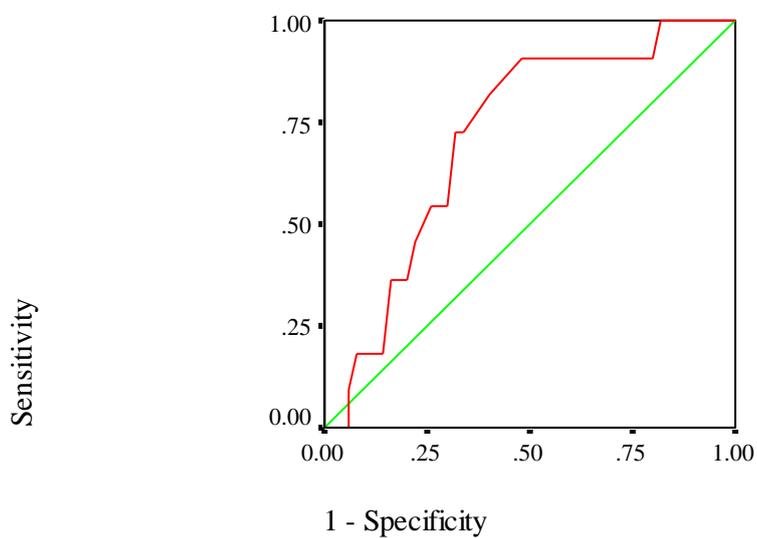
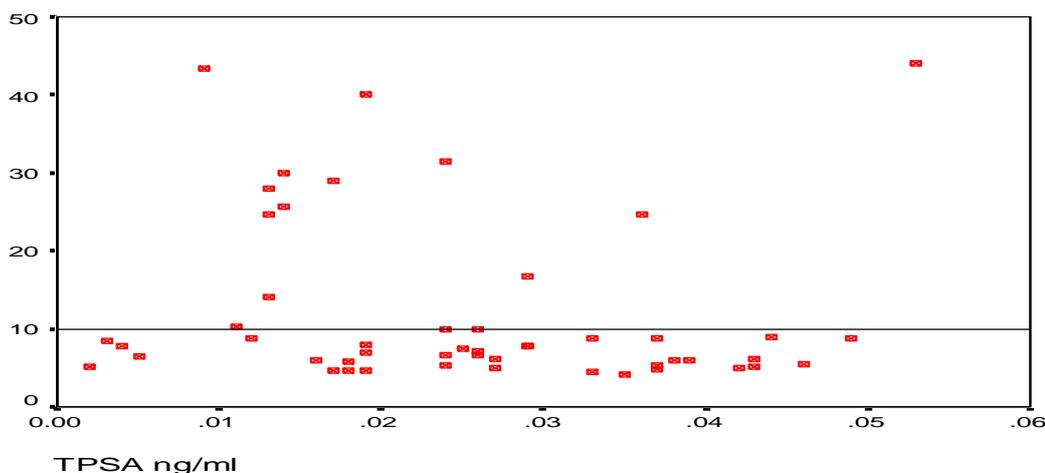


Fig.(7): ROC curve for comparison between AMH and TPSA as diagnostic tool of PCOS.



**Fig 8: correlation between TPSA and AMH level( $r=-0.132$ ,  $p\text{-value}=0.360$ )**

## DISCUSSION

Prostatic specific antigen (PSA) is the most specific prostatic tumor marker in men, PSA can no longer be regarded as a tissue specific or tumor-specific marker for only prostatic tissue, due to recent finding in different female tissues in small amount, because the control is under androgen regulation.

These findings showed a significant difference between the means of total prostate specific antigen (TPSA) in PCOS case ( $0.025 \pm 0.013 \text{ ng/ml}$ ) than normal fertile control ( $0.004 \pm 0.005 \text{ ng/ml}$ ) ( $p\text{-value} 0.001$ ), also showed TPSA was significant higher in case PCOS than in infertile control ( $p\text{-value} 0.004$ ). Similar result was found in other study by (E. Rudnicka *et al.*; in 2016 [2]), which report statistically significant difference in level of TPSA in PCOS than in control ( $p\text{-value} 0.003$ ), While it agrees with other study by Al (Bayatti *et al.*; in 2004) [7]. that found there are significant difference in level of TPSA in PCOS group compared to control group ( $p\text{-value} < 0.001$ ), also agree with other study by Metawie *et al.*; in 2008 [8]. which reported PSA both on 2nd day of cycle and midluteal phase was significantly higher in PCOS than in control group ( $p\text{-value} 0.004, 0.03$ ). This difference it's mainly may due to hyperandrogenism among PCOS (ovarian androgen over production that stimulate the target tissues capable of producing PSA, like breast and periurethral glands [5, 7].

The current study showed the TPSA have ability to predicting infertile PCOS regarding fertile control, at threshold  $0.009 \text{ ng/ml}$ , with sensitivity 92%, and the specificity 90%, area = 0.924, lower bound = 0.871 and upper bound 0.977) and about 0.790 (79.0%)

when regarding infertile control. similar study by E. Rudnicka *et al.*; in 2016 [2] report TPSA: AUC 66.3%, threshold  $0.005 \text{ ng/ml}$  with specificity 63.03%, sensitivity 68.96%, positive LR 1.86, negative LR 0.49 regarding women without PCOS [1].

In this study also demonstrated that the consistency of TPSA to diagnosis PCOs was 0.501 (50.1%); I think may due to different phenotype of PCOS. The present study also include AMH which considered as gold standard separated lab test, which was found to be (100%) sensitivity and 100% specific in predicting PCOS regarding fertile and infertile control, with consistency 0.60 (60%), similar study by Tayrab *et al.*; 2014 [3] that shown AMH is significantly decreased in infertile Sudanese women and significantly elevated in Sudanese women with PCOS, This difference may due to increased synthesis and secretion of AMH by polycystic ovaries [9]. In this study shown very weak, insignificant, negative correlation of TPSA and AMH, the negative correlation may be due to that, there an evidence that AMH and testosterone negatively regulate one another and when AMH concentrations are high, testosterone is low and androgen receptors (AR) are not expressed in the male testes (10). In this investigation also shown the level of TPSA in 16-30 year was not significantly different as compared to >30 year age, but disagree with by SH [11], TPSA and FPSA levels were significantly associated with younger age.

## CONCLUSIONS:

From the results of this study, it is concluded that, the serum levels of TPSA are increased in Sudanese women with PCOS and The accuracy of

TPSA as diagnostic tool for predicting PCOS is good when regarding fertile control, but decrease with infertile without PCOS. But cannot consider as separated lab test and when comparing to AMH, The AMH sensitive and accurate more than PSA. Further studies need to measure PSA in different age above 36yaer, different phenotype and correlate with hirsutism score in Sudanese women. Monitoring PSA level before, during and after treatment. Large number of sample size will be necessary.

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