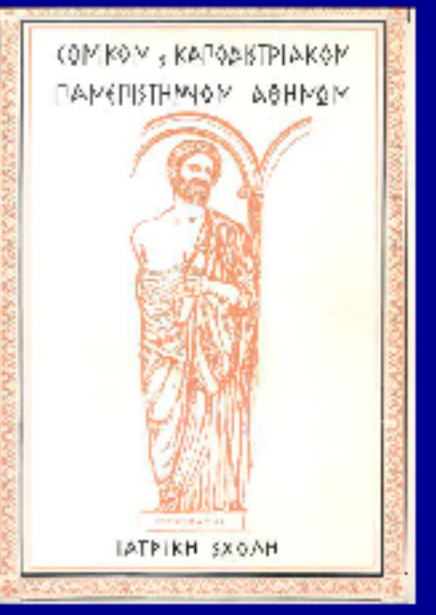


Follicular fluid Bisphenol A levels were higher and correlated with decreased number of oocytes in women with tubal factor infertility compared to polycystic ovary syndrome

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Introduction

Bisphenol A (BPA) is a chemical compound used in the manufacture of polycarbonate plastics and epoxy resins composing a variety of everyday products. BPA was considered a weak environmental estrogen-mimicking compound, binding to both estrogen receptor (ER) α and ER β , with 10-fold higher affinity to ER β .

BPA also acts through a variety of mechanisms other than mimicking, enhancing or inhibiting the activity of endogenous estrogens. BPA exposure negatively impacts ovarian response, number of fertilized oocytes, blastocyst formation and implantation in women undergoing in vitro fertilization (IVF) procedures.

Aim of the study

The aim of the study was to determine BPA levels in polycystic ovary syndrome (PCOS) women and women with tubal factor (TF) infertility who underwent IVF and to investigate their effects in critical endpoints of IVF, the possible association with oocytes number and IVF outcome.

Material and Methods

Eighty two women in reproductive age (41 with PCOS and 41 normo-ovulatory with TF infertility) with mean age who underwent IVF were included in a prospective controlled study in Academic Assisted Conception Unit. Anthropometric parameters were assessed (Table 1).

Table 1. Demographics and comparison of tubal factor and PCOS group.

	Tubal factor (n=41)	PCOS (n=41)	p
Age (years)	38 (37/41)	35 (34/38)	<0.000
BMI status (%)			0.113
Lean (<25 kg/m ²)	65.9% (21.8 kg/m ²)	46.3% (21.5 kg/m ²)	0.562
Overweight/Obese (\geq 25 kg/m ²)	34.1% (27.2 kg/m ²)	53.7% (29.5 kg/m ²)	0.284
Waist circumference (cm)	80.0 (75.0/86.5)	85.0 (74.0/92.0)	0.254
WHR	0.772 (0.749/0.827)	0.815 (0.742/0.875)	0.109
Ferriman-Gallwey score	3 (3/5)	12 (3/18)	<0.000
Smoking (%)			-
Never	51.2%	46.3%	-
Former	14.7%	22.0%	-
Current	34.1%	31.7%	-

We developed a novel gas chromatography-mass spectrometry (GC-MS) method to determine BPA levels in serum, urine and follicular fluid (FF) and their impact on critical parameters of these women undergoing IVF. **Metabolic, and hormonal parameters** were also assessed (Table 2).

Table 2. Comparison of sex steroid levels on the day of oocyte retrieval and IVF outcome

	Tubal factor (n=41)	PCOS (n=41)	p
FSH (mIU/mL)	10.25 (7.84/13.33)	4.57 (2.94/5.75)	<0.000
Testosterone (ng/mL)	0.567 (0.500/0.724)	0.883 (0.583/1.273)	<0.000
E2 (pg/mL)	1240 (796/1640)	1387 (922/2292)	0.097
SHBG (nmol/L)	129.0 (82.7/149.0)	116.0 (85.7/137.0)	0.479
FTI (%)	1.70 (1.23/2.64)	2.70 (1.53/5.34)	0.013
FEI (%)	2.95 (2.18/4.16)	4.55 (3.02/8.00)	0.006
Oocytes collected	8 (5/11)	15 (10/19)	<0.000
Oocytes fertilized	3 (2/6)	8 (5/10)	<0.000
Fertilization rate (%)	37.5%	53.3%	0.575
IVF protocol (%)			-
Antagonist short	36.6%	82.9%	-
Agonist short	58.6%	14.7%	-
Agonist long	0.0%	2.4%	-
Clomiphene	4.8%	0.0%	-
Response to protocol (%)			-
Poor	26.8%	2.4%	-
Normal	68.4%	85.4%	-
High	4.8%	12.2%	-
Male factor (%)			-
No	66.7%	67.7%	-
Yes	33.3%	32.3%	-
Pregnancy (%)			-
No	55.6%	41.0%	-
Yes	44.4%	59.0%	-

FSH: Follicle-stimulating hormone; E2: Estradiol; SHBG: Sex Hormone Binding Globulin; FTI: Free Testosterone Index; FEI: Free Estradiol Index. Data are presented as median (25th/75th percentile). Bold values are statistically significant (p<0.05). Italic values are indicative of a significant difference between groups (0.05<p<0.10).

Table 3. BPA measurements among tubal factor and PCOS women

	Tubal factor (n=41)	PCOS (n=41)	p
Serum BPA (ng/mL)	0.780 (0.390/1.210)	0.580 (0.155/0.933)	0.157
Urinary BPA (ng/mL)	0.985 (0.553/1.623)	1.500 (0.790/2.000)	0.017
Follicular BPA (ng/mL)	1.128 (0.394/2.046)	0.505 (0.138/1.152)	0.041

Data are presented as median (25th/75th percentile). Bold values are statistically significant (p<0.05).

Results

We detected higher BPA levels in serum (0.780 ng/ml vs. 0.580 ng/ml, NS) and FF (1.128 ng/ml vs. 0.505 ng/ml, p<0.05) but lower BPA levels in urine (0.985 ng/ml vs. 1.500 ng/ml, p<0.05) of women with TF infertility compared to PCOS, with a trend towards higher follicular BPA levels in TF women and lower levels in PCOS women after BMI stratification (Table 3 & figure 1). After adjustment for age, BMI and exogenous FSH administration, follicular BPA levels correlated with decreased number of oocytes collected during oocyte retrieval in TF women only (mean decrease of **-1.772 oocytes**, p<0.05) but no significant effect on the number of oocytes fertilized and pregnancy rates of both groups (Table 4).

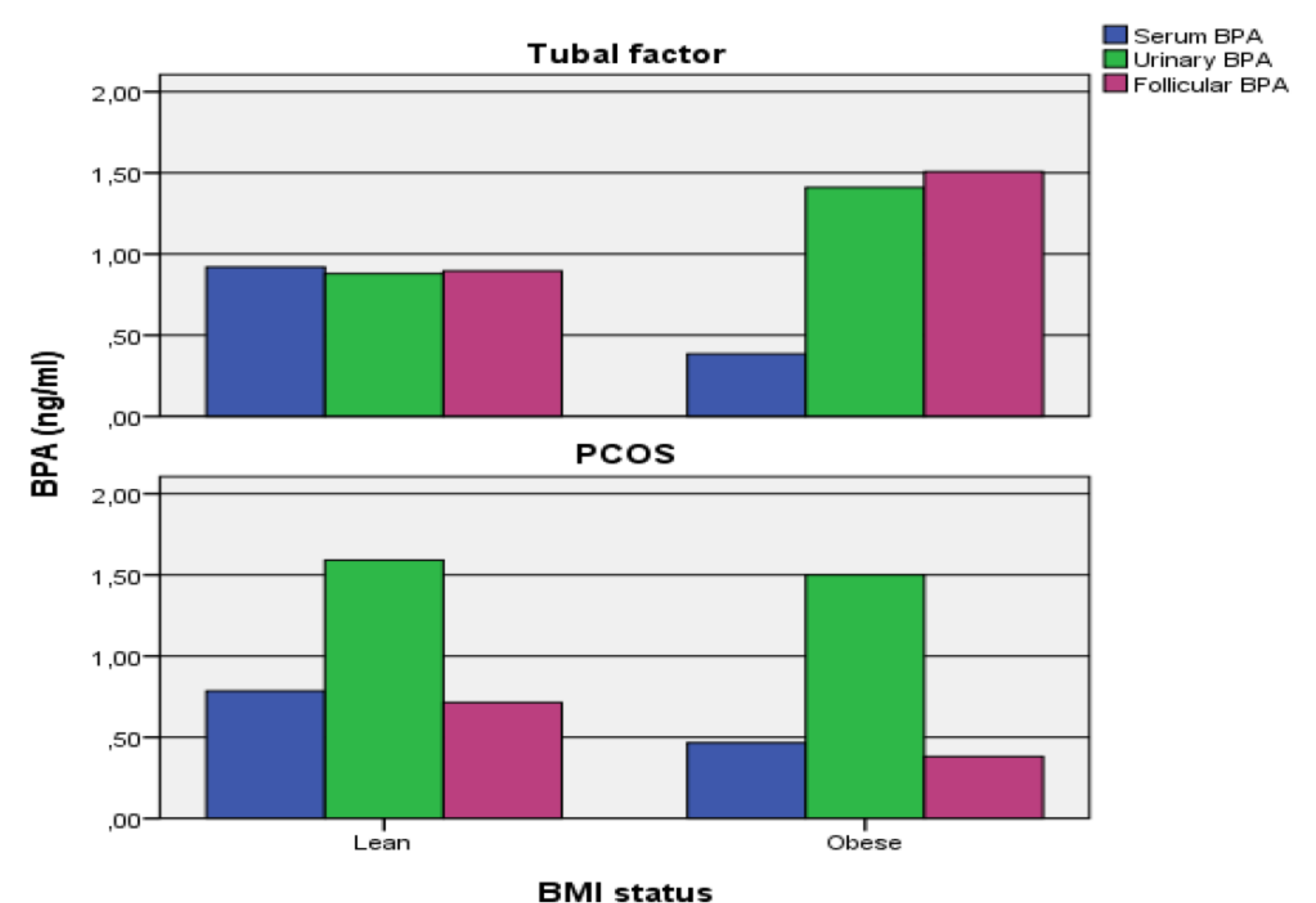


Figure 1. Comparison of BPA levels after BMI stratification among the two groups.

Table 4. Multivariable linear regression models for association between follicular BPA and oocytes collected and fertilized from tubal factor and PCOS group

	Model for oocytes collected ^a				Model for oocytes fertilized ^b			
	Predictors	Beta	95% CI	p	Predictors	Beta	95% CI	p
Tubal factor	Follicular BPA	-1.772	(-3.471/-0.073)	0.041	Follicular BPA	-0.346	(-0.895/0.203)	0.210
	IVF protocol	-5.061	(-7.747/-2.375)	0.001	Age	-0.006	(-0.090/0.077)	0.876
	Age	0.590	(0.363/0.816)	0.000	BMI status	0.141	(-0.713/0.994)	0.740
	FSH	-0.449	(-0.925/0.027)	0.064	FSH	0.019	(-0.146/0.184)	0.817
	BMI status	0.802	(-1.885/3.489)	0.549	Oocytes collected	0.543	(0.448/0.637)	0.000
PCOS	Follicular BPA	0.651	(-1.056/2.357)	0.445	Follicular BPA	0.409	(-0.500/1.318)	0.368
	Age	0.292	(0.110/0.475)	0.002	Age	0.036	(-0.073/0.146)	0.503
	FSH	0.158	(-0.718/1.034)	0.717	BMI status	0.152	(-0.859/1.162)	0.762
	BMI status	1.021	(-0.861/2.903)	0.279	FSH	0.048	(-0.416/0.512)	0.834
					Oocytes collected	0.360	(0.184/0.536)	0.000

^a Model fit: Tubal factor (77.7%, p<0.05), PCOS (89.3%, p<0.05).

^b Model fit: Tubal factor (92.0%, p<0.05), PCOS (89.4%, p<0.05).

CI: Confidence Interval; FSH: Follicle-stimulating hormone.

Bold values are statistically significant (p<0.05). Italic values are indicative of a significant difference between groups (0.05<p<0.10).

Conclusions

The present study showed that BPA levels were higher in FF and correlated with decreased number of oocytes collected during oocyte retrieval in women with TF infertility compared to PCOS.

References

- Wetheril et al. 2007
- Welshons et al 2006
- Kandaraki et al 2011
- Wang et al 2015