

Do Heavy Metals lead to Diminished Ovarian Reserve in Infertile Women?



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Objective

Reproductive decline in women globally is attributable to cultural change and environmental exposure

Heavy metals liberated in the environment, accumulate in the soil, water, and food chain, and do not easily decompose under natural conditions

Heavy metals like Arsenic, cadmium, mercury and lead are commonly found in drinking water, air, cosmetics and foods, notably seafood and rice

Heavy metals form an important aspect of reproductive toxicology and alter reproductive functions in both males and females like a decrease in sperm count, motility, spermatogenesis, follicular atresia, and delay in oocyte maturation

Hence we planned this study to compare the levels of heavy metals in infertile women with diminished ovarian reserve with normal ovarian reserve.

Design

Case control study conducted over a period of one year at Department of Obstetrics & Gynecology KGMU Lucknow

Methodology

Infertile women willing to take part in the study and satisfying the inclusion and exclusion criteria were enrolled

Inclusion criteria

- All the infertile women aged 18-40 years with ovarian reserve test as AMH <0.5 ng/ml., AFC <5, FSH >15 IU/ml & E2 <50 pg/ml

Exclusion criteria

- Uncontrolled thyroid (S.TSH >5 IU/ml) & known adrenal dysfunction.
- Any history of ovarian surgery in past and radiotherapy & chemotherapy in past.
- Known metabolic disorder like galactosemia

Cases : Infertile women with diminished ovarian reserve

Controls: Age matched individuals with normal ovarian reserve

2 ml venous blood sample was collected from each individual in EDTA vial for estimation of heavy metals (ie. As, Pb, Cd, Hg, Cu, Zn, Mg).

Analysis of heavy metals & trace elements in whole blood was done using the microwave digestion method.

ICP/OES was used for the determination of heavy metals and trace elements in a myriad of sample types. The technique is based on the spontaneous emission of photons from atoms and ions that have been excited.

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Results

A total of 146 samples were collected.

Cases

Infertile Women with diminished ovarian reserve (n=73)

Controls

Infertile Women with normal ovarian reserve (n=73)

Demographics and Clinical findings of patients enrolled in the study

S.No.	Parameter	Cases	Controls	P value
1	Age	31.92 ± 5.4	27.79 ± 4.5	<0.0001
2	BMI	24.61 ± 2.4	24.89 ± 1.7	0.417
3	Hindu	60 (82.1%)	70 (95.8%)	??= 7.01,
	Muslim	13 (17.8%)	03 (4.1%)	p= 0.008
4	Illiterate	1 (1.3%)	2 (2.7%)	??= 0.34,
	Literate	72 (98.6%)	71 (97.2%)	p= 0.55
5	Smoking (+)	0	0	-
	Smoking (-)	73 (100%)	73 (100%)	
6	AMH levels	0.125 ± 0.12	2.3 ± 0.09	<0.0001
7	FSH levels	26.36 ± 2.1	7.2 ± 1.8	<0.0001
8	vegetarian	30 (41.0%)	63 (86.3%)	??= 32.26,
	Non vegetarian	43 (58.9%)	10 (13.7%)	p= <0.0001
9	Use of plastic disposable(at least once a week)	12 (16.43%)	0	-
10	Washing of fruits and vegetables(sometimes)	63 (86.3%)	23 (31.5%)	??= 45.27,
	Washing of fruits and vegetables(always)	10 (13.7%)	50 (68.4%)	p= <0.0001
11	Use of unpurified water (Handpumps)	5 (6.8%)	8 (10.9%)	??= 8.70,
	Use of unpurified water (Tap water)	55 (75.3%)	38 (52.0%)	p= 0.012
	Use of purified water (RO)	13 (17.8%)	27 (36.9%)	

Level of metals in enrolled patients in case and control groups

S.No	Heavy metal	CASES		CONTROL		P-VALUE
		MEAN	SD	MEAN	SD	
1.	As 75 Helium KED (cps)	0.15	0.15	0.14	0.13	t=0.4304, p=0.6675
2.	Cd 111 Helium KED (cps)	0.10	0.09	0.06	0.03	t=3.602, p=0.0004*
3.	Hg 202 Helium KED (cps)	2.42	5.50	1.39	1.77	t=1.523, p=0.1299
4.	Pb 208 Helium KED (cps)	6.99	3.59	5.98	1.95	t=2.112, p=0.0363*
5.	Cu 63 Helium KED (cps)	184.56	84.14	178.43	105.56	t=0.3880, p=0.6985
6.	Mn 55 Helium KED (cps)	3.24	7.21	4.58	4.90	t=1.313, p=0.1911
7.	Zn 66 Helium KED (cps)	527.50	290.60	426.93	126.07	t=1.094, p=0.2758

Logistic regression analysis of various parameter with respect to heavy metal (Cadmium and Lead)

	CADMIUM			LEAD		
	aOR	95%CI	P-VALUE	aOR	95%CI	P-VALUE
AGE (year old)	1.04	0.94-1.14	0.2514	1.10	0.89-1.28	0.1548
BMI (Abnormal)	1.01	0.85-1.18	0.1424	1.02	0.88-1.34	0.1148
Food Eating Habits In Disposable Plastics	1.06	0.12-1.841	0.0478*	1.07	0.012-1.658	0.0487*
Does She Wash Fruits & Vegetables Before Eating	0.98	0.25-1.11	0.3481	0.99	0.12-1.34	0.3514
Diet (Non-veg)	1.34	0.99-1.54	0.0404*	1.36	0.97-1.66	0.0398*
Water habit (Tap water)	1.54	0.89-1.89	0.0259*	1.51	0.85-1.79	0.0284*
AMH (<0.5 ng/dl)	1.67	0.02-0.98	0.01984*	1.64	0.03-0.99	0.0199*

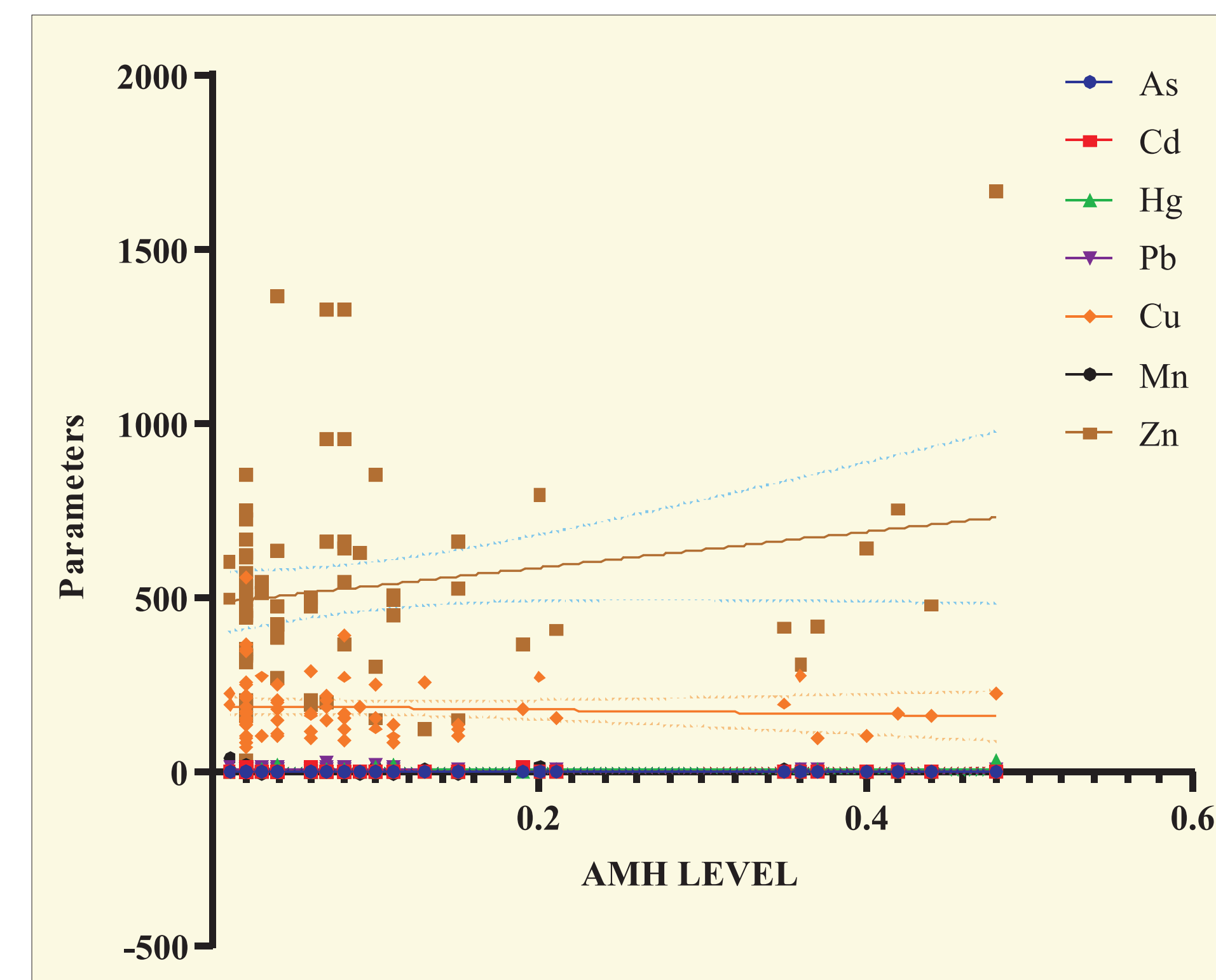
Correlation analysis of Anti Müllerian Hormone (AMH) with level of metals

AMH	Spearman r	95% confidence interval	Correlation	P-VALUE
vs.				
As	-0.2333	-0.3968 to 0.06948	Weak	0.1483
Cd	-0.4167	-0.4510 to 0.003471	Moderate	0.0119*
Hg	-0.12022	-0.2589 to 0.2208	Very Weak	0.8671
Pb	-0.4063	-0.5004 to -0.06031	Moderate	0.0122*
Cu	0.1183	0.1252 to 0.3484	Very Weak	0.3257
Mn	0.2225	0.01841 to 0.4390	Weak	0.0622
Zn	0.07984	0.1632 to 0.3138	Very Weak	0.5081

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Correlation analysis of Anti Müllerian Hormone (AMH) with level of metals



Conclusion

Heavy metals like Pb and Cd were significantly higher in cases. As, Hg, Cu, Zn were found in higher concentration in cases as compared to controls and Mn was found in higher concentration in controls as compared to cases.

Pb and Cd was found in higher concentration in non-vegetarians; who used disposables at least once a week; who consumed tap water

Pb and Cd may affect hypothalamic-pituitary-ovarian axis which affects menstruation and ovulation . They may causes damage to growing follicles reducing AMH and resulting in infertility.

This is a cross-section study, and the significant levels of heavy metals found in our study gives us idea about the effects of heavy metals on woman's fertility and also paves way for further research with larger sample size.

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