

# Relation of Some Heavy Metals with Male Infertility

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## Summary

**Background:** Infertility is defined as a failure of achieve a pregnancy after one year and more of regular unprotected sexual intercourse. The exposure of reproductive system especially the testis to heavy metals has also been associated with male infertility. A large number of metals are toxicants to the reproductive system. **Patients and methods:** Study was performed at the high institute of infertility diagnosis and assisted reproductive technologies in Al-Nahrain University and the Poisoning consultation center / specialized surgeries hospital in the Medical city during the period from November 2018 to April 2019. A total number of 150 men were enrolled in this study who were divided into two groups, the patient and the normal control groups. The patient group included 100 men aged between 20-50 years. The second group included 50 healthy men who have at least two children without any previous history of systemic diseases as a control group. Heavy metals and trace element concentrations were estimated for all the study groups in this study. The aim of current study are evaluation of some trace element concentrations, in serum and whole blood of infertile men and healthy controls. **Results:** The heavy metals Cu, Pb and Cd showed a highly significant increase ( $p < 0.01$ ) in the serum and blood of infertile men ( $159.77 \pm 8.49 \mu\text{g/dl}$ ,  $24.18 \pm 4.30 \mu\text{g/dl}$ ,  $0.31 \pm 0.10 \mu\text{g/dl}$ ) respectively when compared with their concentrations in healthy control men ( $125.14 \pm 10.12 \mu\text{g/dl}$ ,  $15.74 \pm 2.69 \mu\text{g/dl}$ ,  $0.16 \pm 0.03 \mu\text{g/dl}$ ) respectively. The mean levels of Zn showed a highly significant decrease ( $p < 0.01$ ) in the serum of infertile men ( $70.82 \pm 9.48 \mu\text{g/dl}$ ) compared to its mean level in the healthy control group ( $95.70 \pm 11.41 \mu\text{g/dl}$ ). **Conclusions:** this study concluded that some heavy metals were shown to be an indicators for men infertility.

**Keywords:** heavy metals infertility male reproductive.

## Introduction

Infertility was defined as inability to conceive after one year of regular unprotected intercourse<sup>(1)</sup>. Infertility is an ever increasing phenomenon in the modern urban societies<sup>(2)</sup>, and generally, infertility affects about (10-15%) of the couples in the world. The cause of infertility in about (10%) of cases remains unexplained, and the couples are designated as normal infertile couples<sup>(3)</sup>. Male infertility is a common disorder that affects approximately (50%) of infertility cases in the world<sup>(4)</sup>. Male fertility depends upon the coordination between neural and hormonal mechanisms or between male reproductive system and these mechanisms. Thus, any hindering of at least one of these mechanisms will result in infertility<sup>(5)</sup>. The trace elements are micro nutritive elements that exist in minute quantities within the body mass and they are either important via playing different functional roles in the body or non-essential

elements with negative effect on the human body even at very low concentrations<sup>(6)</sup>. Heavy metals are usually dense elements with potential toxicity, especially in environmental context<sup>(7)</sup>. They can be naturally obtained from the earth crust, and became concentrated because human activities. Heavy metals can enter human tissues via food, inhalation and manual handling<sup>(8)</sup>. Skin contact absorption, for instance soil contact, is another possible source of body contamination by heavy metals<sup>(9)</sup>. Because they are difficultly metabolized, toxic heavy metals can bioaccumulate in human's body<sup>(10)</sup>. Those heavy metals may combine with and interfere with the vital cellular element functions<sup>(11)</sup>. Because of sperm's oxidative damage and testicular apoptosis, exposure to heavy metals has also been associated with male infertility<sup>(12)</sup>. Increase in fertility associated with higher miscarriage rates have been noted in the partners of men working in lead battery factories, indicating harmful effects of heavy metals on reproductive success<sup>(13)</sup>.

**Materials and methods:**

Study was performed at the high institute of infertility diagnosis and assisted reproductive technologies in Al-Nahrain University and the Poisoning consultation center / specialized surgeries hospital in the Medical city during the period from November 2018 to April 2019. A total number of 150 men were enrolled in this study who were divided into two groups, the patient and the normal control groups. The patient group included 100 men aged between 20-50 years. The second group included 50 healthy men who have at least two children without any previous history of systemic diseases as a control group. Heavy metals and trace element concentrations were estimated for all the study groups

in this study. Frozen serum was allowed to thaw at room temperature, and assessment of inorganic elements Zn and Cu was performed by Flame atomic absorption spectrophotometry, while Cd was measured by graphite furnace atomic absorption spectrophotometry.

**Finding**

results indicated that 78 (78%) of the 100 cases had abnormal zinc levels, while 22 (22%) of them had normal zinc levels in comparison with the control group which showed that 46(92%) had normal zinc levels and only 4 (8%) had abnormal zinc levels, with a highly significant difference using the Monte Carlo test MCP < 0.01. As shown in table (1).

**Table (1) Descriptive statistic & MCP test between cases and control of serum zinc**

Zn Level	Cases		Control	
	No.	percentage%	No.	percentage%
Normal	22	22	46	92
Abnormal	78	78	4	8
Total	100		50	100

Cu Level	Cases		Control	
	No.	percentage%	No.	percentage%
Normal	20	20	50	100
Abnormal	80	80	0	0.0
Total	100	100	50	100

**Table (2) Descriptive statistic & MCP test between cases and control of serum copper**

While results in table (2) demonstrated that 80 (80%) of the 100 cases had abnormal copper levels, and 20 (20%) of them had normal copper levels when compared with the control group which showed that all the 50(100%) control group had normal copper levels, with a highly significant difference using the Monte

Carlo test MCP < 0.01.

Results of blood lead level estimation in table 3 showed that 33 (33%) of the 100 infertile patients had abnormal lead levels, and 67 (67%) of them had normal leadlevels, while all the control group 50 (100%) had normal lead levels, with a highly significant variation

using the Monte Carlo statistical test  $MCP < 0.01$ .

**Table (3) Descriptive statistic & MCP test between cases and control of blood lead**

Cd Level	Cases		Control	
	No.	percentage%	No.	percentage%
Normal	49	49	50	100
Abnormal	51	51	0	0.0
Total	100	100	50	100

Results of blood cadmium level estimation showed that 51(51%) of the 100 infertile patients had abnormal cadmium levels, and 49 (49%) of them had normal cadmium levels, while all the control group 50 (100%) had normal cadmium levels, with a highly significant difference using the Monte Carlo statistical test  $MCP < 0.01$  as illustrated in table 4.

**Table (4) Descriptive statistic & MCP test between cases and control of blood cadmium**

Pb Level	Cases		Control	
	No.	percentage%	No.	percentage%
Normal	67	67	50	100
Abnormal	33	33	0	0.0
Total	100	100	50	100

**Table (5): Descriptive statistics and t-test between patient group and control group regarding (Zn µg/dl, Cu µg/dl, Pb mg/dl, Cd µg/dl).**

	Groups	N	Mean ±Std.	t-test	P-Value	C.S
Cu	Cases	100	159.77±8.49	22.065	.000	P<0.01(HS)
	Control	50	125.14±10.12			
Zn	Cases	100	70.82±9.48	14.140	.000	P<0.01(HS)
	Control	50	95.70±11.41			
Pb	Cases	100	24.18±4.30	12.684	.000	P<0.01(HS)
	Control	50	15.74±2.69			
Cd	Cases	100	0.31±0.10	10.478	.000	P<0.01(HS)
	Control	50	0.16±0.03			
	Control	50	450.35±131.27			

All the above results discern great variation in levels of heavy metals between the infertile male group and the control group suggesting that heavy metals have effect on male infertility. Results agreed with<sup>(14)</sup>who mentioned in a scientific literature a lot of data on the negative influences of the toxic metals on the human body<sup>(14)</sup>.<sup>(15)</sup>found increase in Cd and Cu concentrations in the serum of infertile men comparison with the control group<sup>(15)</sup>. Inhalation or dermal absorption of heavy metals can significantly increase blood heavy metal levels<sup>(16)</sup>. These findings were consistent with the other studies conducted in Baghdad, Beirut and Al-Najaf which demonstrated that the blood levels of lead, cadmium & other heavy metals were increased among many workers<sup>(17&18&19)</sup>.as depicted in table 5, the mean serum copper concentration in infertile men group was  $159.77 \pm 8.49$   $\mu\text{g/dl}$ , which was significantly higher than the mean serum copper concentration of the healthy control group  $125.14 \pm 10.12$  ( $p < 0.01$ ). Results agreed with<sup>(15)</sup> who found a significant increase ( $p \leq 0.05$ ) in the concentration of Cd and Cu in the serum of infertile men in comparison with the control group. However, many human studies found negative correlations between Cu quantified in the body and spermatozoa quality parameters such as morphology, motility and viability<sup>(20)</sup>.<sup>(21)</sup>Indicated that high doses of Cu had negative effects on sperm motility<sup>(21)</sup>. Similar results were reported by<sup>(22)</sup> in human spermatozoa in Cu accumulation<sup>(22)</sup>. Also showed that serum zinc concentration in infertile men group was  $70.82 \pm 9.48$   $\mu\text{g/dl}$  which was a highly significantly lower than serum zinc of the healthy group  $95.70 \pm 11.41$  ( $p < 0.01$ ). This result was compatible with<sup>(23)</sup> who showed that serum zinc levels of patients with abnormal seminal fluid parameters were lower than those who have normal seminal fluid parameters<sup>(23)</sup>, and similar to the results of<sup>(24)</sup> who showed significant variation between serum zinc of infertile group & fertile group<sup>(24)</sup>. The most rapidly growing organs in the body are the gonads, and zinc metallo-enzymes are the vital enzymes involved in protein and nucleic acid synthesis, therefore, zinc deficiency can result in severe testicular damage, decreases of testicular weight, gonads dysfunction and seminiferous tubule shrinkage<sup>(25)</sup>.Data demonstrated in table 5 showed that the mean blood lead concentration in infertile men was  $24.18 \pm 4.30$   $\mu\text{g/dl}$ , which was significantly higher than its concentration in the healthy control group  $15.74 \pm 2.69$  ( $p < 0.01$ ). These results were compatible with a study of<sup>(26)</sup> who found a highly significant variation between their study groups<sup>(26)</sup>.And with<sup>(27)</sup> who found high levels of lead in the

infertile men in comparison with the controls<sup>(27)</sup>. And also with<sup>(28)</sup> who found that Pb levels were significantly higher in infertile males ( $p=0.001$ ) when compared with the control group<sup>(28)</sup>. Our results were also compatible with the results of<sup>(29)</sup> which showed that seminal and blood plasma cadmium as well as blood plasma lead levels were significantly higher ( $p < 0.01$ ) in azospermic and oligospermic men in comparison with normospermic men<sup>(29)</sup>. Results shown in table 5 indicated that mean blood cadmium concentration in the infertile male group was  $(0.31 \pm 0.10$   $\mu\text{g/dl}$ ), which was significantly higher than its mean concentration in the healthy control group  $(0.16 \pm 0.03$  ( $p < 0.01$ ). Our results were compatible with<sup>(29)</sup> who reported that seminal and blood plasma cadmium as well as blood plasma lead were significantly higher ( $p < 0.01$ ) in azospermic and oligospermic men when compared with normospermic men<sup>(29)</sup>. However,<sup>(30)</sup> observed significant correlations between blood cadmium levels, volume of semen and immature forms of spermatozoa suggesting the need of further studies on blood and semen cadmium levels<sup>(30)</sup>. These results were in agreement with<sup>(15)</sup> who showed a significant increase ( $p \leq 0.05$ ) in the serum concentration of Cd and Cu in infertile group which included azospermia & oligospermia in comparison with the control group<sup>(15)</sup>.

## Conclusions

The heavy metals Cu, Pb and Cd showed a highly significant difference in the serum and blood of infertile men compared to the healthy control men, indicating that the alteration in heavy metal metabolism may be related to the development and even progress of infertility among men. The mean levels of Zn showed a highly significant decrease in the serum of infertile men compared to the healthy control group, indicating that the alteration in zinc metabolism may be related to the development of infertility among men. Concentrations of heavy metals during the progress of life of infertile men were higher than those in healthy men. According to the results of the present study, all heavy metals were shown to be indicators for men infertility. The heavy metals should be monitored routinely in male infertility, which could be helpful in improving the general health conditions and reducing progression of the disease.

**Conflict of Interest:** Non

**Source of Findings:** Non

**Ethical Clearance:** Non

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