Determination of Cadmium Blood level among Infertile Males in Khartoum State

قياس نسبة معدل عنصر فلز الكادميوم في الدم لدى الرجال العُقَم في ولاية الخرطوم

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Abstract

Male infertility is a common disease in the world that affects approximately 15% to 20% of married couples. The study aims to assess serum levels of cadmium among infertile men. Forty men clinically diagnosed were chosen randomly from the Reproductive Health Care Centre in Khartoum State, and forty apparently healthy individuals as a control group, to evaluate the serum levels of cadmium. Serum , cadmium was measured by using the atomic absorption Spectrophotometer. Results were analyzed using Statistical Package for Social Science (SPSS), mean serum levels of cadmium were significantly increased in infertile men patients. (Mean± SD **0.349 ± 0.155** mg/dl versus (0.13 ± 0.082 mg/dl), respectively with ($P< 0.01$), There was a significant week negative correlation between cadmium levels and sperm motility (r=0.493 ; $P< 0.01$), There was a significant negative correlation between cadmium levels and sperm count (r=0.512 ; $P< 0.01$), There was no correlation between cadmium levels and testosterone hormone levels (r=0.165; $P= 0.143$), The serum cadmium measurement was significantly higher in infertile men patients.

The study recommended that Regular measuring of serum Cadmium as biomarkers of male infertility according occupation and area expose to Cadmium element and further investigations are recommended with larger sample size and more parameters should be included such as seminal plasma cadmium and sperm morphology.

Keywords: Cadmium, Male infertility, sperm motility, testosterone hormone.

المستخلص

العقم هو أحد الأمراض الشائعة في العالم, حيث يصيب 15% إلى 20% من الأزواج زيادة نسبة عنصر فلز الكادميوم في الدم يؤدى ترسبه ونخر في الخصيتين ويصيب الرجال بالعقم , تهدف الدراسة إلى قياس نسبة

معدن الكادميوم في الدم لدى الرجال العقم تم اختيار أربعون من الرجال العقم في الفترة بين فبراير إلى أبريل 2018 عشوائياً من مراكز الخصوبة في ولاية الخرطوم كمرضي وأربعون شخصاً على ما يبدو أصحاء كمجموعة مراقبة لتقييم مستوى الكادميوم تم قياس الكادميوم بواسطة جهاز الامتصاص الذري الطيفي تم تحليل النتائج باستخدام الحزمة الإحصائية للعلوم الاجتماعية.

وأظهرت الدراسة أن مستويات الكادميوم قد زاد بشكل كبير في الرجال العقم المرضي، يعني وسط حسابي **(0.155 ± 0.349) مل غرام/ دسم** مقابل (0.082 ± 0.13) مل غرام/دسم على التوالي ($P<0.01$).

كان هناك علاقة سلبية ضعيفة بين مستوى الكادميوم وحركة الحيوانات المنوية (r=0.493; $P<0.01$) وعلاقة سلبية بين مستوى الكادميوم وعدد الحيوانات المنوية (r=0.512 ; $P<0.01$)

كما انه لا يوجد ارتباط معنوي بين مستوي الكادميوم وهرمون الذكورة ,(r=0.165 ; $P=0.143$)

مستوي الكادميوم كان أعلى بشكل ملحوظ لدى الرجال العقم مقارنة بالرجال الاصحاء .

وتوصلت الدراسة لتوصيات تتمثل في أن قياس نسبة معدل معدن الكادميوم في الدم كمؤشر للعقم عند الرجال حسب طبيعة وبيئة العمل و المناطق التي بها معدن الكادميوم مع اعداد دراسات مستقبلية لدى الرجال العقم واخذ عينة كبيرة منهم لتقييم مستوى الكادميوم وتحليل كمي ونوعى لسائل المنوي وهرمونات الذكورة ومقارنة النتائج احصائيا .

1. Introduction

Infertility presents a worldwide reproductive health problem and its etiologic cause remains elusive. According to the WHO, infertility is the inability of a sexually active couple to achieve spontaneous pregnancy in one year of regular unprotected intercourse [(1)]. Epidemiological studies have shown the acute decline in semen quality and human male fertility with underlying geographic variation in prevalence. On a global scale, the disease affects approximately 15% to 20% of married couples [(2)], of which male-factor contributes 50% of cases [(3)] and about 60-75% of male infertility cases are idiopathic [(4)]. The prevalent rate in the UK and the USA is estimated to be 6% and 10% respectively [(5)], with the highest rates in Africa and Central/Eastern Europe [(6)]. When a couple fails to conceive even after two years the couple may be considered infertile [(7)].The term sub-fertile means a male who failed to conceive after one year of regular unprotected intercourse with the same partner and who had a sperm count of less than 20 million/ml [(8)]. The incidence of infertility in a population has important demographic and health implications [(9)]. The prevalence of infertility varies widely, being less in developed countries and more in developing countries where limited resources for investigation and treatment are available [(10)]. Infertility is an important medical and social problem in the world as regards 15% of couples are infertile and 40% are infertile because of male factor infertility and 40% are because of female factor Infertility and in the remainder, both factors are associated. [(11)] Cadmium is a heavy metal, used in industrial activities, agricultural activities and in the widespread use of phosphate-based fertilizers [(12-14)]. High level of cadmium contamination which leads to pollution of the water and air. After cadmium enters the environment, it pollutes air and water and at last is discharged into the food chain, detrimentally affecting living organisms [(15, 16)]. The major source of inhalation cadmium intoxication is smoking, and the human lung resorbs 40-60% of the cadmium content in cigarette smoke [17]. As a result, smokers receive a dose of cadmium daily and generally have cadmium blood levels 4-5 times more than those of nonsmokers [13, 18, 19]. In nonsmokers, most uptake of cadmium is through cadmium contaminated drinking water and food, particularly cereals, such as rice and wheat, and also potato and green leafy vegetables [13, 18, 19, 20]. It has been documented that the total amount of cadmium uptake to the human body depends on the consumed dose. Several factors can increase this uptake, such as low intake of vitamin D, calcium and iron [18]. A higher level of cadmium intake, more than the standard level, has a significant adverse effect on growth rate [21, 22], but its toxic effects on tissues are not the same in all tissues, especially testes [23].

Studies of cadmium toxicity have introduced it as a ubiquitous environmental human carcinogen [24] and one of the best-known reproductive toxicants in a wide variety of animals [25-28]. In humans, chronic exposure to environmentally-relevant cadmium results in high cadmium levels, especially in infertile men [29, 30]. Therefore, in the current study, we describe available literature to determine which part of the male reproductive system is most affected by cadmium and how cadmium causes male fertility problems. [31] Some studies show that cadmium accumulation in the testes has no effect on testicular weight [32-34]. Cadmium enters the seminiferous tubules through a breach of the blood-testis barrier and causes focal testicular necrosis and dystrophy with a consequent reduction in germ cell numbers, leading to infertility. [22, 35, 36, 37] Therefore, severe cellular injury in seminiferous tubules could be due to a high level of peroxidation in the lipid membrane of testicular cells, observed in many studies [21, 22, 35, 38, 39-46]. In one study by Monsefi et al., administration of cadmium chloride caused severe damage to seminiferous tubules, resulting in difficulty in the identification of seminiferous tubules by light microscope and also a consequent reduction in spermatogenesis, as there was no spermatozoid in the lumen of some seminiferous tubules. [22]

Materials and Methods

This analytical cross-sectional case-control study was conducted in Khartoum state. A quantitative method was used to evaluate the serum cadmium levels among infertile men , Sudanese infertile men which came to Ashmiq fertility Center, were considered as case group(N=40), males in a reproductive age group with no complaints of infertility) was considered as control(N=40). Data were collected using a questionnaire, which was designed to collect and maintain all valuable information concerning each case examined**.** Venous blood was collected from each participant in the case group. The sample collected under aseptic conditions and placed in plain containers and centrifuged for 5 minutes at 3000 RPM to obtain serum then samples were kept at -80C until the time of analysis. Plasma was diluted 1:10 with 0.5% v/v HNO3 to determine the concentrations of cadmium using flame atomic absorption spectrophotometer. Testosterone measured by Enzyme-Linked Immunosorbent Assay (ELISA) techniques and sperm motility and a count used microscopic examination.

-Inclusion criteria

Inclusion criteria in the case group were male suffering from infertility

-Exclusion criteria

The criteria of exclusion based on excluding any male have a history of reproductive surgery.

-Ethical consideration

The study was revised and ethically approved by the ethical committee of the

Faculty of Medical Laboratory Sciences, Azaim Alazhari university. Before the specimen was collected, the donors knew that this specimen was collected for research purposes.

-Statistical analysis

Data were analyzed to obtain means standard deviation and correlation of the sampling using statistical package for social science (SPSS) computer Programmed version 20, t-test correlation was used for comparison correlation between variable.

Results

A total of 80 males (40 patients and 40 healthy controls) were included in the study. Age of study group compared with the control group was (Mean ±SD: **37.3 ± 5.2** versus 31.7 ± 5.8), The results of serum cadmium levels and biochemical tests in infertile patients are given in tables and figures:

Table(1) .: Illustrate the mean concentration of cadmium level were significantly increased in infertile patients compared with the control group. (Mean ±SD: **0.349 ± 0.155** mg/ml versus 0.13 ± 0.082 mg/ml), respectively with (P <0.01).

Table(2). Illustrate the correlation between cadmium and other variables.

There was a significant week negative correlation between cadmium level and sperm motility (r=0.493; P <0.01).

There was a significant negative correlation between cadmium level and sperm count (r=0.512; P <0.01).

There was no correlation between cadmium and testosterone hormone (r=0.162; P= 0.317).

Table(1): The mean concentration of cadmium blood level of case and control group

cases	**Cases** **Mean ± Std** **(Min-Max)**	**Control** **Mean ± Std** **(Min-Max)**	P value
Cadmium	**0.349 ± 0.155** (0.06 - 0.578)	0.13 ± 0.082 (0.03 - 0.34)	< ***0.01***

*.*P* value ≥0.05 are considered significant. SD: Standard Deviation.

Independent sample T-test was used for comparison.

Table(2): The correlation (*P* value) of testosterone, sperm motility and count of case and control group

cases	**Cases** **Mean ± Std** **(Min-Max)**	**Control** **Mean ± Std** **(Min-Max)**	P value
Testosterone	18.165 ± 8.139 (3 - 37)	21.40 ± 9.473 (3.9 – 37.5)	***0.106***
Motility	30.7% ± 19.102% (0% – 70%)	**66% ± 6.337%** (50% - 80%)	***< 0.01***
Count	6.108 ± 5.036 (0 - 18)	**75.78 ± 47.620** (1 - 225)	***< 0.01***

*.*P* value ≥0.05 are considered significant. SD: Standard Deviation.

Independent sample T-test was used for comparison.

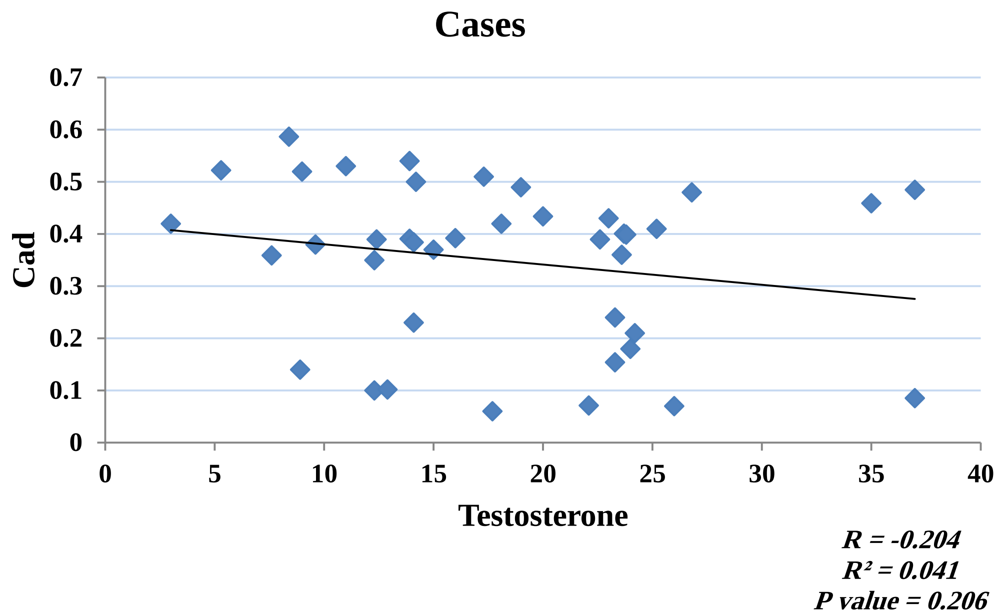

Fig (1) shows the Correlation between Testosterone & Cadmium in Case Study.

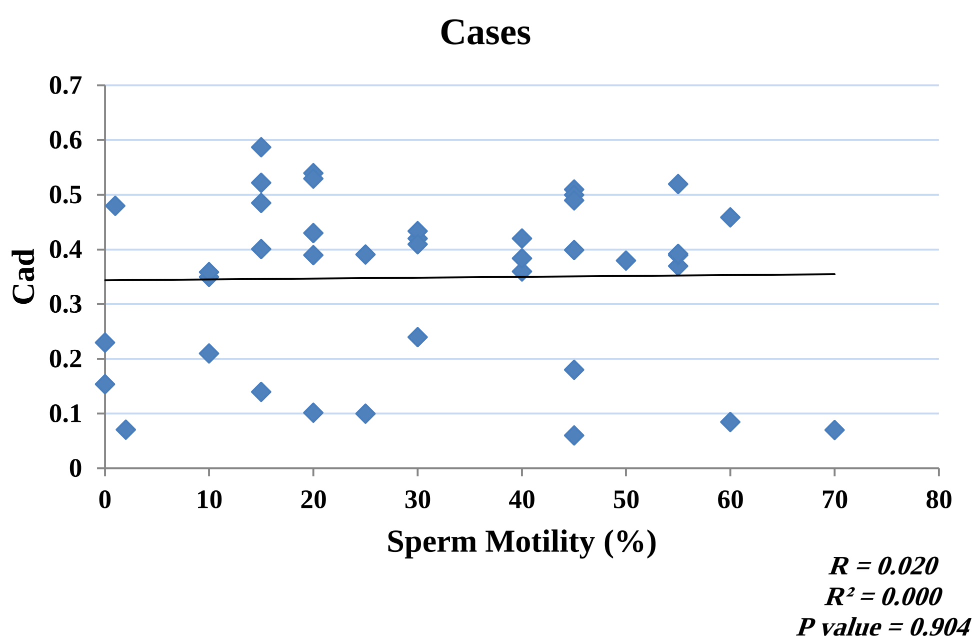

Fig (2) shows Correlation between Sperm Motility & Cadmium in Case Study.

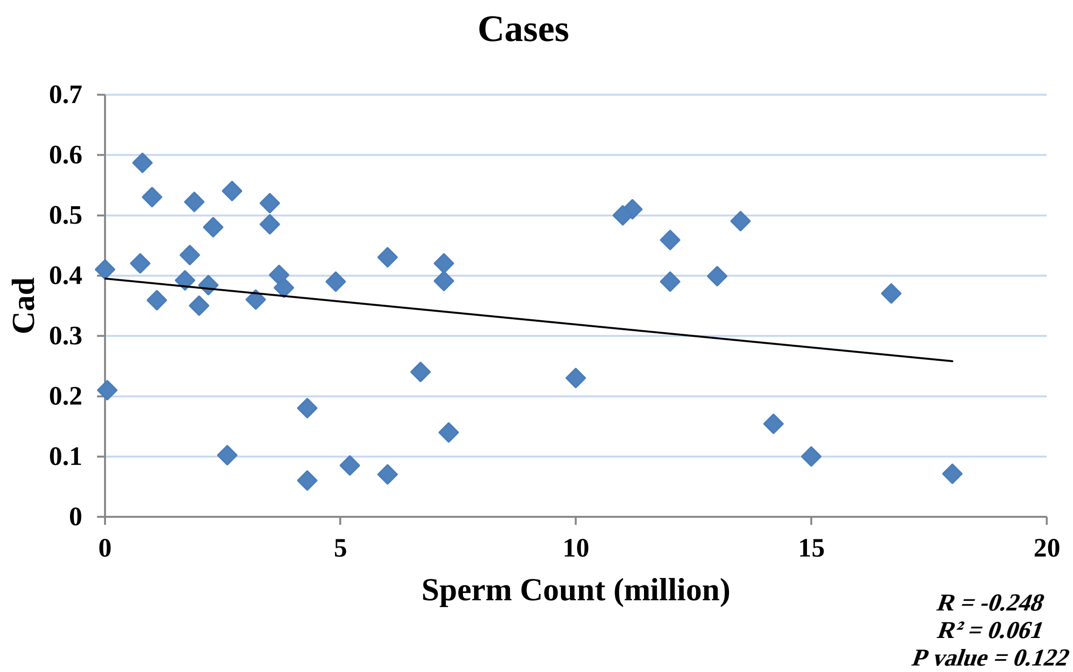

Fig (3) show correlation between Sperm Count & Cadmium for Case Study.

5.1 Discussion

According to the literature, cadmium has adverse effects on the male reproductive system and the testes are the main target of cadmium. Cadmium enters the body through contaminated air, water, and food. It then circulates in the blood and Reaches tissues such as testis, where it accumulates. Cadmium in the testis disrupts the blood-testis barrier, comes into close contact with different cells of testis and, by increasing the production of ROS and decreasing various antioxidants' levels, enhances the lipid peroxidation of cell membranes, causes apoptosis and necrosis of all testicular tissue leading to disturbance of spermatogenesis, reduces sperm's motility and finally leads to infertility.

there are inconsistent reports of association of Cadmium with the decline in semen quality (47), it is plausible that several environmental factors may cause male infertility, particularly that the adverse effects of toxic heavy metals on humans is well documented (48).

However, it is consistent in the literature that male infertility is variable, with a multitude of influencing geographical differences, including environmental and lifestyle factors (48, 49). This study investigated the association of blood Cadmium concentrations with semen quality in non-occupationally exposed infertile Sudanese men undergoing infertility evaluation.

The overall results of this study indicate that high levels of blood Cd reduce human semen quality. We found that Cd in oligospermic men was significantly higher compared to normospermic men.

The present study demonstrated that there is a negative correlation between cadmium level and declines in semen quality. (50)

A number of human studies have reported declines in semen quality associated with cadmium in blood. [50, 51]

Cadmium level are negatively correlated with sperm motility this disagree with a previous study conducted by (Spomenka Teliiman et al) [52] and agree with the study of (*John D. Meeker*, *et. al*). [53]

Also, there is a negative correlation between cadmium and sperm count and found no correlation between cadmium and testosterone level our finding disagrees with the study conducted by (Haouem S, et al 2008). [32]

Testicular testosterone levels are one-hundred-fold higher than normal serum testosterone levels [30], and these high levels are required to support spermatogenesis [31]. It is possible that testicular testosterone levels are more sensitive to the effects of cadmium than are serum levels. Thus, in the absence of testicular testosterone measurements, our findings are consistent with a prior report that cadmium can impair semen quality without effects on male reproductive endocrine function. [54]

5.2 Conclusion

This study conducts that exposure to cadmium at the environmental level influence on male's fertility and lead to change semen-quality parameters.

Recommendations : -

1. Regular measuring of serum Cadmium as biomarkers of male infertility according occupation and area expose to Cadmium element .
2. Further investigations are recommended with larger sample size and more parameters should be included such as seminal plasma cadmium and sperm morphology.

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