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# Effect of environmental factors on ovarian reserve of women living in Aral Sea area

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**Abstract**

Permanent environmental pollution by wastes arising from industries can lead to negative effects on reproductive organs. Normal reproductive function of women depends on the functional capacity of ovaries. This study was designed to detect possible environmental effect on ovarian reserve of women living in Aral Sea area. 160 women in their reproductive age were studied; 80 women from Kuwait in group I and 80 women from Shalkar, Kazakhstan in group II. Women included in this study were evaluated using trans-vaginal ultrasound (TVS) to detect Antral Follicle Count (AFC) as well as Basal Ovarian Volume (BOV). AFC and BOV were compared in both study groups. In this study, there was significant difference between group I and group II regarding; AFC and BOV, which means reduced ovarian reserve as indicated by AFC and BOV of women living in Aral Sea area (Kazakhstan) compared with Kuwaiti women of same age group. This study suggests possible environmental effect on ovarian reserve of women living in Aral Sea area (Kazakhstan). This study, also, concluded that, AFC and BOV is a simple, rapid, non-invasive method for assessment of ovarian reserve.

**Keywords:** Environmental factors, Ovarian reserve, Aral sea area

## 1. Introduction

Permanent environmental pollution by wastes arising from industries can lead to negative effects on reproductive organs (1). Normal reproductive function of women depends on the functional capacity of both ovaries. It is proved that the influence of chemical substances, which increase maximum permissible concentration leads to different morphological and/or functional changes in both ovaries (2). Studies found that sows which were kept in areas of radiation showed a large number of primordial follicles with dystrophic oocytes, granulosa cell hyperplasia and extensive follicular atresia on histological section (3). Lengthening of menstrual cycles, early menopause, benign ovarian cysts or tumors and spontaneous abortions are frequently seen in women exposed to alternating magnetic fields (4).

Exposure to cadmium eco-pollutant released to environment by burning and recycling of products containing this metal, affects lipid peroxidation in ovaries and exerts both immunosuppressive and pro-inflammatory effects in spleen (5). Widespread use of pesticides associated with decrease primordial follicles and increase atretic follicles (6). Dioxins (organochlorine chemical) decrease the secretion of ovarian hormones with subsequent infertility (7). Disaster, of Aral Sea extinction with its toxic effects on human health began in 1960s (8, 9). Uncontrolled use of various pesticides, fertilizers, chemicals and irrational use of water resources led to inverse impregnation of these substances into the sea and frequent toxic dust storms in Aral Sea area (10).

Climatic conditions of Aral Sea region has changed dramatically. Winters become colder; summers are hot and dry with a predominance of sandstorms. Studies conducted in Aral Sea area showed that 41% of population suffers from blood disorder, particularly anemia, 80.6% suffers from respiratory problems and 92% suffers from digestive disorders (11-15). The predominance of any disease in Aral Sea region proves complex chemical contamination. For example, high environmental chromium leads to persistent anemia and various pesticides affects the functional ability

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of female reproductive system (16, 17).

Government of Republic of Kazakhstan adopted a law "On social protection of citizens affected by the environmental disaster in Aral Sea", with implementation of projects for health protection and adoption of preventive measures through boundaries of disaster which was defined by three zones; 1) Zone of ecological disaster (Aral, Kazaly, Shalkar), 2) Zone of ecological crisis (some areas Kyzylorda region), 3) Zones adjacent to ecological crisis (Baiganin, Irgiz, Mugalzhar, Temir) (18-21). Incidence of primary infertility in those areas is about 53%. Environmental factors, intoxication, life style and diet in Aral Sea area are associated with decline of women's reproductive ability and acceleration of premature ovarian aging.

Ovarian reserve refers to the quantity and quality of a woman's current reservoir of oocytes and is closely associated with reproductive potential (22) Measurement of ovarian reserve is very important in predicting woman's response to various fertility treatments and helps us decide an appropriate fertility medication (23). Follicle development is dependent on the interrelationship of many hormones, such as Follicle-stimulating hormone (FSH), Anti-Mullerian hormone (AMH), secreted from anterior pituitary gland and ovaries respectively.

Abnormal levels of these hormones may indicate a woman's diminished ability or inability of conception (23).

Ultrasound parameters as AFC and BOV are also used for evaluation of ovarian reserve (24-28). Previous studies concluded that reduced AFC and BOV are indicators of poor ovarian reserve (28-30). Therefore, this study was designed to compare AFC and BOV in Kuwaiti and Kazakhstan women of same age group to detect possible environmental effect on ovarian reserve of women living in Aral Sea area.

## 2. Materials and methods

### 2.1. Patients

One hundred and sixty (160) women in their reproductive age were included in this cross-sectional multicenter study; Eighty (80) women from Kuwait in group I and Eighty (80) women from Shalkar, Aral Sea area, Kazakhstan in group II. This study was conducted over 3 year from 2011 to 2014 in West Kazakhstan Marat Ospanov state Medical University (ZKGMU) and Ahmadi hospital, Kuwait oil company (KOC) after approval of study protocol by institute ethical committee of both hospitals.

The Purpose of the study and the procedures were explained to all women included in this study and a written informed consent was obtained from each woman.

### 2.2. Procedure

We performed thorough evaluation of all women participated in this study including age, duration of marriage, age of menarche, menstrual history, BMI, documentation of ovulation by TVS and normal uterine cavity. Women with following criteria were included in this study; (I) 30-40 year age (II) regular ovulatory menstrual cycles every 25-35 days; (III) both ovaries present; (IV) no current or past diseases affecting ovaries or sex steroid secretion, clearance or excretion; (V) BMI<25 $kg/m^2$; (VI) no current hormone therapy and (VII) adequate visualization of ovaries at TVS. Women with polycystic ovary syndrome (PCOS), endocrine or medical disorders, endometriosis, previous pelvic surgery, genital malformations and BMI >25 $kg/m^2$ were excluded from this study.

PCOS was defined according to the Rotterdam criteria of ESHRE/ASRM (31). Women included in this study were evaluated using TVS to detect AFC as well as BOV on day 3-5 of their cycles (early follicular phase). AFC is the number of follicles visualized in both ovaries with size from 2-10 mm in early follicular phase by TVS. TVS was done using Philips HD9 (Philips international; Amsterdam; Netherlands) and Hawk 2102 EXL (BK medical, United States, New York) set with trans-vaginal 2D convex probe 4-9 MHz, by a sonographer who was blinded to patients' criteria. To determine diameter of each antral follicle, the mean of measurements in two perpendicular directions was taken. Volume of each ovary was calculated by measuring the three perpendicular directions and applying the following formula: (D1 × D2 × D3 × 0.523). BOV is equal to volumes of both ovaries.

### 2.3. Sample size justification

Required sample size was calculated using G* Power software version 3.17 for sample size calculation (Heinrich Heine Universität; Düsseldorf; Germany), setting α-error probability at 0.05, power (1-β-error probability) at 0.95 % and effective sample size (w) at 0.3. The effective size (w) was calculated as follows: $w = \sqrt{X^2/N}$ , where $X^2$ is the chi-square test and N is the total sample size. Number of participants needed to produce a statistically acceptable figure was 80 women in each group.

### 2.4. Statistical analysis

Statistical analysis was performed using statistical package for social sciences (SPSS) for Windows version 18 (Chicago, IL, USA). Numerical variables were presented as mean and standard deviation (±SD) and t-test was used for comparison between two studied groups as regard quantitative values. A difference with a p-value <0.05 was considered statistically significant.

## 3. Results

In this study, there was no significant difference between group I (Kuwaiti women) and group II (Kazakhstan women) regarding; mean age mean BMI, mean parity, mean miscarriages and mean length of menstrual (Table 1). While, there was significant difference between group I and group II regarding; AFC and BOV which means reduced ovarian reserve of women living in Aral Sea area (Kazakhstan) compared to Kuwaiti women of same age group, (P <0.05) (Table 1).

Table 1. Baseline characteristic, Antral follicle count and basal ovarian volume of two studied groups. Values showed as means ± S.D.

| Variables | Group I | Group II | P value |
|---|---|---|---|
| Age (years) | 33.4±2.46 | 32.7±3.29 | p=0.9 |
| Body Mass Index (BMI), ($kg/m^2$) | 23.3±1.47 | 23.5±2.25 | p=0.9 |
| Parity | 1.2±0.78 | 1.6±0.99 | p=0.98 |
| Miscarriages | 1.2±0.34 | 0.90±0.57 | p=1 |
| Length of menstrual cycle | 28.5±1.37 | 26.9±2.21 | p=0.99 |
| Antral Follicle Count (AFC), (mm) | 6.7±7.1 | 4.2±5.3 | *p=0.005 |
| Basal Ovarian Volume (BOV) | 6.9±6.1 | 4.5±4.2 | *p=0.0005 |

*Significant difference between two groups (P<0.05).

## 4. Discussion

Exposure to environmental toxins will destroy a number of ovarian primordial follicles and it would be of value to assess the ovarian reserve and subsequent reproductive ability of women exposed to environmental hazards. This study was designed to detect possible environmental effects on ovarian reserve of women living in Aral Sea area. There is strong evidence that adult ovarian volume decreases with age as the remaining pool of primordial follicles becomes exhausted (32). As part of the University of Kentucky Ovarian Cancer Screening programme, 13,963 women between 25 and 91 years of age underwent annual TVS. From 58,673 observations of ovarian volume, a statistically significant decrease in ovarian volume was shown with each decade of life from age 30 to 70 years (33). The largest published study of ovarian volume related to age conducted by Pavlik and colleagues, showed significant correlation between primordial follicle population (and ovarian volume (33). This provides good evidence that ovarian volume in women aged 25–51 years is strongly associated with the remaining primordial follicle population (33). Ovarian reserve and reproductive age in healthy pre-menopausal women, who are not using hormonal contraception, can be determined from the measurement of ovarian volume and AFC using TVS (33).

In this study, AFC and BOV were significantly reduced in Kazakhstan women compared to Kuwaiti women of same age, indicating reduced ovarian reserve of Kazakhstan women living in Aral Sea area which may be due to possible environmental effect on ovarian reserve. Women who have reduced mean ovarian volume and reduced ovarian reserve have a very high chance of failure to respond to ovulation induction or exogenous gonadotropins given during In-Vitro Fertilization/Intra-Cytoplasmic Injection (IVF/ICSI) programs (33).

A recent study of both fertile ($n$ = 53) and infertile ($n$ = 62) women conducted by Erdem et al, showed a strong direct association between mean ovarian volume and remaining ovarian reserve (34). Although, Erdem et al, concluded that basal FSH and AFC did not differ between infertile and fertile women (34), Scheffer et al, concluded that the number of small antral follicles measuring in early follicular phase of menstrual cycle was found to have the best correlation with chronological age (35). Larsen et al, concluded that ovarian reserve in childhood cancer survivors with regular menstrual cycles and basal FSH <10 IU/l has shown that female survivors had significantly smaller ovarian volumes and lower number of small antral follicles per ovary than controls (36). Bath et al, concluded that reduced ovarian volumes and reduced serum AMH concentrations, providing clear evidence for diminished ovarian reserve in regularly menstruating pre-menopausal childhood cancer survivors (37).

The ability to make a direct and accurate assessment of ovarian reserve would be of enormous benefit to women who are being considered for assisted reproductive technologies, for women who are considering delaying starting a family for personal or professional reasons (38), or for women exposed to environmental risk factors. This study suggests possible environmental effect on ovarian reserve of women living in Aral Sea area, because of reduced AFC and BOV of women living in Aral Sea area compared to Kuwaiti women of same age. This study, also, concluded that, TVS measurement of AFC and BOV is a simple, rapid and non-invasive method for assessment of ovarian reserve. Hormonal profile evaluation was not included in this study design (cross sectional study) and women refused to participate in this study were faced as limitations during this study. Large prospective case-controlled studies including hormonal markers of ovarian reserve such as; FSH,

AMH and inhibin B are needed to confirm definite environmental effect on ovarian reserve and subsequent women's reproductive ability in Aral Sea area.

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