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Original Research - Quantitative

# The relationship between environmental exposures and hormonal abnormalities in pregnant women: An epidemiological study in Yazd, Iran

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### ABSTRACT

**Problem:** The process of industrialization and lifestyle changes have gradually exposed human societies to a larger number of environmental risk factors, which may cause hormonal abnormalities and congenital anomalies.

**Background:** The current study aimed to investigate the relationship between environmental factors and hormonal abnormalities among pregnant women in Yazd, Iran.

**Methods:** A hundred participants were randomly selected from among a group of pregnant women. According to the screening tests (AFP, free  $\beta$ -HCG, uE3, PAPP-A, and inhibin-A) performed at the genome clinic in Yazd in 2016, the risk of Down Syndrome (DS) was sufficiently high in this group of pregnant women from which the participants were selected. A questionnaire was used to collect data on the degree of the participants' exposure to pesticides at home, use of canned and fast foods, and consumption of greenhouse fruits. The collected data were analyzed by One-way ANOVA and Kruskal–Wallis Test.

**Findings:** The mean of Multiple of Median (MoM) for inhibin-A was significantly higher among pregnant women who often or always used pesticides at home ( $p=0.047$ ). The mean MoM for free  $\beta$ -HCG was significantly higher among pregnant women who often or always used canned foods ( $p=0.024$ ). Finally, the mean MoM for uE3 ( $1.85 \pm 1.30$ ) was significantly higher among pregnant women who never consumed greenhouse fruits ( $p=0.003$ ).

**Conclusion:** It can be concluded that it is possible to reduce environmental exposures affecting hormonal abnormalities among pregnant women by improving nutritional patterns, minimizing the use of pesticides at home, and reducing the intake of canned foods and greenhouse fruits.

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### Statement of significance

### Problem or issue

The process of industrialization and people's change of lifestyle have gradually exposed human societies to a larger number of environmental risk factors, which may cause hormonal abnormalities and congenital anomalies.

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## What is already known

Lifestyle, environmental, occupational and genetic factors have a significant effect on the embryonic development and health in pregnant women. Information on environmental exposures during pregnancy and their impact on the health of the fetus are very limited.

## What this paper adds

There was a significant relationship between hormonal abnormalities (free  $\beta$ -HCG, inhibin-A and uE3) with using pesticides, canned foods and greenhouse fruits, respectively.

## 1. Introduction

The process of industrialization and lifestyle changes have gradually exposed human societies to a larger number of environmental risk factors, which may cause hormonal abnormalities and congenital anomalies.<sup>1</sup> Hormones are chemical messengers that help regulate body functions and hormonal abnormalities occur when hormones are at improper levels.<sup>2</sup> Congenital anomalies can be defined as hormonal or structural or functional abnormalities that occur during intrauterine life, and can be identified prenatally or at birth. These abnormalities can be caused by single gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens and micronutrient deficiencies.<sup>3,4</sup> Generally, abnormalities and congenital anomalies are attributed to three main groups: Genetic factors, environmental factors, and a combination of genetic and environmental factors. Over 35% of hormonal and congenital abnormalities are caused by environmental factors.<sup>5,6</sup> One of the most common congenital anomalies is Down Syndrome (DS) or trisomy-21, which imposes a huge financial burden on families and the larger society, and can lead to increase the stress in families with DS children.<sup>7,8</sup> Therefore, early screening and diagnosis give women the time to discuss their options and receive counseling, so that they can make informed choices.<sup>9</sup>

Many biomarkers related to pregnancy can be used to early screening measure for DS.<sup>10–12</sup> One of the methods of Down syndrome screening during pregnancy is the dual hormone test, measuring alpha-fetoprotein (AFP) and human chorionic gonadotropin (free  $\beta$ -HCG), with a 59% confidence coefficient. Also, the triple test measuring AFP, free  $\beta$ -HCG, and unconjugated oestriol (uE3) with a 69% confidence coefficient, and the quadruple test assessing AFP, free  $\beta$ -HCG, uE3, and inhibin-A with a 76% confidence coefficient can be used to detect DS. All these tests have a 5% margin of error.<sup>13</sup> In a study conducted among Chinese people, the sensitivities of double and quadruple hormone tests were found to be 50% and 66.7%, respectively.<sup>14,15</sup> Low AFP level may indicate chromosomal abnormalities, especially DS. Furthermore, uE3 is 25% lower than the normal level among mothers carrying fetuses with DS. Measuring this factor between 14 and 22 weeks of gestation is a useful marker for DS screening.<sup>15,16</sup> Free  $\beta$ -HCG level is twice that of the normal level among pregnant women carrying fetuses with trisomy-21. AFP, uE3 and free  $\beta$ -HCG hormones are measured in a screening test known as the triple test, which is performed between 15 and 18 weeks of pregnancy.<sup>15,17</sup> Inhibin-A is a heterodimeric protein hormone that is released by granulosa cells of the ovaries in women and sertoli cells of the testes in men. Abnormal increase in the inhibin-A level (as compared to the normal level) increases the chances of woman giving birth to a baby with DS as compared to the background risk

(is a certain risk level, based on maternal age). Pregnancy-associated plasma protein A (PAPP-A) is produced by the evolving placenta and its concentration in maternal serum rapidly goes up after the 7th day of pregnancy. Measuring this protein during the first three months of gestation is a useful marker for DS screening.<sup>14,18</sup>

Some of the environmental factors that can cause hormonal and congenital abnormalities include pesticides (especially pyrethroid insecticides),<sup>19</sup> air pollutants (especially particulate matter, PM2.5),<sup>20</sup> ionizing and non-ionizing radiation, heavy metals (such as lead, mercury and cadmium), occupational factors (such as mechanical vibrations and exposure to chemical solvents), and life style factors (such as smoking, narcotics, alcohol, caffeine, drugs, and food additives).<sup>21–24</sup> Caserta et al. conducted a study on the impact of heavy metals on birth and fetal defects, concluding that exposure to lead, mercury, and cadmium can result in neurological, developmental, and endocrine disorders among babies.<sup>25</sup>

Environmental factors play a significant role in hormonal abnormalities and congenital anomalies in pregnant women. Hence, the current study aimed to investigate the relationship between environmental factors and hormonal abnormalities associated with DS among pregnant women in Yazd, Iran.

## 2. Methods

One hundred participants were randomly selected, based on information in their genetic records, from among a group of pregnant women. In this group, the risk of Down Syndrome (DS) was sufficiently high, according to screening tests performed in the genome clinic in Yazd. A questionnaire was used to collect data on the extent of the participants' exposure to environmental factors. The questionnaire was distributed by the researcher, and the women were invited to complete and return them. The informed consent obtained from the participants at the time of the presence of researcher in the participants home for complete the questionnaire. The questionnaire was validated by feedback from experts in health education, epidemiology, and environmental health. Furthermore, the reliability of the questionnaire was calculated through the Cronbach alpha, which yielded an index of 0.93. The questionnaire consisted of two parts: the first part aimed to collect the participants' demographic information. The second part included questions related to their degree of exposure to environmental pollutants. Environmental factors involved in this study included exposure to pesticides at home, consumption of canned and fast foods, and the use of greenhouse fruits.

### 2.1. Calculating the risk of hormonal abnormalities associated with DS

Concentrations of biomarkers change as the gestational age increases. More specifically, PAPP-A goes up during the first three months of pregnancy. On the other hand, during the second period of three months, the serum level of AFP and uE3 increases, while that of free  $\beta$ -HCG declines. Moreover, inhibin-A level reduces before the 17th week of gestation and surges afterward. It should be noted that different laboratories may report various levels of measurement for biomarkers. Consequently, in order to minimize the effect of such variations on the process of calculating hormone levels, the serum concentration of each marker should be reported as a MoM for similar gestational ages. MoM is calculated with the following formula:

MoM = hormone level measured for the patient/median of gestational age

If MoM values for free  $\beta$ -HCG, AFP, uE3, PAPP-A, and inhibin-A are between 0.5 and 2.5, it means that everything is normal;

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