Full study protocol and statistical analysis plan

Official Title of the study:

Analysis of some heavy metals and some vitamins levels in maternal samples, fetal samples and breast milk for fetal growth restriction.

Date of the document:

May 2020.

Contents:

1. Participant Flow
2. Baseline Characteristics
3. Outcome Measures
4.Endpoints of the study
5.Limitations and Strengths
6. Certain Agreements
7. Results Point of Contact

1. Participant Flow

Recruitment Details

This observational case-control study will be conducted at the Department of Obstetrics and Gynecology, Cengiz Gokcek Public Hospital, Gaziantep, Turkey, between May 2020 and February 2021. The protocol was approved by the Ethics Committee for Clinical Research of Gaziantep University (reference no: 2020/131). The study strictly will be adhered to the principles of the Declaration of Helsinki. All subjects will be included in the study gave oral and written informed consent. 110 women were enrolled in the study in two groups.

Pre-assignment Details

The authors first will be assessed the recruited people to ensure meeting the inclusion and exclusion criteria. The inclusion criteria will be made according to the official documents.

Arm/Group Information *

There are two groups in the study.

Arm/Group Title *

Fetal growth restriction group
Control group

2. Baseline Characteristics

To detect significant difference between groups according to lead levels with a moderate effect size (Cohen's d =0.6), minimum required sample size was estimated as 45 for each group (α=0.05, 1-β=0.80). Power analysis was performed by using G power package version 3.1. Kolmogorov Smirnov and Shapiro Wilk tests will be used to test the normal distribution of data. For comparing groups (FGR/control) the student t-test will be used for variables that have a normal distribution, and the Mann Whitney U test will be used for variables that have not a normal distribution. The ROC analysis will be applied for the determination of cut-off point for variables. Moreover, Spearman correlation test will be used for the relationship of between variables. SPSS for Windows 22.0 and Medcalc programs will be used for statistical analysis. $p<0.05$ will be accepted as statistical significance.

3. Outcome Measures

Primary Outcome Measures : tin (Sn), manganese (Mn), Vanadium (V), Magnesium (Mg), cobalt (Co), nickel (Ni), arsenic (As), chromium (Cr), cadmium (Cd), lead (Pb), mercury (Hg), antimony (Sb), aluminium (Al), zinc (Zn), copper (Cu), selenium (Se), iron (Fe), vitamin D, vitamin A, vitamin B12 and folate concentrations

Secondary Outcome Measures: composite neonatal outcome (infant weight at delivery, placental weight, neonatal intensive care unit hospitalization, and APGAR scores)

Tertiary Outcome Measures: obstetric ultrasound/doppler examination and fetal-maternal assessment

4. ***Endpoints of the study:***

The primary outcome in these analyses will compare tin (Sn), manganese (Mn), Vanadium (V), Magnesium (Mg), cobalt (Co), nickel (Ni), arsenic (As), chromium (Cr), cadmium (Cd), lead (Pb), mercury (Hg), antimony (Sb), aluminium (Al), zinc (Zn), copper (Cu), selenium (Se), iron (Fe), vitamin D, vitamin A, vitamin B12 and folate concentrations in FGR group and control group.

5.Limitations and strengths:

Our study has some strengths. These metals will be measured blood, urine and hair samples. So, these measurements may not reflect the metals exposure levels only recent exposure and will reflect before and during pregnancy.

6. Certain Agreements

This work will be supported by the Scientific Research Project Fund of Yozgat Bozok University.

7. Results Point of Contact

Corresponding Author: Ali Ovayolu, Department of Obstetrics and Gynecology, Cengiz Gokcek Women's and Children's Hospital, Gaziantep, Turkey, drovayolu@yahoo.com

Address: Osmangazi Mahallesi, Cengiz Gokcek Kadın Hastaliklari ve Dogum Hastanesi, 27010 Gaziantep, Turkey

GSM: +90 (532) 640 40 60

Tel.: +90.342 360 08 88

Fax: +90.342 360 02 90