Research Article

Fetuin A Concentration in the Second Trimester Amniotic Fluid of Fetuses with Trisomy 21 Appears to Be Lower: Phenotypic Considerations

S. Iliodromiti, 1, 2 N. Vrachnis, 1 Evangelia Samoli, 3 Z. Iliodromiti, 1 C. Pangalos, 4 N. Drakoulis, 5 G. Creatsas, 1 and D. Botsis 1

1 2nd Department of Obstetrics and Gynecology, University of Athens Medical School, Aretaieion Hospital, 124B Vas. Sofias Avenue, 115 26 Athens, Greece
2 West of Scotland Deanery, Obstetrics and Gynaecology, Glasgow, G3 8BW, UK
3 Department of Hygiene, Epidemiology and Medical Statistics, University of Athens Medical School, 115 27 Athens, Greece
4 Diagnostic Genetic Centre, 115 28 Athens, Greece
5 Department of Pharmaceutical Technology, School of Pharmacy, University of Athens, 157 71 Athens, Greece

Correspondence should be addressed to N. Vrachnis, nvrachnis@med.uoa.gr

Received 23 July 2011; Revised 21 November 2011; Accepted 21 November 2011

Academic Editor: Teresa Zelante

Copyright © 2012 S. Iliodromiti et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Objective. We investigated whether the concentration of the glycoprotein fetuin A is altered in the second trimester amniotic fluid of trisomy 21 pregnancies compared with euploid pregnancies. Methods. 25 pregnancies with an extra chromosome 21 were matched for maternal and gestational age with 25 pregnancies with normal karyotype. Levels of fetuin A in amniotic fluid were measured by a commercially available enzyme-linked immuno sorbent assay (ELISA) kit. Results. The median concentration of fetuin A in amniotic fluid of trisomy 21 pregnancies (5.3 ng/ml) was statistically significantly lower (P value = 0.008) compared with that in euploid pregnancies (6.8 ng/mL). Conclusion. Lower levels of fetuin A in trisomy 21 may indicate an association with altered metabolic pathways in this early stage that could potentially be associated with features of the syndrome, such as growth restriction or impaired osteogenesis.

1. Introduction

Down’s syndrome (DS) occurs in about one out of every 500 to 1000 live births [1]. The majority of the cases result from an extra copy of human chromosome 21, while the remainder are due to mosaicism or an extra part of chromosome 21. The phenotypic characteristics of DS vary significantly among individuals. Features such as short stature, reduced growth velocity [2], and reduced bone density [3] have been described in fetuses, children, and adults with DS.

Fetuin A, also known as alpha-2-HS (Heremans-Schmid) glycoprotein, is mainly expressed in the liver, the tongue and placenta in humans [4]. It occurs in high serum and amniotic fluid concentrations during fetal life [5] and is involved in development-associated regulation of calcium metabolism and osteogenesis [6]. It also accumulates in bones and teeth as a major fraction of noncollagenous bone proteins [7]. Fetuin A also plays a positive role in insulin resistance in humans and is associated with metabolic syndrome [8, 9].

We investigated whether altered concentration of fetuin A is present in the second trimester in pregnancies with trisomy 21 (DS) in order to elucidate the presence of possible metabolic pathways in utero. We hypothesized that levels of fetuin A in amniotic fluid of trisomy 21 pregnancies (5.3 ng/ml) was statistically significantly lower (P value = 0.008) compared with that in euploid pregnancies (6.8 ng/mL). Conclusion. Lower levels of fetuin A in trisomy 21 may indicate an association with altered metabolic pathways in this early stage that could potentially be associated with features of the syndrome, such as growth restriction or impaired osteogenesis.
in trisomy 21 rather than add new information to the already studied field of prenatal diagnosis.

2. Methods

The study was set up in a university hospital, a private hospital, and a genetic center. Amniotic fluid samples were collected from women who underwent amniocentesis in the second trimester of pregnancy because of advanced maternal age, pathological sonographic features, family history of inherited disorders, or abnormal first trimester biochemical screening for DS. Gestational age was estimated by an early booking scan. Multiple pregnancies and pregnancies with fetuses with gross anatomical abnormalities were excluded. Fetal karyotype was checked by QF-PCR (quantitative fluorescent polymerase chain reaction) analysis and confirmed via conventional cytogenetic cultures.

Twenty-five pregnancies having a single fetus with an extra chromosome 21 were identified and matched for maternal and gestational age with 25 uncomplicated singleton pregnancies with normal karyotype that were delivered at term. The Ethical Committee of the University Hospital approved the study protocol. Written informed consent was obtained from the participants.

Samples of amniotic fluid were centrifuged, and supernatants were stored in polypropylene tubes at −80°C until the date of quantitative determination of fetuin A. Levels of total fetuin A in the amniotic fluid were measured by a commercially available enzyme-linked immunosorbent assay (ELISA) kit (BioVendor-Laboratorní medicína a.s.). The sensitivity, intra-assay and inter-assay coefficient of variation for fetuin A were 0.35 ng/mL, 3.5%, and 5.4%, respectively. Analysts were blinded to the clinical information.

For the statistical analysis, we applied the nonparametric Mann-Whitney test for the comparison of the fetuin A levels between the two groups, since the measured hormone was not normally distributed.

3. Results

Table 1 presents characteristics of the women as well as the distribution of fetuin A according to the fetuses status. Age and gestational week were similar between the two groups ($P = 0.513$, $P = 0.216$, resp.), although women that carried a fetus with trisomy 21 were slightly older and had the amniocentesis at a later stage. More specifically, 80% of the women with a DS fetus were under 40 years of age as opposed to 90% of women with euploid fetuses. The median levels of fetuin A in cases with trisomy 21 were 5.3 ng/mL as compared with 6.8 ng/mL in controls. Fetuin A was statistically significantly ($P = 0.008$ from the Mann-Whitney test) higher in amniotic fluid from euploid pregnancies compared with the levels from pregnancies with fetuses with DS. Figure 1 presents the concentrations of fetuin A in amniotic fluid from euploid and trisomy 21 pregnancies plotted against individual patients. In addition, gestational age is correlated with fetuin A; the more advanced the gestation, the higher the concentration of the hormone in amniotic fluid for both groups ($r = 0.44$, $P = 0.029$ for euploid pregnancies and $r = 0.55$, $P = 0.005$ for DS pregnancies). On the other hand, its levels are not correlated with maternal age ($P = 0.42$). There is a considerable overlap during the early second trimester in the levels of fetuin A in amniotic fluid between euploid and trisomy 21 pregnancies, but this becomes less apparent as the gestation advances, the majority of the euploid pregnancies having a higher concentration of fetuin A regardless of gestational week.

4. Discussion

To our knowledge, fetuin A has not previously been studied in the human amniotic fluid. The composition of amniotic fluid is similar to that of fetal plasma up to the commencement of keratinization of the fetal skin, which starts at around 20 weeks and is completed by 25 weeks [11]. The amniotic fluid serves as an extension of the fetal extracellular...
5. Conclusion

Our findings support the hypothesis that certain features of DS may be associated with altered concentrations of fetuin A in the early 2nd trimester amniotic fluid. Our data, although limited, could prompt further research into fetuin A and other proteins related to metabolism in the first half of pregnancy that should result in a better understanding of the physiopathological changes associated with DS. However, we are far from developing in utero treatments that will regulate factors that are reduced or increased with the aim of improving the pathological features of DS. Nonetheless, this approach may be of particular public health importance, especially in countries or individuals where the termination of pregnancy for DS is not legal or acceptable.

To our knowledge, this is the first study to measure the concentration of fetuin A in human amniotic fluid. Although there are limitations to our study, our data are likely to contribute to elucidation of the metabolic and inflammatory pathways in DS that are related to fetuin A from the early stage of the second trimester. Additional research is required to further explain the observed difference.

Abbreviations

DS: Down’s syndrome
IUGR: Intrauterine growth restriction
AHSG (fetuin A): Alpha-2-HS glycoprotein or alpha-2-Heremans-Schmid glycoprotein.

Funding

This work was supported by private funding.

Conflict of Interests

The authors have no conflict of interests to disclose.
References


Submit your manuscripts at http://www.hindawi.com