IMR Press

Original Research

Can serum biochemical markers be used to establish a relationship between idiopathic polyhydramnios and antenatal aneuploidy?

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DOI:10.31083/j.ceog4805172

Submitted: 11 December 2020 Revised: 28 January 2021 Accepted: 14 February 2021 Published: 15 October 2021

Background: Polyhydramnios is a common cause of adverse pregnancy outcomes. The prediction of polyhydramnios in early pregnancy may lead to improved treatments and will diminish these adverse outcomes. *Objective*: This study aims to investigate the role of biochemical markers in antenatal screening tests to predict idiopathic polyhydramnios. *Methods*: Patient records were retrospectively evaluated in this case-control group study. Pregnant women (160 in total) were included in the study (this included 47 pregnant women diagnosed with idiopathic polyhydramnios and 113 healthy pregnant women as a control group). *Results*: Alpha-fetoprotein, unconjugated estriol, and total beta-human chorionic gonadotropin values were similar in both groups (p = 0.296, p = 0.573, p = 0.284). There was no significant difference between the group diagnosed with idiopathic polyhydramnios and the control group when the first-trimester screening test parameter, pregnancy-associated plasma protein-A, was examined (p = 0.102). *Conclusion*: Biochemical markers examined in prenatal screening tests in the first and second trimesters were insufficient to predict idiopathic Polyhydramnios. The reasons for this are that our study was retrospective, and the patient population was low. We believe that a prospective study with a larger population of patients should be conducted for more meaningful results.

Keywords

Antenatal screening; Biochemical markers; Polyhydramnios

1. Introduction

Polyhydramnios is defined as a condition that results from increased amniotic fluid production or decreased consumption. The diagnosis is made by ultrasonography and clinical evaluation with an incidence ranging from 1% to 2%. A single quadrant measurement of >8 cm, or the sum of four quadrant measurements over 24 cm in ultrasonographic sizes is indicative of Polyhydramnios. Polyhydramnios may be idiopathic or associated with a variety of fetal disorders and has been associated with an increased risk of various adverse pregnancy outcomes [1–4].

Sonographic evaluations, first/second-trimester prenatal serum screening tests, and cell-free fetal DNA tests are widely used in obstetrics. Biochemical markers screened in the first-trimester include maternal serum beta-human chorionic gonadotropin (beta-hCG or free beta-hCG subunit) and maternal serum pregnancy-associated plasma protein-A (PAPP-A). In addition, serum Alpha-fetoprotein (AFP), hCG, and unconjugated estriol (E3) are often screened in the second-trimester [5]. Maternal serum levels of first- and second-trimester markers for aneuploidy are associated with adverse obstetric outcomes [6].

This study investigated whether prenatal serum screening tests could predict the development of idiopathic Polyhydramnios, which may negatively affect maternal and fetal outcomes.

2. Material-methods

This case-control retrospective study enrolled pregnant women who gave birth between 2018 and 2020 in Çanakkale State Hospital. Prior to data collection, the required sample size had been calculated using G*Power 3.1 (Faul, Erdfelder, Buchner, & Lang, 2009), assuming an alpha of 0.05 and an effect size of 0.50, power analysis suggested that 144 participants (48 for the patient, 96 for the control groups) were required to have 80% power. In this study, 160 pregnant women were included (47 pregnant women diagnosed with idiopathic Polyhydramnios at 20–24 weeks of gestation and 113 healthy pregnant women). Local ethics committee approval was obtained for this study. We defined idiopathic Polyhydramnios as excluding fetuses with congenital anomalies, additional placental anomalies, ultrasonographic and serological findings of TORCH, maternal diabetes or gestational diabetes, Rh/Rh isoimmunization, presence of comorbid conditions, fetuses with minor markers examined in the ultrasonographic evaluation, and multiple gestations were excluded [7]. Additionally, pregnancies with abnormal first trimester and second-trimester screening markers

Table 1. Comparison of the control group and patients diagnosed with idiopathic Polyhydramnios according to demographic characteristics and perinatal results.

Variables	Idiopathic polyhydramnios (n = 49)		Control (n = 116)		p
	Mean ± Sd	Median	Mean ± Sd	Median	
Age	32.02 ± 5.69	30	27.85 ± 5.25	26	<0.01*
BMI	29.03 ± 4.62	28.0	29.08 ± 4.20	29	0.96
Gravida	2.14 ± 1.11	2.1	2.24 ± 1.08	2.0	0.56
Parity	0.84 ± 0.921	1.0	0.89 ± 0.821	1.0	0.72
Abortus	0.34 ± 0.64	0.0	0.33 ± 0.62	0.0	0.88
Birth week	37.3 ± 1.46	37.0	39.2 ± 1.0	39.3	<0.01*
Apgar 1.min	8.82 ± 0.62	9.0	8.92 ± 0.47	9.0	0.04*
Apgar 5.min	9.82 ± 0.69	10	9.94 ± 0.35	10	0.04*
Birth weight	3162 ± 463	3120	3396 ± 386	3355	<0.01*

* $p < 0.05$ Statistically significant.

were also excluded from the study. Pregnant women in the control group consisted of healthy pregnant women with matching age and body mass index (BMI). The first trimester "combined test" included both sonographic determination of nuchal translucency (NT) and the determination of biochemical markers associated with aneuploidy: pregnancy-associated plasma protein-A (PAPP-A) and free-beta or total hCG which were performed at 11 + 0 to 13 + 6 weeks of gestation respectively. For the second trimester, the biochemical markers alfa fetoprotein (AFP), unconjugated estriol (uE3) and human chorionic gonadotropin (hCG) were determined at 15 + 0 to 18 + 6 weeks of gestation. The PAPP-A multiple of the median (MoM) values in the first-trimester screening tests for all patients and the MoM values of the second-trimester screening test biochemical markers (AFP, E3, hCG) in addition to demographic characteristics such as age, gravida, parity, gestational age were retrospectively obtained from the hospital records.

3. Results

The main characteristics and results of the pregnant women diagnosed with idiopathic Polyhydramnios and the control group are shown in Table 1. The mean age was significantly higher in the idiopathic polyhydramnios group (32.02 ± 5.69 vs. 27.85 ± 5.25) compared to the control group ($p < 0.01$). No statistically significant difference was found in terms of BMI, gravida, parity, and abortion values between pregnant women diagnosed with idiopathic Polyhydramnios and healthy pregnant women. The week of birth was found to be significantly lower in the idiopathic polyhydramnios group (37.3 ± 1.46 vs. 39.2 ± 1.0) compared to the control group ($p < 0.01$). Mean birth weight was found to be significantly ($p < 0.01$) lower in the idiopathic polyhydramnios group (3162 g ± 463 vs. 3396 g ± 386) compared to the control group.

The first and second trimester serum screening test parameters are shown in Table 2. AFP MoM, E3 MoM, and total HCG MoM values scanned in the second trimester were found to be similar between the group diagnosed with idiopathic Polyhydramnios and the control group ($p = 0.296$, $p = 0.573$, $p = 0.284$ respectively). No significant difference was found between the group diagnosed with idiopathic Polyhydramnios and the control group when the first-trimester screening test parameter PAPP-A MoM value was examined ($p = 0.102$).

4. Discussion

We planned to investigate whether there is a role of serum biochemical markers in antenatal aneuploidy screening tests in predicting idiopathic Polyhydramnios, which may negatively affect maternal and fetal gestational outcomes. There was no difference between the idiopathic Polyhydramnios and the control group with regards to serum screening parameters. This is the first study in the literature that investigates the serum screening parameters in idiopathic polyhydramnios cases.

In the first and second trimesters, prenatal screening tests can recognize aneuploidies like Down's syndrome and reveal its relationship with maternal and fetal results [8]. Decreased PAPP-A values during early gestation have been shown to predict Down's syndrome and be associated with intrauterine death, fetal growth retardation, preeclampsia, gestational diabetes mellitus, and preterm labour. According to the current literature, it has been reported that increased AFP MoM, β-HCG, and lower E3 levels in prenatal screening tests in the second trimester are associated with poor pregnancy outcomes. The findings of this study reveal that these biochemical markers are insufficient to predict idiopathic Polyhydramnios during pregnancy [9–14].

Amniotic fluid protects the fetus from trauma, prevents compression of the umbilical cord, and protects against infections. It includes the environmental and growth factors necessary for normal development of the fetal lungs, gastrointestinal system, and musculoskeletal system. Amniotic fluid abnormalities should be considered as high-risk conditions. To predict them in the early stages of pregnancy is essential for the management of these pregnancies [15].

There are a limited number of studies in the literature to

Table 2. Comparison of the control group and pregnants with idiopathic Polyhydramnios in terms of PAPP-A, Alpha-fetoprotein (AFP), Unconjugated estriol (uE3), and Human chorionic gonadotropin (hCG) results.

Variables	Idiopatik Polihidroamnios (n = 49)		Control (n = 116)		*p*
	Median	Minimum–Maksimum	Median	Minimum–Maksimum	
PAPP-A MoM	1.14	0.29–4.18	1.41	0.29–9.20	0.102
Alpha-fetoprotein (AFP) MoM	1.00	0.62–2.92	0.98	0.28–2.76	0.296
Unconjugated estriol (uE3) MoM	0.82	0.24–10.60	0.94	0.32–2.16	0.573
Human chorionic gonadotropin (hCG) MoM	0.96	0.24–3.00	0.94	0.38–2.66	0.284

predict idiopathic Polyhydramnios. Previous reports have tried to estimate development of this condition by using biochemical and ultrasonographic markers. The role of antenatal surveillance in predicting pregnancies complicated by idiopathic Polyhydramnios is uncertain due to the lack of definitive studies [16, 17].

It is well known that idiopathic Polyhydramnios is a risk factor for placental abruption and increased intrapartum/perinatal mortality and morbidity in both term and preterm fetuses. There are studies on the effectiveness of serum screening tests to predict placental abruption, and it has been reported that reduced serum levels of PAPP-A could have an increased risk of placental abruption [18]. According to the data of our study, although the PAPP-A values of the idiopathic polyhydramnios group were lower than the control group, no statistical difference was found.

As a result, in our study, biochemical markers performed in prenatal serum screening tests at first and second trimesters were unable to predict idiopathic Polyhydramnios. The reasons for this could be that our study was retrospective, and the patient population was small. Serum screening biomarkers may play an essential role in the management of pregnancies complicated by idiopathic Polyhydramnios and possible placental abruption in the later stages of pregnancy. These markers could be integrated into clinical practice to improve outcomes. Identification of fetuses with idiopathic polyhydramnios could help clinicians focus on preventive measures, including hospitalization and more intensive surveillance, and decide delivery timing. We believe that a prospective study with a larger patient population should be conducted for more meaningful results.

5. Conclusions

Biochemical markers have an essential role in cases of idiopathic polyhydramnios. We think that further studies will reveal this relationship more clearly. In this respect, our study will shed light on other studies.

Author contributions

OS & SBA led this research, including proposal write up and designed the instrument. OS & HET collected data in the field, analyzed, and wrote the manuscript. HET, TA & SBA contributed to the study design and the final version of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was conducted under the principles of the Declaration of Helsinki. Hospital Local Ethics committee approval was received for this study (ethics committee no: 280/4779, 02/11/20). This study was designed as a retrospective assessment of data, and therefore, informed consent were not required.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interest.

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