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Association of placental cysts with increased fetal anomalies and growth restriction: An observational cohort study

Plasental kistlerin artmış fetal anomalilerle ve büyüme kısıtlılığı ile ilişkisi: Gözlemsel kohort çalışması

Göksun İPEK[1], Esra Gülen YILDIZ[1], Ayşe Gülçin BAŞTEMUR[1], Salim ERKAYA[1]

[1]Department of Obstetrics and Gynecology, Ministry of Health, Ankara City Hospital, Ankara, Turkey

ABSTRACT

Aim: To investigate the placental cysts in every aspect and evaluate associations with fetal anomalies, fetal growth, accompanying maternal diseases, and obstetric outcomes.

Materials and Methods: The presented cohort study was conducted with twenty pregnant women diagnosed with placental cysts. Maternal age, obstetrical histories, maternal diseases, ultrasonographic characteristics of cysts, additional ultrasound findings, and fetal anomalies were recorded at the time of diagnosis and each examination. Pregnancy outcomes; birth weight, gestational age at birth, APGAR scores, neonatal intensive care unit (NICU) admissions, amniotic fluid disorders, and fetal growth restriction (FGR) were recorded for all participants. Data were evaluated according to diagnosis time, size of the cyst at diagnosis and at birth, fetal anomalies, and obstetric outcomes.

Results: All cysts were single. Five of them increased in size with follow-ups. The mean follow-up duration was 12 weeks. There were 9 FGR (64.3%). Six of the FGR patients had cyst sizes >5 cm. There were eight fetal anomalies; 5 were heart-associated, and 3 had a single umbilical artery. The frequency of C/S in delivered patients was 78%, and preterm delivery was 35.7%.

Conclusion: The presented study showed that placental cysts have clinical importance due to their potential risk for FGR and accompanying fetal anomalies. Appropriate patient follow-ups for cyst size enlargements and anomaly screening, especially for cardiac evaluation, might be important for placental cyst management. Also, uterine artery Doppler measurements and prophylactic acetylsalicylic acid use might be under consideration. However, the clinical utility of uterine Doppler examination and prophylactic use of acetylsalicylic acid needs further studies.

Keywords: Placental cyst; fetal anomalies; fetal growth restriction; adverse perinatal outcomes

ÖZ

Amaç: Plasental kistleri her yönüyle araştırmak ve fetal anomaliler, fetal büyüme, eşlik eden maternal hastalıklar ve obstetrik sonuçlarla ilişkisini değerlendirmek.

Gereçler ve Yöntem: Bu kohort çalışması plasental kist tanısı alan yirmi hamile kadınla yürütüldü. Tanı anında ve her muayene sırasında anne yaşı, doğum öyküsü, maternal hastalık, kistlerin ultrasonografik özellikleri, ek ultrason bulguları ve fetal anomaliler kaydedildi. Hamilelik sonuçları; doğum ağırlığı, doğumdaki gebelik haftası, APGAR skorları, yenidoğan yoğun bakım ünitesine (YYBÜ) yatış, amniyotik sıvı bozuklukları ve fetal büyüme geriliği (FBG) kaydedildi. Veriler tanı zamanına, tanı anındaki ve doğum zamanındaki kist boyutlarına, fetal anomalilere ve obstetrik sonuçlara göre değerlendirildi.

Bulgular: Kistlerin tamamı tekil idi. Takiplerinde beş tanesinin boyutu arttı. Ortalama takip süresi 12 haftaydı. 9 FBG (%64,3) vardı. FBG hastalarının altısında kist boyutları >5 cm idi. Sekiz fetal anomali mevcuttu; 5'i kalple ilişkiliydi ve 3'ünde tek umbilikal arter vardı. Doğum yapan hastalarda sezaryen sıklığı %78, erken doğum oranı ise %35,7 olarak belirlendi.

Sonuç: Sunulan çalışma, plasental kistlerin FBG ve eşlik eden fetal anomaliler açısından potansiyel risk taşımaları nedeniyle klinik öneme sahip olduğunu göstermiştir. Kist boyutunun büyümesinin takibi ve anomali taraması, özellikle kardiyak değerlendirme şeklinde uygun hasta takipleri plasental kist yönetimi açısından önemli olabilir. Ayrıca uterin arter Doppler ölçümleri ve profilaktik asetilsalisilik asit kullanımı da düşünülebilir. Ancak uterin arter Doppler incelemesinin klinik faydası ve asetilsalisilik asitin profilaktik kullanımı için daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Plasental kist; fetal anomaliler; fetal büyüme geriliği; olumsuz perinatal sonuçlar

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Sorumlu Yazar/Corresponding Author: Göksun İPEK, Üniversiteler Mahallesi 1604. Cadde, No: 9. Çankaya, Ankara, Türkiye
E-mail: drgoksunipek@gmail.com

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INTRODUCTION

Identifying placental hypoechoic lesions is essential to determining patients at risk of subsequent complications in pregnancy and delivery. Hypoechoic lesions in the placenta surrounded by normal parenchyma are defined as lacunas and lakes based on vascular flows (1). However, placental cysts differ from lakes and lacunae and are identified as hypoechoic lesions protruding from the placental fetal surface to the amnion. Placental cysts are referred by different terms in the literature; including mostly 'membranous cysts', 'chorionic cysts' and 'sub-amniotic cysts' (2-5). The prevalence of placental cysts is 5-7% (6). Despite the high prevalence of cysts, the diagnosis is made mostly incidentally, and the clinical importance of cysts remains unknown.

The etiology of placental cysts has yet to be fully elucidated. The cyst wall microscopically consists of amniotic and chorionic membranes. Special cells called 'X-cells' surround cysts, but their function is unknown. Their possible secretory activity and contribution to cyst formation were reported in the literature (2, 4, 7).

In the literature, there are only a few studies about placental cyst outcomes, most of which are case reports. Controversial findings about accompanying diseases and adverse outcomes are reported in the literature. Fetal growth restriction (FGR) and preterm delivery are mostly reported adverse outcomes related to placental cysts (4, 5, 8).

We evaluated our experience with placental cysts for any association with fetal anomalies, fetal growth, accompanying maternal diseases, and obstetric outcomes to determine what clinical significance these cysts may have.

MATERIAL AND METHODS

The presented cohort study was conducted on 20 patients incidentally diagnosed and recorded with placental cysts. Patients whose cyst location, shape, structure and dimensions were not fully described were excluded from the study. Patients were obtained either by scanning the hospital patient database or outpatient follow-ups from January 2021 to January 2023. The study was approved by the Institutional Review Board of the Ankara Bilkent City Hospital Ethics Committee (approval number: E2-23-4716).

All patients were included in the study after giving written informed consent. Maternal age, obstetrical histories (gravity, parity, miscarriage, and living children), and maternal diseases were recorded at the time of diagnosis with ultrasonographic characteristics of cysts (location of cyst and size). All patients were numbered and followed up until delivery. Additional ultrasound findings, fetal anomalies, and cyst characteristics were recorded at each examination. Pregnancy outcomes; gestational age at birth, birth weight, APGAR scores in the first and fifth minutes, neonatal intensive care unit (NICU) admission, amniotic fluid disorders, delivery methods; either cesarean section (C/S) or vaginal birth (VB) and fetal growth restriction were also recorded for all participants. Obstetric and perinatal outcomes were evaluated and compared with the literature.

RESULTS

Maternal age ranged between 23 and 40 years. Ten patients did not have any maternal diseases. In the other patients, there were six cases of diabetes mellitus (3 type-2 DM and 3 GDM), four cases of hypertension (2 gestational hypertension (GHT) and 2 chronic hypertension (CHT)), four cases of goiter, and two other maternal diseases. There were two twin pregnancies and 18 singleton pregnancies. Maternal demographic characteristics are shown in Table 1.

All cysts were single. When the patients were grouped according to diagnosis weeks, there were 5 patients in the first-trimester group, 9 patients in the second-trimester group, and 6 patients in the third-trimester group. The mean diagnosis week was 22 (9 - 36) weeks. Cysts were grouped depending on their diagnosis time sizes. Group 1(<2 cm) included 3 patients, group 2 (2-5 cm) included 11 patients, and group 3 (>5 cm) included 6 patients. There were four cysts at the placental cord insertion site (PCIS). Examples for placental cyst images and measurement method are shown in Figures 1 a and b.

There were eight fetal anomalies, and the most accompanying were cardiac and cord anomalies. Five anomalies were heart-associated anomalies with 3 major cardiac anomalies and 2 cardiac echogenic focus with VSD, and 3 of the patients had a single umbilical artery. There were 2 patients who had non-cardiac anomalies; one had an amniotic band disruption sequence, and the second had multiple anomalies but did not have invasive genetic tests. Two patients terminated due to amniotic band distraction sequence and cystic hygroma with multiple anomalies (Table 2).

After the exclusion of 2 terminated patients, there were 18 patients. There were four patients whose pregnancy outcomes could not be obtained. Case 11 had a di-di twin pregnancy; one of the fetuses, which had a placental cyst with the hypoplastic right ventricle, was observed intrauterine exitus, and the case was delivered at 35 weeks. Patient number 11 and the remaining 13 pregnancies' outcomes are shown in Table 3.

Table 1. Demographic characteristics of patients

Patient Number	Age	Gravidity	Parity	Disease
1	24	1	0	None
2	29	2	1	Type-2 DM
3	36	3	2	None
4	36	4	3	Goiter, GDM
5-twin (Mono-di)	32	1	0	GDM
6	33	3	1	None
7	31	2	0	GHT-preeclampsia
8	23	2	0	None
9	28	1	0	None
10	33	1	0	None
11-twin (Di-di)	23	3	1	Asthma
12	35	7	1	None
13	24	1	0	None
14	38	4	3	GHT-preeclampsia
15	23	2	1	Epilepsy
16	28	6	4	Type-2 DM, CHT, Goiter
17	40	4	2	Type-2 DM, CHT, Goiter
18	24	2	0	None
19	37	4	2	None
20	40	3	2	GDM, Goiter

*DM, diabetes mellitus; GDM, gestational diabetes mellitus; GHT, gestational hypertension; CHT, chronic hypertension; Mono-di, monochoronic – diamniotic twin; Di-di, dichoronic-diamniotic twin

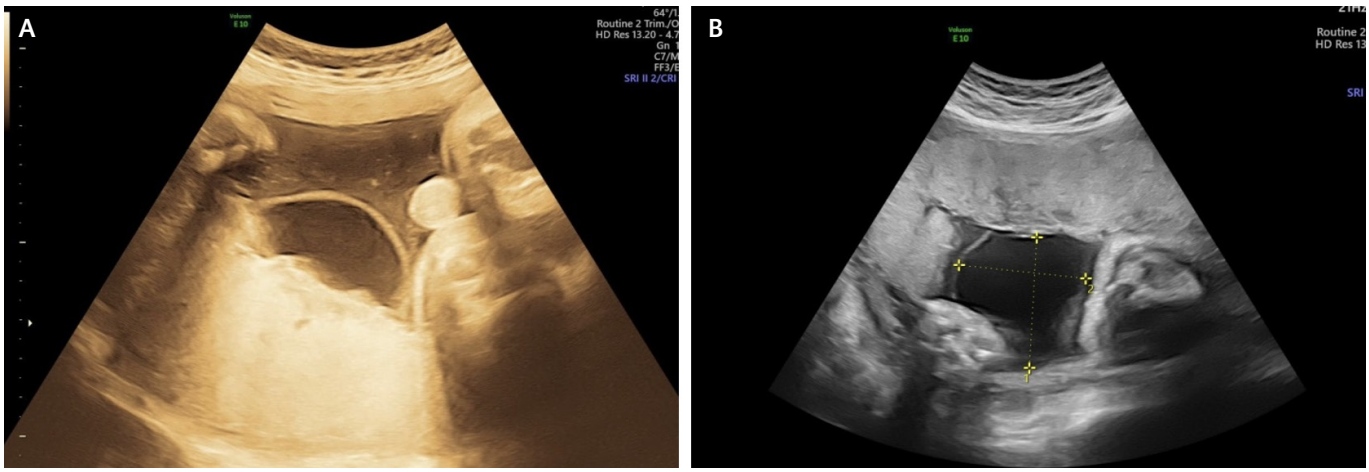

Figure 1. A and B. Images of a placental cyst and cyst measurement method

The frequency of C/S was 78.5%. There were five preterm deliveries (35.7%). Two who delivered before <34 weeks were diagnosed with severe preeclampsia. Two preterm deliveries had twin pregnancies. The fifth patient, who had a previous cesarean section, had severe uterine contractions and was delivered via c/s due to the risk of uterine rupture.

The mean follow-up duration was 12 weeks. No cyst was larger than >5 cm in the first trimester. The percentage of cysts larger than 5 cm was 33% in the second trimester and 50% in the third trimester. There were 9 FGR (64.3%). FGR patients were evaluated according to cyst's specialties, 5 had an increased cyst size with follow-ups. There were only 4 patients whose cyst size did not change during follow-up; cases 7 and 14 had severe preeclampsia and required emergency delivery only after 2 and 3 weeks of clinical follow-ups, case 19 was diagnosed at 36 weeks and delivered only after one week, and case 5 was mono-di twin pregnancy with possible confounder factor for FGR.

Table 2. Placental cyst characteristics and ultrasound findings

Case number	Diagnosis Week	Group	First Size (mm)	Last Size (mm)	PCIS	Growth pattern	Delivery Week	Additional Ultrasound Findings
Diagnosis in the first trimester								
1	13	1	15*12	-	No	-	MT	Cystic hygroma, encephalocele, AVSD, clenched hand, single umbilical artery
2	11	2	20*25	-	No	-	MT	Amniotic band distraction sequence, right lower extremity does not exist
3	12	2	21*27	ND	No	-	NR	Cardiac echogenic focus
4	9	2	26*23	ND	No	-	NR	None
5-twin (mono-di)	12	2	44*14	40*13	No	Same in 24w	36	None
Diagnosis in the second trimester								
6	20	1	18*20	ND	Yes		NR	Aorta hypoplasia
7	24	1	11*13	15*15	No	Same in 2w	26	None
8	18	2	35*20	40*45	No	Increase in19w	37	None
9	16	2	30*25	35*27	No	Same in 24w	40	Bilateral cleft lip and palate, hypertelorism, lobar holoprosencephaly
10	20	2	30*40	50*40	No	Increase in 19w	39	None
11-twin (di-di)	28	2	31*29	51*45	Yes	Increase in 7w	35	*Right ventricle hypoplasia and single umbilical artery
12	16	3	63*37	67*32	No	Same in 21w	39	None
13	23	3	34*58	58*42	No	Same in 16w	39	None
14	22	3	30*50	32*50	No	Same in 3w	25	None
Diagnosis in the third trimester								
15	31	2	24*35	32*38	No	Same in 8w	39	None
16	30	2	27*40	36*53	No	Increase in 8w	38	None
17	31	2	38*27	38*30	No	Same in 5w	36	None
18	29	3	59*46	NR	Yes		NR	None
19	36	3	52*40	50*44	No	Same in 1w	37	Cardiac echogenic focus
20	33	3	50*31	68*28	Yes	Increase in 4w	37	Single umbilical artery, bilateral choroid plexus cysts

*PCIS, placental cord insertion site; NR, not reached; MT, medical termination; AVSD, atrium-ventricle septal defect; w, week; Mono-di, monochoronic – diamniotic twin; Di-di, dichoronic-diamniotic twin

When the FGR outcomes were evaluated for the last sizes of cysts, six patients had >5 cm cysts, two patients had 2-5 cm cysts (case 8 had a 4.5 cm cyst which increased in size, and case 5 had twin pregnancy), and case 7 had <2 cm cyst and delivered at 26 weeks because of severe preeclampsia. FGR cases were also evaluated according to diagnosis time size groups. There were 1 FGR case in group 1, 5 cases in group 2, and 3 cases in group 3. There were 5 cases without FGR; in all cases, cyst size remained the same in follow-ups.

APGAR scores for all cases were above 7 at the first minute except for cases 7 and 14 (preterm birth with severe preeclampsia) and case 11 with multiple anomalies.

Table 3. Pregnancy outcomes

Patient number	Delivery week	Delivery method	C/S indication	Birth weight	APGAR	FGR	NICU
5-twin (mono-di)	36	C/S	Twin	2395/2445	7-8/7-9	Yes	Yes
7	26	C/S	Severe preeclampsia	550	4-6	Yes	Yes
8	37	C/S	Fetal distress	1885	7-8	Yes	Yes
9	40	VB		4000	5-7	No	Yes
10	39	C/S	CPD	2625	9-10	Yes	No
11-twin (di-di)	35	C/S	Twin preterm (right fetus IU-EX)	1650/1200*	7-8/0-0	Yes	Yes
12	39	C/S	Previous C/S	4000	8-9	No	No
13	39	VB		3700	8-9	No	No
14	25	C/S	Severe preeclampsia	410	2-4	Yes	Yes
15	39	C/S	Previous C/S	3840	8-9	No	No
16	38	VB		3065	7-9	Yes	No
17	36	C/S	Previous C/S	3285	7-9	No	No
19	37	C/S	CPD	2450	8-9	Yes	No
20	37	C/S	Previous C/S	2310	7-9	Yes	No

*FGR, fetal growth retardation; NICU, neonatal invasive care unit; C/S, cesarean section; VB, vaginal birth; CPD, cephalo-pelvic disportion, IUEX, intra uterine exitus; Mono-di, monochoronic – diamniotic twin; Di-di, dichoronic-diamniotic twin

In all cases, ultrasound diagnoses were confirmed histopathologically. Four placental cysts were at the umbilical cord insertion site; follow-up information for cases 6 and 18 could not be reached. Case 11 was a mono-di twin, and one of the fetuses with cyst and hypoplastic right ventricle died, and case 20 was growth restricted.

DISCUSSION

The present study found an increased FGR frequency associated with placental cysts. Preeclampsia, developing on the basis of gestational hypertension, and diabetes mellitus were mostly seen as maternal complications in the study group. There were also an increased number of fetal anomalies, and the cardiac and umbilical cord anomalies mostly accompanied ultrasound findings. To the best of our knowledge, this was the first study evaluating the association between placental cysts and fetal anomalies.

Placental cysts' etiology and clinical importance have remained controversial because of the limited studies that mostly report cases. Some authors found cysts associated with FGR and suggested clinical and ultrasound follow-up, whereas others considered them harmless and clinically not meaningful (3, 4).

FGR was described as a related outcome with placental cysts in the literature, and this study's findings were compatible with the literature. In the presented study, most of the FGR cases' cyst sizes were >5 cm, and increased growth patterns were seen. In the literature, in a retrospective evaluation, multiple cysts and cyst sizes larger than 4.5cm were found to be associated with FGR, similar to the presented study. In this research, researchers showed no relation with the cyst of the umbilical cord insertion site (5). In another study, researchers hypothesized that larger cysts and cysts at the PCIS had a higher risk for FGR because of interference with cord circulation. For this purpose, two case reports demonstrated an association between PCIS and FGR (3, 4). Our study did not have adequate case numbers for determining any relationship with FGR.

In a case report and review of the literature study, the FGR ratio was reported as 13%, and the preterm delivery ratio was reported as 37% (8). In another study, the preterm delivery ratio was reported as 20% (9). The preterm delivery ratio was similar to the literature in the presented study, whereas the FGR ratio was higher than in the literature. A possible reason for the increased FGR ratio could be hypoxia of the fetus due to the cyst.

The literature reported cysts mostly in women with diabetes mellitus and rhesus incompatibility (4). In our study, diabetes and

hypertension were mainly seen maternal diseases in concordance with the literature.

In the presented study, there were an increased number of fetal anomalies; the most accompanied were cardiac and cord anomalies. In the literature, there was no study in this context.

This study shows that placental cysts have clinical importance due to their potential risk for FGR and accompanying fetal anomalies. Placental cyst diagnosis can be made accurately and easily by ultrasound, even in the first trimester. Appropriate patient follow-ups for cyst size enlargements and anomaly screening, especially for cardiac evaluation, might be important for placental cyst management. Blood pressure measurements and oral glucose tests for gestational diabetes have increased importance for such patients. Also, uterine artery Doppler measurements and prophylactic acetylsalicylic acid use might be under consideration.

Strengths of the present study were its higher patient number than the literature, ultrasound follow-ups until delivery, and obstetric outcomes. The limitation of this study was that it involved mostly perinatology unit patients, and these group results may not reflect low-risk pregnant population outcomes.

CONCLUSION

The presented study showed that placental cysts have clinical importance due to their potential risk for FGR and accompanying fetal anomalies. Appropriate management for this special group necessitates ultrasound examinations for fetal well-being, cyst size and growth pattern, and anomaly screening, considering the increased risk for fetal anomalies and growth restriction. The clinical utility of uterine Doppler examination and prophylactic use of acetylsalicylic acid needs further studies.

Ethics Committee Approval

The study was approved by the Institutional Review Board of the Ankara Bilkent City Hospital Ethics Committee (approval number: E2-23-4716).

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Conflict of interest

The authors declare that there are no conflicts of interest.

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