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ORIGINAL ARTICLE – OPEN ACCESS

Analysis of Risk Factors for Ultrasonographic Graf Type IIa (–) Hips in Developmental Dysplasia: A Hospital-Based Case-Control Study with Follow-Up Outcomes

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ABSTRACT

Objective: To examine the association of Graf type IIa(-) hips with maternal and infant risk factors in newborns and to evaluate the follow-up outcomes.

Materials and Methods: Two different risk analyses were performed. In the first analysis, Graf type I hips were grouped as "controls," and Graf type II were grouped as "cases." In the second analysis, all the Graf type I and Type IIa(+) hips were grouped as "controls," and all Graf type IIa (-) hips were considered as "cases." Maternal age, presence of consanguinity, pregnancy, and smoking were considered as maternal risk factors. Sex, birth weight, gestational age, associated congenital anomalies, and family history were considered as infant risk factors. Further, we determined the risk factors for Graf type IIa and type IIa (-) hips.

Results: The study population included 73 cases (11.4%) and 569 controls (88.6%), including 322 (50.2%) male and 320 (49.8%) female infants. Graf type IIa hips revealed significant differences for gestational age (>42 wk), birthweight (>3500 g), and maternal age (≤20 y). At follow-up, all Graf type IIa(+) hips became Graf type I mature hips. In contrast, three Graf type IIa(–) hips (3/12, 25%) required additional treatment.

Conclusion: Significant risk factors for Graf type IIa(-) hips were female sex, gestational age of >42 wk, and birthweight of >3500 g. Almost one-quarter of Graf type IIa (-) hips may require additional treatment. Thus, significant risk factors for Graf type IIa(-)should be remembered in clinical practice.

Keywords: Hip dysplasia, screening, ultrasonography, graf type II, risk factors

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INTRODUCTION

A hip ultrasonography uses sound waves to produce images of joints, muscles, ligaments, tendons, bone, and soft tissues. This method helps in diagnosing hip abnormalities and can be used in infants to identify developmental dysplasia of the hip (DDH) (1, 2). Graf developed an ultrasonography classification scheme for ultrasound (US) classification system for DDH of the hip in infants using a standard coronal view of the mid-acetabulum (3, 4). In the measurement of the acetabular inclination angle (a) and the cartilage roof angle (b), the Graf method categorizes hips into four (4) main types, subdivided into nine (9) subtypes, ranging from normal hips to severely dysplastic hips to dislocated hips (4). Type IIa are physiologically immature and have two subtypes: type IIa(+) and IIa(–). Both IIa subtypes have an (a) angle between 50° and 59° at 6 wk of age. Hips with an (a) angle between 55° and 59° are classified as type IIa(+) where hips with an (a) angle between 50° and 54° are classified as type IIa(–). As the hip joint matures, there can be risk, and although most (Graf) type IIa will resolve themselves, 10% of the infants born initially with (Graf) type IIa may develop into a true dysplastic hip (5). Graf recommends treatment for type IIa(–) hips to ensure the valuable time of opportunity for regular acetabular development is not missed, and follow-ups for type IIa(+) hips is performed (6). Thus, we recommend that (Graf) type IIa(–) hips are identified in particular for a good understanding of the risk factors to aid the identification of hips abnormalities.

Although confirmed DDH risk factors are oligohydramnios, breech presentation, female sex, and primiparity (7, 8), there is limited information in the literature regarding (Graf) type IIa(–) hip risk factors. A better understanding of the risk factors for this type IIa(–) hips would allow better screening and identification of potential DDH cases. Here, we aimed to determine the relationship between ultrasonographic (Graf) type IIa(-) hips and maternal and newborn infant risk factors screened for DDH, including a follow-up after 3 mon.

MATERIALS and METHODS

Study Place and Design

Başkent University Medical School, Case-control analysis.

Ethic Approval

The Ethical Committee of Başkent University, Faculty of Medicine, approved this study (number: KA20/253).

Patients and Data Collection

All the infants admitted to the orthopedic outpatient clinic for DDH screening between May 2015 and November 2017 were included in the present study. With the first 3 mon after birth, the infants included in the study presented for US hip screening and were assessed with either normal hips (types Ia and Ib) or physiologically immature hips [types IIa(+) and IIa(–)] as per the Graf criteria (4). Our institution covers infants aged <6 wk old; these infants were also included in the study. We excluded premature infants and infants with mild dysplasia (IIb) and DDH (IIc, D, IIIa, IIIb, and IV) to allow comparison of the control group with (Graf) type IIa patients.

For the final analysis, two (2) case-control groups were formed for analyzing the following risk factors:

1. (Graf) type I were categorized as "controls" and (Graf) type IIa, including IIA(+) and IIa(-), were categorized as "cases.
2. (Graf) type I and type IIa(+) hips only were included in the control group and (Graf) type IIa (-) hips were categorized as "cases" (Fig. 1).

A 6–13 MHz linear-array transducer (HFL38e; SonoSite Inc.) was used, and the US was performed by a pediatric orthopedist (C.T.) with >15 y of experience in hip US. The US images were interpreted by the same authors (OS and C.T.).

Risk factors and various parameters related to DDH were researched from the literature (1, 9–12), and a consensus meeting was held. The following two categories of risk factors were established: maternal and infant characteristics. Maternal risk factors were considered as the presence of consanguinity (first and second degree); maternal age; any pregnancy complications, such as breech positioning or oligohydramnios; and smoking. The following infant risk factors were considered: birth weight, sex, gestational period, associated congenital anomalies, and family history. Maternal age, gestational age, and birth weight were categorized as follows: <20 y, 20–35 y, and >35 y; <38 wk, 38–42 wk, and >42 wk; and ≤3500 g and >3500 g, respectively. The obstetric database and neonatal clinical notes were used as the source of information.

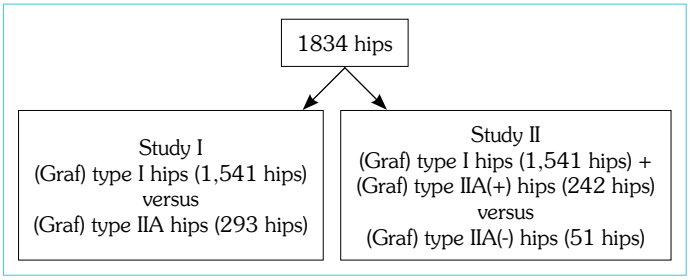

Figure 1. Flow chart of the patients enrolled in the study

Statistical Analyses

The software SPSS version 11.5 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. Categorical data for (Graf) type IIa (yes or no) was compared with a chi-square or Fisher's exact test. The outcome of (Graf) type IIa (dependent variable) was dichotomous (yes or no); therefore, binary logistic regression was performed for risk factor assessment. Detection of the risk level for all factors with statistical significance was then performed using backward stepwise multiple logistic regression. Individual models

Table 1. Frequencies of variables (risk factors) and cross tabulations for cases and controls with statistical comparison results

Variable	n	Percentage	Graf type I (%)	Graf type IIa (%)	p
Sex					
Male	322	50.2	298 (92.5)	24 (7.5)	0.002
Female	320	49.8	271 (84.7)	49 (15.3)	
Gestational age (week)					
35–42	560	87.2	513 (91.6)	47 (8.4)	0.001
>42	82	12.8	56 (68.3)	26 (31.7)	
Birthweight (gram)					
≤3500	341	53.1	309 (90.6)	32 (9.4)	0.001
>3500	301	46.9	260 (86.4)	41 (13.6)	
Congenital abnormalities	8	1.2	7 (87.5)	1 (12.5)	0.919
Maternal age (y)					
≤20	12	1.9	8 (66.7)	4 (33.3)	
20–30	487	75.9	431 (88.5)	56 (11.5)	0.039
≥30	143	22.3	130 (90.9)	13 (9.1)	
Pregnancy complication	7	1.1	6 (85.7)	1 (14.3)	0.807
Smoking history	61	9.5	50 (82.0)	11 (18.0)	0.085
Family history	12	1.9	9 (75.0)	3 (25.0)	0.133
Consanguinity	31	4.8	30 (96.8)	1 (3.2)	0.143
Multiple pregnancies	8	1.2	6 (75.0)	2 (25.0)	0.091

were developed to allow backward stepwise regression comparison. First, logistic regression analysis included all the variables whereby unadjusted odds ratios were calculated. Variables were then taken out of the model once the probability of the probability ratio statistic based on the maximum probability estimates was >0.10. Predictor variables for each category were then compared against the initial "reference category." Finally, adjusted odds ratios were calculated for each variable at 95% confidence interval (CI). Statistical significance was when the p level was <0.05.

RESULTS

The study included 1,834 hips of 917 infants, including 422 (46.1%) male and 495 (49.8%) female infants. The median patient age was 6.5 wk (range 3–24 wk). The median age was 6.4 wk for the cases and 6.7 wk for the controls (range 3–12 wk). An US median age was 6.1 wk (range 3–24 wk) for female infants and 6.9 wk (range 3–24 wk) for male infants. There were 293 cases of hips of both (+) and (–) (Graf) type IIa (15.9%; 272 infants consisting of 167 female and 105 male infants). There were 1.541 (Graf) type I mature hip controls (84.1%; consisting 271 females and 298 males). The rate of (Graf) type IIa (p=0.002) was significantly higher in female infants. The study group frequencies and the cross tabulations for infant and maternal risk factors are shown in Table 1.

Analysis: Follow-Up Phase

Repeat US were performed on 293 hips of 272 infants aged 3 mon. During this period, none of the (Graf) type IIa(+) hips were treated, and a Pavlik harness was used for the treatment (Graf) type IIa(–) hips. The (Graf) type IIa(+) and (Graf) type IIa(–) case-split was 242 hips (82.6%) and 51 hips (17.4%), respectively. Further treatment of type IIa was given to 4.1% (3 of 73) of the patients. All (Graf) type IIa(+) hips became (Graf) type I mature hips at follow-up without needing treatment; however, three (Graf) type IIa(–) hips (3 of 12, 25%) needed further treatment (closed reduction with general anesthesia and spica cast) after follow-up US at 3 mon of age as per our treatment program. There was no significant difference between males and females with regard to treatment need (p=0.073).

Logistic Regression Analysis for the Study Groups

Stepwise logistic regression was applied to study the cases and study controls with five steps for each group. Step 1 results of the logistic regression model are shown in Table 2 for the study groups including all variables [unadjusted OR with (Graf) type IIa as the dependent variable] as well as maternal and infant risk factor distribution among the cases and controls.

Significance was found in the stepwise logistic regression model at step 5 for "Group 1" with a chi-square value of 90.267 (p<0.001) with a prediction rate of 99.5%. For group 1 [all (Graf) type IIa], the significant risk factors were sex (female), gestational period (>42 wk), maternal age (≤20 y), birth weight (>3500 g), and smoking (Table 3).

Significance was found in the stepwise logistic regression model at step 5 also for "Group 2" with a chi-square value of 88.412 (p<0.001) with a prediction rate of 99.5%. Group 2 [(Graf) type IIa (-) hips] significant risk factors were sex (female), gestational period (>42 wk), and birth weight (>3500 g) (Table 4).

Table 2. Characteristics of the study groups with unadjusted odds ratios and 95% confidence intervals

	Group 1		Group 2	
Variables	**Unadjusted OR 95% CI**	**p**	**Unadjusted OR (95% CI)**	**p**
Sex				
Male	1 (reference)		1 (reference)	
Female	**2.245**	0.002	**2.534**	0.035
	1.34–3.75		1.65–4.01	
Gestational age (w)				
35–42	1 (reference)		1 (reference)	
>42	**5.068**	0.001	**4.421**	0.012
	2.91–8.80		2.78–7.89	
Birth weight (g)				
≤3500	1 (reference)		1 (reference)	
>3500	**2.876**	0.031	**1.697**	0.012
	1.96–9.45		1.47–7.58	
Congenital abnormalities	**1.115**	0.919	**0.793**	0.772
	0.13–9.19		0.09–8.31	
Maternal age (y)				
20–30	1 (reference)		1 (reference)	
≥30	**0.770**	0.419	**0.642**	0.321
	0.40–1.45		0.52–1.78	
≤20	**3.848**	0.032	**3.523**	0.059
	1.12–13.19		1.42–12.89	
Pregnancy complication	**1.303**	0.808	**1.201**	0.792
	0.15–10.97		0.53–8.72	
Smoking history	**1.842**	0.041	**1.236**	0.261
	0.91–3.72		0.87–2.87	
Family history	**2.667**	0.148	**2.173**	0.326
	0.70–10.08		0.56–11.51	
Consanguinity	**0.250**	0.175	**0.461**	0.581
	0.03–1.85		0.45–2.09	

OR: Odds ratio; CI: Confidence interval; w: Week; g: Gram; y: Year

DISCUSSION

To our knowledge, this is the first study in the literature to analyze the risk factors for (Graf) type IIa(–) physiologically immature hips. While (Graf) type IIa normalized spontaneously in most cases, especially (Graf) type IIa(–) hips, normalization may not occur and treatment is required in infants. On this basis, an understanding of the risk factors for (Graf) type IIa(–) hips in particular is critical for avoiding identification of the development of true hip dysplasia and late treatment.

Progression of (Graf) type IIa and requirements for US screening remain uncertain. Some authors believe that routine screening is unnecessary and ay lead to over-diagnosis and overtreatment. They further point to the majority of infant patients who normalize

Table 3. Adjusted odds ratios and 95% confidence intervals for study group 1 (the association of all Graf type IIa hips and risk factors)

	Adjusted OR	95% CI	p
Sex			
Male	1 (reference)		0.013
Female	5.967	1.098–8.776	
Gestational age (w)			
35–42	1 (reference)		0.001
>42	6.179	3.397–10.159	
Birth weight (g)			
≤3500	1 (reference)		0.027
>3500	3.745	1.831–7.679	
Maternal age (y)			
20–30	1 (reference)		
≥30	0.647	0.315–1.613	0.513
≤20	5.731	1.591–21.367	0.015
Smoking	2.597	1.297–5.219	0.037

OR: Odds ratio; CI: Confidence interval; w: Week; g: Gram; y: Year

Table 4. Adjusted odds ratios and 95% confidence intervals for study group 2 (the association of all Graf type IIa (-) hips and risk factors)

	Adjusted OR	95% CI	p
Sex			
Male	1 (reference)		0.038
Female	1.414	0.841–2.951	
Gestational age (w)			
35–42	1 (reference)		0.025
>42	2.748	1.569–5.832	
Birth weight (g)			
≤3500	1 (reference)		<0.05
>3500	3.612	2.162–6.838	

OR: Odds ratio; CI: Confidence interval; w: Week; g: Gram

without treatment (13–15). In contrast, other authors support US screening for the early identification of the development of true hip dysplasia that requires treatment. Kosar et al. (16) studied 529 infants with (Graf) type IIa and determined that US findings were worse in >5% within the follow-up period. The authors' opinion is that determined that US screening to identify development of true hip dysplasia early (type IIa). Omeroglu et al. (17) evaluated 285 type IIa and determined that treatment was required in 35 (Graf) type IIa(–) hips and 1 (Graf) type IIa(+) hip. Further, the authors determined that the rate of planned follow-ups that were not performed was quite high, and the management of (Graf) type IIa requires careful management in newborn infants (17). These study results are partially consistent with literature. The further treatment rate for (Graf) type IIa was 4.1% [all (Graf) type IIa (-) hips] in our study, in line with that reported in the literature. Unlike the study by Omeroglu et al. (17), no sex-related difference was found in this study. The authors believe that irrespective of sex, (Graf) type IIa(–) hips require careful management in newborn infants.

DDH risk factors have been analyzed in several studies (1, 7, 9, 10, 12, 13, 18). DDH risk factors are generally reported as female sex, positive family history, and breech cases (19, 20). Hundt et al. (1), performed a meta-analysis on 30 studies, and the authors determined that breech cases, female sex, positive family history, and clicking hips at clinical examination increase the DDH risk. Ortiz-Neira et al. (13) also performed a meta-analysis whereby they concluded that US screening should be performed to confirm DDH in high-risk groups; high-risk groups include females, those with the left hip affected, breech cases, first order of birth, and family history. The authors concluded on similar risk factors as literature with similar results, and further that risk factors are common between DDH and (Graf) type IIa.

Female sex is generally accepted as a key risk factor for DDH (9, 21). The previously mentioned meta-analysis by de Hundt et al. (1) indicated a significant increase in DDH in female infants with an OR of 3.8. Omeroglu et al. (17) showed that (Graf) type IIa occurs 2.7 times higher in female infants. This study concluded that (Graf) type IIa is more common in female than in male infants. Previous studies have shown similar findings; in this study, females have a high-risk of (Graf) type IIa(–) hips, but with a lower imbalance to males (1.5 times more cases).

Factors commonly analyzed for patients with DDH are gestational period and birthweight, with the incidence of DDH being widely accepted to be lower in low-birthweight and premature infants (22). Bower et al. (23) indicated that a higher rate of DDH is observed with a birthweight of >3500 g and a gestational period of >42 wk. Patterson et al. (24) concluded in their study on 243 infants that all patients with DDH had a gestational period of ≥39 wk, consistent with the present findings. We did not find any previous study that analyzed (Graf) type IIa(–) hips concerning birthweight and gestational period. However, our results showed that double the risk of (Graf) type IIa(–) hips with a gestational period of >42 wk and birthweight of 3500 g increases the risk.

Multiple studies (1, 7, 24) concluded that maternal age is a DDH risk factor. For example, Chan et al. (7) studied 1,127 infants and concluded that maternal age is a risk factor, whereby a maternal age of 30–34 y was a stronger risk factor than a maternal age of ≤20 y. Our study had similar results; found that a maternal age of 20–30 y had half of the risk of having infants with (Graf) type IIa. In contrast, maternal age did not seem to be a risk factor for Graft type IIa(–) hips. The authors' opinion is that while maternal age of <20 y or >30 y is a risk factor for Graft type IIa, especially as a maternal age of <20 y involved a five times risk of having infants with Graft type IIa compared with maternal age 20–30 y.

The present study has the following limitations:

- This was a single-center hospital-based case-control study; multicenter studies allow more cases and controls.
- Other risk factors, such as parity and delivery type, were not analyzed.
- Given the number of cases, the low predictor rate was considered as a study limitation.

The authors recommend further detailed analysis on all possible risk factors in future trials.

CONCLUSION

The major risk factors for (Graf) type IIa(–) hips are gestational period of >42 wk, female sex of the infants, and birth weight >3500 g. An analysis of follow-ups within 3 mon of birth indicated that 4.1% of (Graf) type IIa(–) hips could develop into DDH. Therefore, the authors recommend an US screening program to identify (Graf) type IIa(–) hips that could develop into DDH so that early treatment can be administered.

Ethics Committee Approval: The Başkent University Medicine and Health Sciences Research Ethics Committee granted approval for this study (date: 16.06.2020, number: 94603339-604.01.02/16837).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – BH, OŞ; Design – OŞ; Supervision – İCT; Resource – İCT; Materials – OŞ; Data Collection and/or Processing – BH; Analysis and/or Interpretation – BH, OŞ; Literature Search – BH; Writing – OŞ, BH; Critical Reviews – İCT.

Conflict of Interest: The authors have no conflict of interest to declare.

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