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Fetal macrosomia and associated factors to perinatal adverse outcomes, in Yaounde, Cameroon : a case control study.

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Abstract

Objective

To Identify risk factors of perinatal complications amongst macrosomic babies in a reference hospital structure.

Method

We conducted a case-control institutional based study. Cases and controls of singleton livebirths were extracted from the maternity registry from January 2017 to December 2019 The case population consisted of mother and child macrosomic couples with perinatal complications. The control group consisted of couples without perinatal complications. Matching was done on age and sex. The main primary end point was the risk factors for complications. Data were analyzed using R, software version3.0 in adjusted and unadjusted analysis with $p<0.05$ threshold considered statistically significant.

Results

Out of 362 couples, we had 186 cases and 176 controls. Maternal age ≥30 years (p=0.024); non-screening for gestational diabetes (p=0.027); history of caesarean section (p=0.041); weight gain ≥16 kg (p<0.001); maternal HIV (p=0.047); birth weight ≥4500g (p=0.015) and birth height ≥ 52.7 ±1.7cm (p=0.026) were risk factors.

Conclusion

The delivery of a macrosomic baby remains problematic in this setting. The improvement of the maternal-fetal prognosis requires quality prenatal surveillance and management by a multidisciplinary perinatal team involving obstetricians, endocrinologists and neonatal pediatricians.

Key words : fetal macrosomia, gestational diabetes, maternal obesity, birth weight, fetal growth

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INTRODUCTION

Fetal macrosomia(FM) is an impairement of fetal growth in excess mainly due to hyperinsulinemia. It is defined by a birth weight (BW) above 4000g or 4500g irrespective of gestational age or a BW above 90 or 95th percentile on growth charts according to the term at delivery. These babies are described as large for gestational age(LGA) in comparison to those appropriate or small for gestational age [1,2]. The main causes of fetal macrosomia are grouped into 3 main categories which are diabetes during pregnancy, excess weight gain during pregnancy and obesity [1-3]. Fetal macrosomia can lead to life-threatening complications for both mothers and babies. Among mothers it is common to identify a high rate of caesarean delivery, obstetrical maneuvers, tearing of the perineum, postpartum hemorrhage and the dreaded shoulder dystocia. Among babies, traumatic deliveries can result in brachial plexus palsy, fractures, neonatal asphyxia, and many metabolic complications such as hypoglycemia, hypocalcemia, hyperbilirubinemia. [4,5]. Overall FM can affect 20% of livebirths worldwide, regarding the threshold retained for its definition. In Cameroun, this prevalence rates has been reported from 5 -31% notably when included the prevalence of diabetes mellitus in pregnancy [5-6]. In general, fetal macrosomia remains a challenge around the world, with no critical reduction over the recent years, and its rates are parallel to the trends of obesity and diabetes during pregnancy. Beyond the perinatal period, neonatal macrosomia is a determinant of diseases in adolescence and adulthood, notably obesity, hypertension and metabolic syndrome[7]. To improve the prevention of FM, several interventions are carried out among others: improving timely screening of gestational diabetes, adopting local guidelines for management of delivery of macrosomic babies ; all of these must be preceded by increased efforts for education to limit excessive weight gain during pregnancy [8,9]. Within a context of ressource limited settings, we conducted this institutional facility based study to analyze risk factors associated to complications amongst macrosomic babies. The aim of the study was to identiy risk factors of perinatal adverse outcomes in case of fetal macrosomia in order to update guidelines on prevention of FM including management of delivery and of babies large for gestational age.

METHODS

STUDY OBJECTIVE, DESIGN SETTING AND POPULATION STUDY

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We performed a case-control study, with presence/absence of a perinatal complication, amongst babies with macrosomia as primary endpoint.The sample size was determined assuming a frequency of macrosomia equals to 7.5% , a confidence level of 95%, a relative precision of 50%, and an expected Odd Ratio of 2. Given all these, the minimum sample size was estimated at 170 for each group (presence vs absence of perinatal complication) giving a required total of 340 patients.

The study took place at the maternity of Essos hospital center (EHC). EHC is a third level facility in Yaoundé, hosting a maternity of 2500 to 3000 annual deliveries. The studied population comprised all macrosomic babies and their mothers. For the propose of the study, macrosomia was defined as a BW of 4000g or above. Cases were macrosomic mothers and babies pairs with complications and control were mothers and macrosomic babies pairs without complications. Singleton In-Born cases and controls, were matched for sex and gestational age after exclusion of genetic cause of macrosomia.

STUDY PERIOD

The study included all the singleton livebirths from January 2016 to december 2019.

PROCEDURE-VARIABLES

Cases and controls after being extracted from perinatal registers (maternity and neonatology department) were matched for sex and age. The variables collected were qualitative and quantitative under the following categories

1- **socidemographic** : maternal age, occupation, marital status, ethnicity, religion, education
2- **clinical and obstetrical** : parity, gestational term, fetal presentationweight gain during pregnancy, past story of mellitus diabetes, duration of the labour, previous macrosomic baby, mode of delivery, maternal perinatal complications.
3- **Fetal variables** : Apgar score, weight, height, head circumference and perinatal complications.

PRIMARY ENDPOINT -AND STATISTICAL ANALYSIS

The main primary endpoint were the risk factors for complications. Cspro software version 7.3 was used for data entry, while R software version 3.6.2 was used for all data analysis. Chi 2/Exact Fisher test was applied where applicable for testing the association between the primary endpoint and other qualitative variables. While the Anova/Kruskall Wallis test was used when applicable to test the association between the primary endpoint with quantitative variables. Logistic regression was used to

estimate the odds ratio, to measure the magnitude of association between the primary endpoint and different covariates of the study.

Ethical consideration

Administrative authorisation was issued and ethical clearance for the study obtained from the Institutional Review Board (IRB) of the Essos Health Centre (Reference: N°2020/08/CE-CHE). All data were kept in strict confidentiality by using specific identifiers and restricted access.

RESULTS

POPULATION STUDY AND CHARACTERISTICS OF CASES AND CONTROLS

A total of 362 macrosomes and their mothers were included, consisting of 186 cases and 176 controls.

Descriptive analyzes showed that the mothers in the case group were older (31.3±5.3years vs 29.1±5.3years; p=0.012) (Table 1) . Compliance with the eight CPN model was found more in the controls (47.7% vs 19.4%; p= 0.002). Non-screening for gestational diabetes was more common in cases (26.9% vs 4.3%; p<0.001). Weight gain during pregnancy was lower in controls (16.02 ±4.01 kg vs 18.75 ±3.25; p<0.001). The case group had more mothers with a history of caesarean section for fetal macrosomia (8.1% vs 0.6%; p=0.007). Fetal birth weight ≥4500 g was found more in the case group (17.7% vs 1.7%; p<0.001). The mean birth height of the cases was greater than that of the controls (52.7cm ± 1.7cm vs 51.8cm ± 1.5cm). (see Table 2 and 3)

Complications of FM

The main complications found in the mothers were delivery by caesarean section, more often emergency than elective (26.5%), lesions of the genital canal, 20.2% followed by instrumental delivery in 10.5% of cases, Postpartum hemorrhage occurred in 7.2% of cases. There were no maternal deaths. Amongst newborns, metabolic complications (19.6%) were more frequent than respiratory complications (12.4%), dystocic presentations (6.3%) or traumatic injuries(1.7%) (see Table 4). The neonatal case fatality rate was 2.8%.

Factors associated to complications of fetal macrosomia

The maternal risk factors for perinatal complications amongst mothers of babies born with macrosomia were: maternal age ≥30 years (OR: 3.31, 95% CI 1.19-9.57, p=0.024); non-screening for gestational diabetes (OR: 3.77; 95 CI 1.22-13.16, p=0.027); history of caesarean section (OR: 3.47; 95 CI1.07-11.95, p=0.041); weight gain ≥16 kg (OR=3.38; 95 IC1.80-6.54, p<0.001) and maternal HIV (OR: 6.23; 95 IC1.18-49.42, p=0.047).

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The fetal risk factors for perinatal complications in macrosomic mother-child couples were: birth weight ≥4500g (OR: 7.12; 95 IC 1.61-40.52, p=0.015) and birth height ≥ 52.5 ±1.7cm (1.26; 95 CI 1.03-1.56, p=0.026).In addition, multiparity (OR: 0.09, 95% CI 0.03-0.23, p<0.001) and great multiparity (OR: 0.30; 95% CI 0.10-0.81, p=0.019) were protective factors.(see Table 5)

DISCUSSION

One of the particularities of this study is that it compares the factors associated with complications in babies weighting 4000g or above. This is contrary to previous studies comparing babies with macrosomia to those weighting less than 4000 g [10-12]. Our work seems to document that within our population, complications are more frequent in case of poor prenatal follow-up and as such reinforces the recommendations for good antenatal follow-up advocated by the World Health Organization [13]. This good prenatal follow-up includes, among other things, screening for gestational diabetes, the absence of which increases the risk of macrosomia, thus confirming data from previous studies. However, in our context, the timing of this remains worrying and the consensus of experts seems to recommend a blood glucose test for all women from the first prenatal consultation and a new measurement between 24 and 28 weeks for those at risk and even earlier [14-15]. Unsurprisingly, our study confirms the deleterious effect of excessive weight gain on the risk of macrosomia as well as the existence of obesity prior pregnancy. In our study, excessive weight gain beyond 16 kg requires sustained attention. However, this result must be tempered, as it was not correlated with pre-pregnancy weight [16,17]. The risk of complications seems to increase with the age of the mothers as well as with the existence of a past story of caesarean section including multiparity. These data are consistent with those found in similar populations of sub-Saharan Africa [12, 18,19, 20].

What is striking in this study is the high rate of emergency and non-elective caesarean section testifying of the late detection of macrosomia, probably during labor. This reinforces the need for good clinical follow-up by regular measurement of symphysis fundal height associated to abdominal circumference[21]. In addition, the absence of influence of third term ultrasonography to predict

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macrosomia in our study is consistent with previous reports in the literature and emphazises the need to use a multiparametric ultrasound model including umbilical vein flow for optimal performance and accuracy to diagnose macrosomia[22,23]. Finally, in newborns, the parameters most associated with complications within this population of over 4000 g were those with over 4500 g and over 52.7 cm of height. Such thresholds have previously been described for weight, but data on height are wandering and sometimes slightly higher[24]. At last, the HIV factor found in this study should without doubt be linked to the therapies taken by HIV infected women, some of those drugs may induce metabolic effects, in particular disturbing the metabolism of carbohydrates and lipids. This could therefore suggest to reinforce metabolic monitoring of HIV infected pregnant women under antiretroviral therapy[25]..

CONCLUSION

All the results of this work confirm the need to improve prevention of macrosomia in our context. This may require to strengthen antenatal care of all pregnant women, to systematize screening for gestational diabetes; to limit weight gain during pregnancy to 16 kg: The personalized obstetric care protocol should be implemented when the estimated fetal weight of the expected child is greater than 4500 g with attention to height greater than 52.7 cm .

CONFLICT OF INTEREST : None

FINDING : No funding was received for this study

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Table 1 : Distribution of socio-demographic characteristics of mothers according to perinatal complications and non-complications of macrosomia and the respective unadjusted OR.

		Macrosomia without Complication N= 176, 48.6%	Macrosome with at least 1 complication N= 186, 51.4%	Undajusted OR (95CI, p)
Marital status	Single	77 (43.8)	85 (45.7)	-
	Married	99 (56.2)	101 (54.3)	0.92 (0.61-1.40, p=0.709)
Education	None	1 (0.6)	10 (5.4)	-
	Primary	13 (7.4)	17 (9.1)	0.13 (0.01-0.82, p=0.067)
	Secondary	52 (29.5)	77 (41.4)	0.15 (0.01-0.81, p=0.073)
	Higher	110 (62.5)	82 (44.1)	0.07 (0.00-0.40, p=0.014)
Profession	White coolar	29 (16.5)	24 (12.9)	-
	Private	50 (28.4)	60 (32.3)	1.45 (0.75-2.82, p=0.269)
	Informal	53 (30.1)	76 (40.9)	1.73 (0.91-3.32, p=0.095)
	Student	44 (25.0)	26 (14.0)	0.71 (0.34-1.48, p=0.363)
Maternal Age years	< 25	30 (17.0)	15 (8.1)	-
	25-30	56 (31.8)	55 (29.6)	1.96 (0.97-4.13, p=0.067)
	30-35	51 (29.0)	64 (34.4)	2.51 (1.24-5.27, p=0.012)
	35-40	33 (18.8)	38 (20.4)	2.30 (1.07-5.09, p=0.035)
	40 et plus	6 (3.4)	14 (7.5)	4.67 (1.55-15.54, p=0.008)
Age	Mean (SD)	29.9 (5.3)	31.3 (5.2)	1.05 (1.01-1.10, p=0.012)

OR : Odd Ratio

CI : Confidence Interval

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Table 2 : Distribution of the characteristics of the prenatal follow-up of macrosomic mother-child couples in EHC according to the presence or absence of perinatal complications and the respective unadjusted ORs.

		Couples without Complication N= 176, 48.6%	Couples with complication N= 186, 51.4%	Unadjusted OR (95CI, p)
Third trimester ultrasound	Yes	171 (97.2)	153 (82.3)	-
	No	**5 (2.8)**	**33 (17.7)**	**7.38 (3.06-21.97, p<0.001)**
Screening for gestational diabetes	Yes	170 (96.6)	136 (73.1)	-
	No	**6 (3.4)**	**50 (26.9)**	**10.42 (4.67-27.78, p<0.001)**
Number of antenatal visits	0-1	1 (0.6)	12 (6.5)	-
	2-3	32 (18.2)	93 (50.0)	0.24 (0.01-1.30, p=0.181)
	4-7	**59 (33.5)**	**45 (24.2)**	**0.06 (0.00-0.34, p=0.009)**
	8 et plus	**84 (47.7)**	**36 (19.4)**	**0.04 (0.00-0.19, p=0.002)**
Body Maas Index(BMI)	Thinness	6 (3.4)	4 (2.2)	-
	Normal	76 (43.2)	58 (31.2)	1.14 (0.31-4.65, p=0.840)
	Overweight	85 (48.3)	99 (53.2)	1.75 (0.48-7.03, p=0.399)
Weight gain during pregnancy (kg)	**Mean (SD)**	**16.02 (40.1)**	**18.75 (32.5)**	**1.03 (1.02-1.04, p<0.001)**
	≤16 kg	89 (50.6)	38 (20.4)	-
	>16 kg	**87 (49.4)**	**148 (79.6)**	**3.98 (2.52-6.38, p<0.001)**
Fundal height (cm)	**Mean (SD)**	**36.3 (1.3)**	**37.0 (3.1)**	**1.25 (1.09-1.44, p=0.002)**

OR : Odd Ratio

CI : Confidence Interval

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Table 3: Distribution of EHC macrosomic mother-child couples according to paraclinical and fetal anthropometric parameters and unadjusted OR.

		Témoins N= 176, 48.6%	Cas N= 186, 51.4%	OR non-ajustes (95CI, p)
Mean estimated fetal weight on 3rd trimester ultrasound (g)	**Mean (SD)**	**3946.6 (291.1)**	**4141.2 (437.3)**	**1.00 (1.00-1.00, p<0.001)**
Gestational Age	< 37 SA	3 (1.7)	3 (1.6)	-
	37 SA-41SA6J	170 (96.6)	176 (94.6)	1.04 (0.19-5.66, p=0.966)
	42 SA et plus	3 (1.7)	7 (3.8)	2.33 (0.28-21.10, p=0.428)
Gender	Male	114 (64.8)	118 (63.4)	-
	Female	62 (35.2)	68 (36.6)	1.06 (0.69-1.63, p=0.792)
Birth Weight(g)	4000-4500	173 (98.3)	153 (82.3)	-
	≥4500	**3 (1.7)**	**33 (17.7)**	**12.44 (4.35-52.43, p<0.001)**
Head Circumference Mean (cm)	**Mean (SD)**	**36.0 (0.8)**	**36.3 (1.1)**	**1.35 (1.09-1.70, p=0.008)**
Mean Height (cm)	**Mean (SD)**	**51.8 (1.5)**	**52.7 (1.7)**	**1.43 (1.25-1.66, p<0.001)**

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Table 4: **Maternal morbidity and mortality of macrosomic mother-child couples in** EHC

Maternal' complications	N=362	%
• Instrumental delivery	38	10.5
• Emergency cesarean	71	19.6
• Elective C-section	25	6.9
• Genital laceration	73	20.2
• Gestaional Diabete	21	5.8
• Post partum fever	11	3.0
• Eclampsia ou pré éclampsia	31	8.6
• Post partum hemmorage	26	7.2
• Maternal deaths	0	0
Newborn Complications		
Respiratory distress		
• Mild and moderate respiratory distress	37	10.2
• Severe respiratory distress	8	2.2
Total	45	12.4
Other Complications		
• Anemia	1	0.3
• Hypocalcémia	17	4.7
• Hypoglycémia	34	9.4
• newborn jaundice	19	5.2
Total	71	19.6
Traumatic Complications:		
• Fracture of the humerus	1	0.3
• Collarbone fracture	2	0.6
• Obstetric brachial plexus palsy	3	0.8
Total	6	1.7

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Tableau 5 Multivariate analysis of maternal factors associated with perinatal complications in fetal macrosomia (adjusted ORs)

		OR ajustes (95CI, p)
Education	Aucun	-
	primaire/secondaire	0.20 (0.01-1.66, p=0.190)
	Supérieur	0.15 (0.01-1.21, p=0.117)
Age maternel	17-24	-
	25-29	2.28 (0.85-6.38, p=0.108)
	30-40	**3.31 (1.19-9.57, p=0.024)**
	≥40	**11.25 (2.23-63.76, p=0.004)**
Third trimester ultrasound	Yes	-
	No	1.18 (0.34-4.57, p=0.804)
Screening of gestational diabetes	Yes	-
	No	**3.77 (1.22-13.16, p=0.027)**
Number of antenatal visits	0-1	-
	2-3	0.39 (0.01-5.10, p=0.527)
	4-7	0.11 (0.00-1.54, p=0.145)
	≥8 e	**0.06 (0.00-0.82, p=0.050)**
Previous C-section	No	-
	Yes	**3.47 (1.07-11.95, p=0.041)**
Previous macrosomic baby	**Yes**	**19.24 (2.74-396.73, p=0.011)**
Fundal Height (cm)	37.0 (3.1)	0.87 (0.29-1.22, p=0.569)
Weight Gain	moins de 16 kg	-
	plus de 16 kg	**3.38 (1.80-6.54, p<0.001)**
HIV	Non	-
	Oui	**6.23 (1.18-49.42, p=0.047)**
Parity	Primiparous	-
	Pauciparous	0.53 (0.23-1.18, p=0.121)
	multiparous	**0.09 (0.03-0.23, p<0.001)**
	great multiparous	**0.30 (0.10-0.81, p=0.019)**
Birth Weight (g)	4000-4500	-
	4500 et plus	**7.12 (1.61-40.52, p=0.015)**
Foetal Height (cm)	**52.7 (1.7)**	**1.26 (1.03-1.56, p=0.026)**