Congenital Malformations And Metabolic Disorders On The Gestational Diabetes In Ouagadougou (Burkina Faso)

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Abstract

Introduction: Neonatal health is still a concern in low-income countries. This work aims to describe neonatal congenital malformations in children born from mothers with diabetes or gestational diabetes in urban health facilities south of the Sahara.

Patients and methods: This is a longitudinal descriptive study conducted from August 1, 2015 to July 31, 2016 on stratified random sampling of 21 neonates of diabetic mothers with congenital malformation. Cardiac malformations were suspected in the presence of clinical signs (respiratory distress, cyanosis) and confirmed by Doppler echocardiography

Results: Two hundred and seventy-two mothers developed diabetes during pregnancy and 21 newborns were malformed (7.7%). The mean age of mothers was 28.8 years and 28.6% of these women were multiparous. On diagnosis, the average age of the newborns was 4 days and 40% of them had a birth weight higher than 4000g. Cardiac malformations were predominant (52%) followed by central nervous system malformations (33%. The pattern of developing cardiac malformations was respiratory distress in 10 cases (47%) and these malformations were dominated by inter ventricular communication (36%). The pattern of developing cardiac malformations was respiratory distress in 10 cases (47%) and these malformations were dominated by inter ventricular communication (36%. One newborn died (4%).

Conclusion: Heart malformations are the number one killer of newborns in diabetic pregnancies. Improving obstetric and perinatal prognosis requires multidisciplinary collaboration with pre-conceptual programming and appropriate management of pregnancy and diabetes.

INTRODUCTION

The prevalence of gestational diabetes is on the rise and now accounts for 3 to 15% of pregnancies worldwide [1]. The combination of diabetes and pregnancy is a heterogeneous entity that includes pre-existing and pregnancy-specific diabetes.

The proportion of neonates with congenital malformations is reported to be 3.4% in France [2], metabolic disorders are nearly 10% [5,13] and deaths from congenital malformations are estimated to be around 7% of the total number of neonatal deaths [9]. In Burkina Faso, the incidence of newborn malformations associated with diabetes is not known and metabolic disorders are poorly documented. The increase in the frequency of malformations and complications in diabetes is related to the state of fetal hyperglycemia. The heart and brain of the newborn are the organs most affected by diabetes. Although work on neonatal morbidity and mortality in neonates of diabetic mothers is frequent, those focusing more specifically on malformations are rare, particularly in Africa. In Burkina Faso, the incidence and circumstances are poorly documented.

We therefore proposed to study in Burkina Faso the neonatal complications of maternal diabetes and particularly malformations in order to help target health interventions for this at-risk group.

METHODS

Our study covers the maternity services of 17 health facilities in the city of Ouagadougou. The health region of

the central plateau averages between 75,000 and 85,000 deliveries a year and has no pediatric / neonatal service. The majority of cases requiring neonatal attention are transferred to our national reference center, CHU Charles De Gaulle. This descriptive study covers a population of approximately 1,900,000 inhabitants and 50,000 births in the city of Ouagadougou.

This was a longitudinal descriptive study conducted over a 12-month period (August 1, 2015 to July 31, 2016). The population included all newborn from diabetic mothers or mothers with gestational diabetes with a congenital malformation according to the following criteria:
1) 0-28 days of life at transfer to a health facility,
2) birthplace in the city of Ouagadougou and
3) at least one paraclinical examination to determine the risk of injury

We performed random stratified random sampling of health structures. This random sampling helped to estimate the denominator by evaluating 17 health centers in a proportionality in the echelons of the different health structures of the city of Ouagadougou.

We defined diabetes in pregnancy according to the WHO definitions, which requires a glucose tolerance disorder leading to a hyperglycemia of variable severity starting or diagnosed for the first time during pregnancy, whatever the treatment necessary and evolution in the postpartum period [1,2]. This definition actually includes two different entities that must be distinguished: 1) diabetes, most often type 2 (T2D2), preexisting to pregnancy and found only on the occasion of pregnancy and which will persist after delivery, and 2) the abnormality of carbohydrate tolerance actually appeared during pregnancy, usually in second part and disappearing at least temporarily postpartum.

In terms of congenital malformations, we retained all the morphological and / or functional abnormalities of a tissue, an organ that existed from birth [3], according to Priscilla White's classification which distinguishes several classes according to gravity, age of onset, and duration of diabetes [20]. We collected sociodemographic data, the reference pattern in the department, the personal and family pathological antecedents, the clinical and paraclinical signs, and the fate of newborns. The collected data were entered and processed on a micro-computer using the Epi info 3.5.1 software. Continuous variables were expressed as mean and standard deviation (SD) and discontinuous variables as absolute and relative frequencies. Chi-square and Fisher tests were used. The result of the odds ratio calculation (OR) was used to analyze the factors associated with malformations. The materiality threshold was set at $p < 0.05$. All parents of malformed children gave verbal consent for inclusion in the study. For the denominator, the parents did not individually agree. The data come from a therapeutic relationship in each center and were anonymized before entry for analysis in this work. Due to the epidemiological and non-interventional nature of the study, the Ethics Commission of Burkina Faso was not solicited. The findings of the study were made available to interested parents.

RESULTS

During the 12-month period of the study, we found 272 diabetic women in our 17 participating centers that deliver on average 70% of women in the city of Ouagagougou. We recorded 21 newborns with congenital malformations. During this same period, our 17 centers participating in the study reported at birth 272 mothers with diabetes, which leads to an incidence during pregnancy for the city of Ouagadougou of 12.9% (272/21).

Characteristics of diabetic mothers of children with malformations

Mothers of malformed children averaged 28.8 years (range 20-37 years) and their characteristics are shown in Table I. It should be noted that the socio-economic status was globally low with 76% without income-generating activities. Two women (9%) were on oral antidiabetic drugs, 3 mothers (14.28%) were on insulin therapy, 2 mothers (9%) were on diet only, and 14 women (66%) were not under antidiabetic treatment.

Characteristics of diabetic mothers of children without malformation

The mean age of newborn mothers without malformation was 25.8 ± 5.5 years with extremes of 16-38 years. Mothers without income-generating activities (housewives, pupils and students) numbered 175, or 70% of mothers. The mean age of newborn mothers without malformation was 25.8 ± 5.5 years with extremes of 16-38 years.

Characteristics of newborns with malformations

The characteristics of newborns are summarized in Table II. On arrival, we noted an age between 0 and 5 days in 52% of

cases, the average weight was 3600 ± 25g (range = 2350 to 5550g) and the average size of 51cm. One newborn died during the neonatal period, 4% of newborns with malformations.

The reference pattern was in 43% (9/21) cases of respiratory distress, followed by jaundice 19% (4/21) and fever 14% (4/21). It should be noted that 48% (10/21) of newborns had metabolic disorders, as were hypoglycemia and hypocalcemia, but not the same neonates.

Congenital malformations

The types of congenital malformations found in the 21 neonates of diabetic mothers were dominated by cardiac malformations in 52% (11/21) cases, followed by central nervous system malformations (33%), and skeletal malformations (10%).

The detail is given in Table III. Cardiopathies were non-cyanogenic in nine neonates (82%) (Table III).
Among the malformations of the central nervous system, 4 cases (57%) were observed with hydrocephalus followed by 2 cases (28%) with anoxo-ischemic leukoencephalopathy, and then 1 case (14%) with holo-pros encephalopathy. The skeletal malformations were essentially a case of equine varus clubfoot and a newborn with a pectus excavatum.

A neonate had left renal dysplasia associated with nephrromegaly. We found a newborn with trisomy 21 and another case of poly-malformative syndrome associating a cardiac malformation, a malformation of the central nervous system and skeletal malformation. We followed these newborns during the neonatal period and we reported one case of death among the 21 newborns is 4%.

Table 1

Maternal characteristics of neonates with malformations (n = 21)

Mother's Profession	**n**	**Percentage (%)**
Housewife	12	57
Civil servants	5	24
Students	4	19
Parity		
Primiparae	8	38
Multiparous	6	29
Mother's medical background		
Hypertension	3	14
HIV Infection	2	10
Hemoglobinopathies	2	10
Asthma	1	5
Obstétrical ultrasound		
Done	13	62
Normal **(of done)**	11	85
Polyhydramnios **(of done)**	2	15
Antidiabetic treatment		
Insulin therapy	3	14
Oral antidiabetic	2	10
Diet alone	2	10

Table 2

Characteristics of neonates with malformations (n = 21)

Birth Characteristics		n	Percentage (%)
Female gender		5	24
Sex ratio	3,2		
Term of pregnancy at birth			
On term		19	90
Post-term		1	5
Premature		1	5
Birth weight			
Average weight	3600 ± 25g		
Extremes of weight	2350 to 5550g		
Low weight <2500 g)		1	5
Excessive weight (>4000 g)		8	38
Birth size			
Average height	51± 0,5 cm		
Extremes of height	46 to 61 cm		
Age at hospitalization			
Average Age	4 ± 1 days		
Extremes of age	1 - 21 days		
Delivery			
Low way		13	62
Eutocic Delivery		9	43
Dystocic childbirth		4	19
Dystocia of the shoulder		2	10
Paralysis of the plexus		2	10
Caesarean		8	38
Resuscitation at birth			
Apgar less than or equal to 3		0	0
Apgar between 4 and 6		3	14
Number of resuscitated newborns		3	14
Duration of the resuscitation		9,3 to 7,5 min	
Respiratory distress (according to Silverman score)		10	48%

Table 3

Distribution of congenital malformations (n = 21)

Types of heart malformations	Percentage (%)	Heart diseases (%)
	11	***52***	
Non-cyanogenic congenital heart disease	*9*	*43*	*82*
Arterial Canal	4	19	*36*
Interventricular Communication (CIV)	3	14	*27*
Atrial Communication (CIA)	1	5	*9*
Associated Form (CIA & CIV)	1	5	*9*
Cyanogenic congenital heart disease	*2*	*10*	*18*
Transposition of large vessels (TGV)	1	5	*9*
Pulmonary Stenosis	1	5	*9*
Nervous System	***7***	***33***	
Skeletal	***2***	***10***	
Kidney	***1***	***5***	
Genetics (Trisomy)	***1***	***5***	

DISCUSSION

Among diabetic women in the city of Ouagadougou, the incidence of neonatal malformations was 7, 7% which is comparable to the incidences reported by Lepercq [3] and Cheung [4]: with 7.2% and 9.2% respectively. In contrast, Baliutavicana [5] in her study without echo-cardiac exploration reported only an incidence of 1.6%

Diabetic mothers and pregnancy

Socio-economic situation

The average age of our diabetic mothers was 29 years and 25% were under 25 years old. In established diabetes it is advisable to anticipate pregnancy because of the scarcity of vascular lesions and fœto- maternal complications [6]. This argument, however, seems unimportant in our population which was poorly followed and where pregnancy is unlikely to have been planned according to maternal condition. The average age corresponds to our general population of pregnant women and is comparable to those found by Agarwal (30 years) [7] and Deslandes (31 years) [8]. In our study one third of the women were multiparous. In the Lefebure study [9], multiparity did not seem to be a factor favoring congenital malformations during gestational diabetes. On the other hand, an inverse link between the socio-economic situation and the prevalence of malformations of newborns has already been demonstrated [1] and the majority of our mothers had a low socio-economic level, considering that 76 % had no income.

Pregnancy follow-up

In our study, 62% of mothers were able to have obstetrical ultrasound follow-up and 2 of 14 (15%) had hydramnios. It is not possible to determine if this is a factor leading to obstetric consultation with ultrasound, but it is a considerable number. Other authors, Rachdi [13] and Luwawu [14] report similar figures with 18% and 20% respectively, and Maizi [15] 22% in Morocco. Hydramnios are more common in diabetic women, often reported between the 20th and the 26th week of amenorrhea and are correlated with the development of macrosomia, congenital malformations, and prematurity. It is considered to develop on fetal polyuria and is all the more common and abundant when diabetes is poorly balanced [10].

Only 5 out of 21 women with diabetes had treatment. Two women (9%) were taking oral antidiabetic drugs and 3

mothers (14%) undergoing insulin therapy

Delivery

The trigger rate and caesarean section are generally high in parturients with gestational diabetes treated or not. In our collective 8/21 (38%) women delivered by caesarean section, which is well above the national average of 20%. While the recommendations for clinical practice of the National College and Obstetricians French (CNGOF) [10] do not recommend a trigger or a caesarean section in cases of balanced gestational diabetes, the trigger remains recommended in case of complications and / or macrosomia; caesarean section is recommended in case of estimated fetal weight greater than 4500g [16].

In our collective, two thirds (13/21) women gave birth vaginally, close to the figures reported by Maizi [15] and Gandaho [17] in Morocco by 62% and 61% respectively. On the other hand, they remain lower than those of Deslande [8], Carlotti [18] and Rachidi [13] which are respectively 77%, 80% and 83%. It can be hypothesized that more regular monitoring of diabetic women can reduce the rate of caesareans.

In Morocco and France, where the cited studies come from, there is also a general increase in the frequency of cesarean section in diabetic parturients. It went from 38.2% in 2002 to 39.3% in 2009 in Morocco and from 20.8% to 23% in France, representing an increase of 2.17%. The reasons for increasing cesarean sections in gestational diabetes are multiple and difficult to analyze, since there is often a combination of objective reasons (stagnation of cervical dilatation, uncommitted and / or dystocic presentation, macrosomia) and subjective (lack of a priori belief of the obstetrical team about the chances of vaginal delivery in case of macrosomia, suspicion of foeto-pelvic disproportion) [19].

In Iran, however, this rate dropped by 8.5%, from 87.1% in 2005 to 78.6% in 2008 [4]. The introduction of triggering led to a reduction in caesarean section practice. It is recommended that these contraindications be avoided at 40 weeks of amenorrhea in the absence of complications, and 38 weeks of amenorrhea if the diabetes is poorly balanced or in the presence of pregnancy-induced hypertension or fetal macrosomia or hydramnios [13]. Excessive fetal growth is the second indication of triggering apart a disease trigger (fetal rhythm abnormality, Manning score, pregnancy HTA, and intrauterine growth retardation). Prolonged pregnancy is dangerous in diabetics as it leads to a higher risk of macrosomia and an increased rate of caesarean section.

Malformed newborns and their complications

Malformations

Our main goal was the description of neonatal malformations associated with diabetes during pregnancy. Heart malformations were the most common birth defects in our community and accounted for half of all malformations. Our data confirm the inverse association between congenital heart disease and maternal diabetes reported earlier for Burkina Faso [10]. The incidence of malformations of 12.9% (21/272) in the population of diabetic women in Ouagadougou is much higher than the incidence of malformations in the general population [10]. In our collective the reported death was of cardiac cause, but the small number of cases does not allow extensive conclusion. Cardiac malformations are two to three times more common in neonates of diabetic mothers [20].
They present the leading cause of death for these children with more than 50% attributable to this pathology [21]. Since cardiac malformations are supposed to develop before the 7th embryonic week, they would already be constituted at the time of the first obstetric consultation for a rule delay. Prevention of heart disease would therefore require a 'prenuptial' or public health intervention to detect young women with diabetes, which is still difficult to imagine in our Burkinabe population. Primary nutritional prevention is therefore at present a public health priority, especially for girls and women of childbearing age. Gestational diabetes is detected late, it would prevent complications, but not malformations. Interventricular communication was the dominant congenital heart disease in our series. It is usually the most common cardiac malformation, as already observed in several studies in Burkina Faso [11] and Togo [12], and the type of malformation does not seem specific to maternal diabetes.
The high number of patent arterial ducts is certainly due to the neonatal period. Some of these situations will likely normalize until the end of the first year of life [22]. Even excluding the arterial duct in malformations, 7/17 malformations remain of cardiac origin. The malformations of the central nervous system covered 7/21 found malformations and was the 2nd position as in the literature.

If we exclude the arterial duct (n = 4) and the anoxic-ischemic leuco-encephalopathies (n = 2) that could be established lesions at birth during difficult deliveries, we stay with 5/15 important in malformations.
Finally, the other malformations included skeletal lesions (2 cases) in 3rd rank [10] but it is difficult to pronounce on such a small number. We also found 1 case of trisomy 21 and a poly-malformative syndrome associating a cardiac malformation, central nervous system as well as skeletal.

Further neonatal complications

In our group of malformed children, postnatal complications were common. Macrosomia is common when diabetes is poorly balanced [20] with a frequency doubled compared to a normal pregnancy [13].
Macrosomia is common when diabetes is poorly balanced [20] with a frequency doubled compared to a normal pregnancy [13]. Its frequency during gestational diabetes in the literature is reported at 20% to 30% [10]. Our study that selects children with malformations finds an incidence of 8/21, or 40%, comparable to that of Gandaho (50%) [17] and Luwawu (60%) [14]. The differences can probably be explained by varying degrees of pregnancy monitoring and glycemic balances between parturients. In our series, a newborn was hypotrophic, and this low rate which is comparable to the works of Lefebure [9], Carlotti [18] and, Gandaho [17] with 4.7%, 5.3% and 3.6% respectively. Hypotrophy is correlated with vascular complications of diabetes, often type I more advanced, which was the case in our situation.

Prematurity was exceptional with only one case in our group, similar to that reported by Carlotti [18] (4.5%) and Rachdi (2%) [13]. This result is lower than other figures reported in the literature, closer to the general incidence of prematurity in Africa with 16.7% (Maizi) [15], 14.5% (Gandaho) [17] and 12.1% (Lefebure) [9]. Once again, a selection bias could explain our low figure, but it does not seem at least that diabetes during pregnancy significantly increases prematurity.

Neonatal respiratory distress is more common in neonates of diabetic mothers, probably related to a decrease in surfactant synthesis [22] [16] and amniotic fluid resorption. In our series, half (10/21) of newborns had a respiratory disorder, similar to that reported by Cheung (42.9%) [4] but much higher than that found by Rachdi (13.33%) [12] and Gandaho (10.9%) [6]. It is possible that this difference can be explained by a virtually non-existent maternal follow-up of the mothers in our group, at least as regards diabetes. Only 3 mothers received insulin and 4 additional dietary follow-up or with oral antidiabetic agents.

Moreover, the difference in caesarean section rates between different publications could also explain some of the discrepancies. Metabolic complications are related to fetal hyperinsulinemia, which itself depends on the degree of maternal metabolic control. In our study, half of malformed newborns (10/21) had hypoglycaemia. This incidence is very high in comparison with Rachdi [12] and Baliutavicienne [5] who report 5% and 11% respectively. This very frequent complication testifies to poor monitoring of blood glucose levels in our group and poor early neonatal care. Early management and improvement of maternal glycemic control during pregnancy may significantly reduce neonatal hypoglycaemia [5,6] and potentially the brain development of newborns. These interventions therefore have an important clinical target in our population.

Hypocalcemia is explained by increased needs of the child's macrosome [21], but is often asymptomatic. The very high incidence of 10/21 in our malformed newborns is probably a selection effect. The search for hypocalcemia was prompted by malformations. In addition, the reported rates are around 2.5% Rachdi [12].

Neonatal mortality

In our collective we have noted a death. Nevertheless, neonatal mortality remains a major concern for neonates of diabetic mothers. The reported rates are 7% in Tunisia [13], 10% in Morocco [17] and 9% in French overseas territories [9]. The low rate of our collective is probably due to the selection of newborn survivors.

CONCLUSION

Our study focused on diabetic mother's newborns who had a malformation. A selection bias that is difficult to avoid therefore follows and must be taken into account for interpretation. By extrapolating to the general population, our study showed an association with neonatal malformations and maternal diabetes during pregnancy. The most common malformations were in the heart and central nervous system. Our epidemiological data clarify a public health problem. Preventing fetal malformations requires a pre-conceptional intervention to avoid conditions of obesity favoring diabetes and gestational diabetes; it therefore

particularly concerns the nutrition of girls and women. To prevent neonatal complications, it would be necessary to detect and treat glucose intolerance as early as possible during the current pregnancy. The health of future newborns therefore depends on young girls today.

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