

# Neonatal complications of diabetes in pregnancy: Study of 393 cases

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## RÉSUMÉ

Le diabète chez les femmes enceintes constitue une situation à haut risque tant pour la mère que pour le fœtus. Malgré les progrès de la néonatalogie, la morbidité néonatale demeure élevée. Nous avons mené une étude rétrospective descriptive sur une période de 8 mois (janvier-août 2020) au centre de maternité de Bizerte en Tunisie, incluant les nouveau-nés issus de grossesses diabétiques (diabète avant la grossesse ou gestationnel).

L'objectif était de préciser l'incidence des complications néonatales des grossesses associées au diabète. Dans cette étude, 393 nouveau-nés et 388 mères diabétiques ont été inclus. La prévalence du diabète pendant la grossesse était de 19,06%. Le diabète gestationnel était le type le plus fréquent, représentant 16,81% des naissances, et il a été diagnostiqué à temps selon les recommandations dans 67,3% des cas. Des anomalies à l'échographie obstétricale ont été observées dans 10,3% des grossesses. Les infections vaginales et les infections des voies urinaires étaient fréquentes chez les mères diabétiques, avec des taux respectifs de 19,8% et 9,1%. La plupart des accouchements étaient à terme. La prévalence de la prématurité était 9,4%. Les nouveau-nés de mères diabétiques avaient un poids moyen de 3386,84 g, dont 19% étaient hypertrophiques et 4,83% hypotrophiques. Les morbidités courantes chez ces nouveau-nés comprenaient une détresse respiratoire transitoire (52,6%) et une infection bactérienne néonatale précoce (42,1%). Des malformations congénitales étaient présentes dans 7,6% des cas. Des traumatismes obstétricaux sont survenus dans 10,9% des cas. L'hospitalisation des nouveau-nés a été nécessaire pour 33,3%, principalement en raison de la détresse respiratoire néonatale. La durée moyenne de séjour à l'hôpital était de 4 jours. Un seul décès a été enregistré dans la population étudiée.

Le diabète pendant la grossesse augmente le risque de morbidité néonatale, principalement la détresse respiratoire, les malformations congénitales, les traumatismes obstétricaux et les troubles métaboliques. Pour minimiser ces risques, une meilleure gestion de la grossesse, un dépistage efficace et une prise en charge adéquate du diabète gestationnel sont essentiels pour réduire la morbidité néonatale.

## ABSTRACT

Diabetes in pregnant women is a high-risk situation for both mother and fetus. Despite improved management, neonatal morbidity remains very high. We conducted a retrospective descriptive study during 8 months (January- August 2020) in the maternity center of Bizerta in Tunisia, including newborns from diabetic pregnancies (pre-gestational or gestational diabetes). The main objective was to focus on the incidence of complications during diabetes-associated pregnancies. In this study, 393 newborns and 388 diabetic mothers were included. The prevalence of diabetes during pregnancy was 19.06%. Gestational diabetes was the most common type, representing 16.81% of births, and it was timely diagnosed in 67.3% of cases. Obstetrical ultrasound abnormalities were found in 10.3% of pregnancies. Vaginal infections and urinary tract infections were prevalent in diabetic mothers, at 19.8% and 9.1%, respectively. Most pregnancies reached full term, with a 9.4% prevalence of prematurity. Newborns of diabetic mothers had an average weight of 3386.84 g, with 19% being hypertrophic and 4.83% hypotrophic. Common morbidities in these newborns included transient respiratory distress (52.6%) and early neonatal bacterial infection (42.1%). Congenital malformations were present in 7.6% of cases. Obstetric trauma occurred in 10.9% of cases. Newborn's hospitalization was needed for 33.3%, mainly due to neonatal respiratory distress. The average hospital stay was 4 days, and there was one recorded death in the study population.

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Diabetes during pregnancy increases the risk of various neonatal problems, including respiratory distress, congenital issues, trauma during childbirth, and metabolic disorders. To minimize these risks, improved pregnancy management, effective screening, and proper gestational diabetes management are crucial for reducing neonatal morbidity.

**Key words:** newborn, diabetes, gestational diabetes, morbidity, mortality.

## Introduction

The International Diabetes Federation (IDF) estimates that 21.8% of women aged between 20 and 49 in the MENA (Middle East and North Africa) region have hyperglycemia during pregnancy [1].

The incidence of fetal and neonatal morbidity and mortality increases in the presence of diabetes during pregnancy [2]. These complications are variously described within literature. Nevertheless, in Tunisia, limited studies have been conducted to elucidating these particular complications.

The aim of our study was to precise the incidence of neonatal morbidity and mortality during diabetes-associated pregnancies in the maternity center of the Habib Bougatfa University Hospital in Bizerte (MCB), Tunisia.

## Methods

A retrospective study over 8 months (January -August 2020) at MCB, which was type 2A maternity at the time of the study. We included newborns of diabetic mothers, born at MCB or transferred from another medical center during the first 48 hours of life. Diabetic mothers were women with pre gestational or gestational diabetes. We have adopted the criteria of the International Association of Diabetes and Pregnancy Study Group (IADPSG) [3] and the American Diabetes Association 2021 (ADA) [4] to diagnose gestational diabetes.

We did not include the babies whose mothers had, in addition to diabetes, other chronic diseases that could have an impact on the pregnancy and fetus, such as arterial hypertension, hypothyroidism, severe heart disease, progressive renal or hepatic disease, psychiatric or neurological pathology, or a progressive inflammatory or infectious disease. Data were collected from post-partum charts and newborn hospitalization records.

## Results

A total of 393 newborns and 388 diabetic mothers were included in the study. The prevalence of diabetes during pregnancy was 19.06 %. The mean age of the mothers was 31 years and 7 months (extremes 20-48 years). Gestational diabetes was the most frequent type of diabetes. It represented 16.81% of the total number of women who have given birth during the study period, and 96% of diabetic ones. Gestational diabetes was diagnosed on time according to ADA recommendations in 67.3%

of cases (252 mothers). For the remaining cases (122 mothers), it was diagnosed late by fasting blood glucose tests. When gestational diabetes was diagnosed during the second trimester of pregnancy, 95.63% of the mothers were put only on dietary measures. The association with insulin was necessary in 4,36% of cases. No preconception programming was carried out for mothers known to be diabetic prior to pregnancy. Obstetrical ultrasound abnormalities were found in 10.3% of cases. Morphological ultrasound was performed in 36.59% of pregnancies. It was pathological in 8.45% women. The antenatal malformations diagnosed were congenital malformations were pyelocaval dilatation in 2.8% of cases and esophageal atresia in one case.

The prevalence of vaginal infection and urinary tract infection among diabetic mothers was 19.8% and 9.1% respectively.

The majority of pregnancies were carried to term, and the prevalence of prematurity was 9.4%. The mean term of delivery was 39 weeks of amenorrhea. The upper delivery route was the most frequent (57%). Instrumental vaginal delivery was indicated in 2% of cases. Indications for cesarean delivery are displayed in Table 1.

**Table 1 :** The different indications for cesarean delivery

| <b>Indication</b>                                     | <b>Number</b> | <b>Percentage</b> |
|---|---------------|-------------------|
| <b>Acute fetal distress</b>                           | 101           | 45,3%             |
| <b>Biscarred uterus</b>                               | 63            | 28,3%             |
| <b>Seat presentation</b>                              | 19            | 8,5%              |
| <b>Transverse presentation</b>                        | 8             | 3,6%              |
| <b>Macrosomia</b>                                     | 14            | 6,3%              |
| <b>Preeclampsia</b>                                   | 8             | 3,6%              |
| <b>Failure to engage</b>                              | 5             | 2,2%              |
| <b>Placenta previa</b>                                | 3             | 1,3%              |
| <b>High myopia</b>                                    | 1             | 0,4%              |
| <b>Elderly primipara who refuses vaginal delivery</b> | 1             | 0,4%              |
| <b>Total</b>  | 223           | 100%              |

Poor adaptation to extrauterine life was noted in 1.28% of cases. The mean weight of newborns of diabetic mothers (NBDM) was 3386.84 g. NBDM were hypertrophic compared to their birth term in 19% of cases, and hypo trophic in 4.83%. The other morbidities diagnosed are shown in Table 2.

**Table 2:** The different morbid states in newborns of diabetic mothers

| <u>Morbid state</u>                             | <u>Diabetic mothers' newborns</u> |
|---|-----------------------------------|
| <u>Neonatal respiratory distress</u>            | <b>76(19,30%)</b>                 |
| <u>Neonatal jaundice</u>                        | <b>53(13,50%)</b>                 |
| <u>Polyglobulia</u>                             | <b>79(20,10%)</b>                 |
| <u>Congenital malformation</u>                  | <b>30(7,60%)</b>                  |
| <u>Obstetrical trauma</u>                       | <b>43(10,90%)</b>                 |
| <u>Early-onset neonatal bacterial infection</u> | <b>57(14,50%)</b>                 |
| <u>Hypoglycemia</u>                             | <b>35(8,90%)</b>                  |
| <u>Hypocalcemia</u>                             | <b>12(3,10%)</b>                  |
| <u>Hypotonia</u>                                | <b>4(1%)</b>                      |
| <u>Convulsion</u>                               | <b>1(0,30%)</b>                   |

Transient respiratory distress (52.6%) and early neonatal bacterial infection (42.1%) were the most common causes of respiratory distress in NBDM. At birth, a congenital malformation was found in 7.6% of cases. The different types of congenital malformations in our population are summarized in Table 3.

**Table 3 :** Frequency and type of congenital malformations in newborns of diabetic mothers

| <u>Malformation type</u>  | <u>Frequency and percentage</u> | <u>Clinical signs</u>   |
|---|---------------------------------|---|
| <u>Urogenital</u>   | 10(2,54%)                       | - Hypospadias (6 newborns)<br>- Bent penis (1 newborn)<br>- Pyloric ectasia (3 newborns)  |
| <u>Musculoskeletal</u>  | 7(1,78%)                        | - Clubfoot (4 newborns)<br>- Craniosynostosis (1 newborn)<br>- Tongue lock (2 newborns)   |
| <u>Cardiac</u>  | 4(1,02%)                        | - Ventricular septal defect (4 newborns)  |
| <u>Vascular</u>   | 4(1,02%)                        | - Angioma (4 newborns)  |
| <u>Poly malformative syndrome and chromosomal abnormalities</u> | 4(1,02%)                        | - Goldenhar syndrome + ventricular septal defect (1 newborn)<br>- Holt-Oram syndrome + pyloric dilatation (1 newborn)<br>- Pyloric dilatation + bilateral hexadactyly + angioma (1 newborn)<br>- Trisomy 21 (1 newborn) |
| <u>Digestive</u>  | 1(0,25%)                        | - Esophageal atresia (1 newborn)  |

Obstetric trauma (10.9%) was severe in 3.1% of cases. Hospitalization was indicated in 33.3% of cases. The main cause for hospitalization was neonatal respiratory distress. The remaining causes are summarized in Table 4.

**Table 4 :** Frequency and percentage of the hospitalization causes in newborns of diabetic mothers

| <u>The hospitalization cause</u>     | <u>Frequency</u> | <u>Pourcentage</u> |
|--------------------------------------|------------------|--------------------|
| <u>Neonatal respiratory distress</u> | 76               | 58%                |
| <u>Heel blood glucose monitoring</u> | 29               | 22,1%              |
| <u>Neonatal jaundice</u>             | 18               | 13,7%              |
| <u>Hypoglycemia</u>                  | 5                | 3,8%               |
| <u>Prematurity</u>                   | 3                | 2,3%               |
| <b>Total</b>                         | <b>131</b>       | <b>100%</b>        |

The average length of hospital stay was 4 days. Only one death was recorded in our study population.

## Discussion

Diabetes during pregnancy is a real public health problem. Its incidence is significantly increasing these days due to obesity and type 2 diabetes. Nearly 3 to 10% of pregnancies are complicated by a glycemic regulation disorder [4]. In our series, its frequency during pregnancy was estimated at 19.06 % which is much higher than those reported in the study of Firouzeh and Mahdaviani [5] in Iran in 2004, and KayMcfarland and Ezzat [6] in the United States in 1985 (2.6%).

For diabetic pregnancies, the mothers' most common obstetrical antecedents are macrosomia, spontaneous miscarriage and prematurity, which were evaluated respectively at 25.7%, 23% and 8.1% in a study conducted in Bamako (7), 42%, 24% and 8% in a study conducted in Marrakech (8) and 22.7%, 22.7% and 14.9% in our study.

The simultaneous presence of diabetes and pre-eclampsia during pregnancy increases the risk of maternal-fetal complications and requires adequate management [9]. In our study, the coexistence of toxemia gravidarum with diabetes during pregnancy was found in 17% of cases. This rate was high compared to 6.2% at the Mayotte hospital [10], 7.4% in Bamako [11] and 12.8% in Tunisia [12], but lower than the 23.76% rate in Tlemcen [13].

The main embryonic anomalies detected on antenatal ultrasound are : macrosomia, hydramnios, abortion, in utero fetal death and congenital malformations, with variable prevalence in the literature [11,12,14].

According to the literature, the main risk factors for gestational diabetes are : overweight, maternal age greater than or equal to 35 at the time of pregnancy, first-degree family history of type 2 diabetes, personal history of gestational diabetes and personal history of fetal macrosomia [15-18].

First treatment of gestational diabetes is dietary therapy. Insulin was the preferred hypoglycemic treatment in cases of poor control by dietary therapies [16,19]. In our study, glycemic control in gestational diabetes was achieved by dietary measures in 95,63% of cases. For pregestational diabetes,

oral antidiabetics do not have marketing authorization during pregnancy [20].

In cases of diabetes associated with pregnancy, the high route is the preferred method of delivery, with an estimated frequency of 56.7% in our study, 68% in the Dhouibi series [12] and 78.9% in the Ashour et al. series [21]. The lower prevalence of vaginal deliveries in diabetes can be explained by the interventionist attitude of obstetricians, the high frequency of previous caesarean deliveries and the high frequency of fetal macrosomia [22, 23]. Macrosomia is one of the most frequent complications of diabetes in pregnancy [24].

Maternal hyperglycemia during pregnancy causes fetal hyperglycemia, resulting in hyperinsulinemia. This extra glucose in the fetus is stored as body fat [25]. A study of 17,094 mothers and infants in 15 centers in 9 countries conducted by Metzger et al. showed a linear correlation between maternal blood glucose levels, fetal hyperinsulinism, and birth weight above the 90th percentile [26]. Moreover, lipid concentrations in pregnant diabetic mothers (especially triglycerides) were found to be strongly correlated with fetal growth [27].

The prevalence of macrosomia in our study was higher than the prevalence reported by Dhouibi et al (15.5%) [8], Moumen et al (14%) [16] and Christophe Olivesi (5.2%) [17], but lower than Boiro et al. (29.29%) [2] and Drabo et al (48.4%) [7].

Newborns of diabetic mothers are generally more likely to develop neonatal respiratory distress due to premature birth, surfactant maturation abnormalities and caesarean section births, which increase the risk of respiratory distress through delayed resorption of pulmonary fluid [24,28,29].

As for metabolic complications, the high frequency of hypoglycemia in NBDM is explained by transient hyperinsulinism that hinders the adaptive mechanisms initiated at birth to regulate blood sugar according to the prandial state [30].

Its prevalence in our study (8.9%) was lower compared to the prevalence reported in the study of Al-Nemri et al (11.8%) [31], but higher compared to the prevalence reported by Drabo et al (6.1%) [7]. The mechanism of hypocalcemia in the NBDM is not completely clarified and appears to be related to functional hypoparathyroidism [32].

In our study, hypocalcemia was found in 3.10% of NBDMs. Our results were similar to those of Mounhil et al [8], Boiro et al. [2] and Tshiala Fany [33], with a prevalence of 2.32%, 3.03% and 2.86% respectively.

According to the literature, both pre-gestational and gestational diabetes increase the risk of congenital anomalies [34-36].

Fetal exposure to hyperglycemia in early pregnancy may contribute to increased oxidative stress. This leads to high levels of fetal cells apoptosis, increasing the risk of malformation. In addition, deficient activity of the transcription factor involved in defense mechanisms against oxidative stress (ALX3)

may increase the risk of congenital anomalies due to maternal hyperglycemia [37].

Obstetric trauma is generally attributed to macrosomia, notably shoulder dystocia [24,35]. Its incidence varies from 0.2% to 2.8% in the general population. It can even reach a rate of 9% in diabetic pregnancies. The risk increases with the child's weight; however, for the same weight, the frequency of shoulder dystocia is multiplied by 2 in macrosomia born to diabetic mothers, due to the increase in thoracic volume and biacromial diameter, explaining the high frequency of brachial plexus elongation [38].

## Conclusion

Diabetes during pregnancy is a high-risk situation for the newborn. Respiratory distress, congenital malformations, obstetric trauma, metabolic and hematological disorders are the main neonatal morbidities associated with this pregnancy. Great efforts are needed to better conduct pregnancy programming in diabetic mothers, screening and management of gestational diabetes during pregnancy to reduce the risk of neonatal morbidity.

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## Conflicts of interest

No conflict of interest to declare

## References

- [1] Fédération internationale du diabète. Atlas du diabète de la FID. 10<sup>ème</sup> ed. Bruxelles: 2021.
- [2] Boiro D, Guéye M, Seck N, Ndongo AA, Thiongane A, Niang B, et al. Les nouveau-nés de mère diabétique au service de néonatalogie du chu de Dakar (Sénégal). *J Pediatr Pueric*. 2017;30(4):150-5.
- [3] E. Wery, A. Vambergue, F. Le Goueff, D. Vincent, P. Deruelle. Impact des nouveaux critères de dépistage sur la prévalence du diabète gestationnel. *J Gynecol Obstet Biol Reprod*. 2014;43(4):307-13.
- [4] Classification and Diagnosis of Diabetes: Standards of medical care in diabetes-2021. *Diabetes Care*. 2021;1:44:S15-33.
- [5] N. Firouzeh N, A. Mahdaviyani,. Comparison of morbidities between infants of pregestational and gestational diabetic mothers. *MJIRI*. 2004;18(1):9-13.
- [6] KF. McFarland, E. Hemaya. Neonatal Mortality in Infants of Diabetic Mothers. *Diabetes Care*. 1985;1:8(4):333-6.
- [7] AM. Drabo. Diabète et grossesse dans le csref de la commune [Bamako]: Université des Sciences des Techniques et des Technologies de Bamako; 2019.

- [ 8 ] N. Moumhil. Diabète et grossesse: à propos de 50 cas . [Marrakech]: Université Cadi Ayyad faculté de médecine et de pharmacie Marrakech; 2013.
- [ 9 ] D. Gordin, C. Forsblom, PH Groop, K. Teramo, R. Kaaja. Risk factors of hypertensive pregnancies in women with diabetes and the influence on their future life. *Ann Med.* 2014;21:46(7):498–502.
- [ 10 ] C. Olivesi. Diabète et grossesse à Mayotte: étude d'une cohorte de 178 grossesses compliquées d'un diabète . [Bordeaux]: Université Bordeaux 2; 2016. .
- [ 11 ] Z. DaoSeydou, A. Demebele, B. Traore, S. Konate, K. Sidibe, M. Minkailou, D.Dao S et al. Diabète et grossesse au centre de santé de référence de la commune II de Bamako, Mali. *Remapath.* 2019;19–23.
- [ 12 ] N. Dhouibi. Morbi-mortalité des nouveaux-nés de mères diabétiques . Faculté de médecine de Tunis; 2019.
- [ 13 ] H. Senouci H. Nouveau né de mère diabétique [mémoire : médecine]. Tlemcen; 2017.
- [ 14 ] F. Dilmi. Complications Sanitaires et nutritionnelles des nouveau-nés de mères diabétiques. [Algérie]; 2021.
- [ 15 ] Texte des recommandations. *J Gynecol Obstet Biol Reprod.* 2010;39(8):338–42.
- [ 16 ] Haute Autorité de Santé. Rapport de synthèse sur le dépistage et le diagnostic du diabète gestationnel. 2005 Jul.
- [ 17 ] K. Amazian , I. Ouahidi, A. Housni. Dépistage du diabète gestationnel : étude descriptive transversale dans des centres de santé marocains. *Revue Francophone Internationale de Recherche Infirmière.* 2018 Mar;4(1):64–70.
- [ 18 ] A. Vambergue, AS. Valat, P. Dufour, M. Cazaubiel, P. Fontaine, F. Puech. Pathophysiology of gestational diabetes. *J Gynecol Obstet Biol Reprod (Paris).* 2002;31(6 Suppl):4S3–10.
- [ 19 ] F. Mosora. Étude INDAO : comparaison de l'effet du glyburide et de l'insuline sous-cutanée sur les complications périnatales lors du traitement du diabète gestationnel. . *Pharmactuel .* 2019;52(4):201.
- [ 20 ] E. Fougere. Le diabète gestationnel. *Actualités Pharmaceutiques.* 2019;58(586):57–9.
- [ 21 ] A. Salima, A. Moktar, J. Hanan, A.B. Bashir. Study on Infants of Diabetic Mothers in Neonatal Intensive Care Unit of Misurata Teaching Hospital –Libya/2015. *Research in Pediatrics & Neonatology.* 2018;(5):29–1.
- [ 22 ] A. Fournié, J.-F. Le Digabel, F. Biquard,, C. Vas seur, P. Gillard, P. Descamps. Les indications obstétricales dans le diabète gestationnel : déclencher ou ne pas déclencher. *Journal de gynécologie obstétrique et biologie de la reproduction.* 2002;31(6):4S21–9.
- [ 23 ] DJ. Rouse, J. Owen. Prophylactic cesarean delivery for fetal macrosomia diagnosed by means of ultrasonography-A Faustian bargain? *Am J Obstet Gynecol.* 1999;181(2):332–8.
- [ 24 ] M. Saint-Faust, U. Simeoni. Devenir des enfants nés de mère diabétique. *Médecine des Maladies Métaboliques.* 2012;6(4):300–4.
- [ 25 ] KC.Kamana, S. Shakya, H. Zhang. Gestational Diabetes Mellitus and Macrosomia: A Literature Review. *Ann Nutr Metab.* 2015;66(Suppl. 2):14–20.
- [ 26 ] BE. Metzger, B. Persson, LP. Lowe, AR. Dyer, JK. Cruickshank C., Deerochanawong et al. Hyperglycemia and Adverse Pregnancy Outcome Study: Neonatal Glycemia. *Pediatrics.* 2010;1:126(6):e1545–52.
- [ 27 ] KWhyte, H. Kelly, V. O'Dwyer, M. Gibbs, A. O'Higgins, MJ. Turner. Offspring birth weight and maternal fasting lipids in women screened for gestational diabetes mellitus (GDM). *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2013;170(1):67–70.
- [ 28 ] Y. Li, W. Wang, D. Zhang. Maternal diabetes mellitus and risk of neonatal respiratory distress syndrome: a meta-analysis. *Acta Diabetol.* 2019;56(7):729–40.
- [ 29 ] D. Mitanchez. Complications foetales et néonatales du diagnostic gestationnel : mortalité périnatale, malformations congénitales, macrosomie, dystocie des épaules, traumatisme obstétrical, complications néonatales. *J Gynecol Obstet Biol Reprod (Paris).* 2010;39(8):S189–99.
- [ 30 ] E. Motte-Signoret. Hypoglycémie néonatale. *Perfectionnement en Pédiatrie.* 2018;1(1):48–54.
- [ 31 ] AM. Al-Nemri, F. Alsohime, AH. Shaik, GA. El-His si, MI. Al-Agha, NF. Al-Abdulkarim, et al. Perinatal and neonatal morbidity among infants of diabetic mothers at a university hospital in Central Saudi Arabia. *Saudi Med J.* 2018;39(6):592–7.
- [ 32 ] RC. Tsang, IW. Chen, MA. Friedman, M. Gigger, J Steichen, H. Koffler, et al. Parathyroid function in infants of diabetic mothers. *J Pediatr.* 1975;86(3):399–404.
- [ 33 ] F. Tshiala. Hypocalcémie chez les nouveau-nés à terme de mère diabétique : étude observationnelle rétrospective à l'hôpital de la mère et de l'enfant de Limoges. [Limoges]; 2017.
- [ 34 ] R. Gabbay-Benziv. Birth defects in pregestational diabetes: Defect range, glycemic threshold and pathogenesis. *World J Diabetes.* 2015;6(3):481.
- [ 28 ] D. Mitanchez. Foetal and neonatal complications in gestational diabetes: perinatal mortality,

congenital malformations, macrosomia, shoulder dystocia, birth injuries, neonatal complications. *Diabetes Metab.* 2010;36(6):617-27.

- [ 36 ] O. Lajili, Y. Htira, A. Temessek, I. Hedfi, S. Ben Amara, F. Ben Mami. Incidence of maternal and fetal outcomes in women with gestational diabetes. *Tunis Med.* 2022;100(3):241-6.
- [ 37 ] P. García-Sanz, M. Mirasierra, R. Moratalla, M. Vallejo. Embryonic defence mechanisms against glucose-dependent oxidative stress require enhanced expression of Alx3 to prevent malformations during diabetic pregnancy. *Sci Rep.* 2017;24:7(1):389.
- [ 38 ] I. Jordan, P. Audra, G. Putet. Nouveau-nés de mère diabétique. *EMC - Pédiatrie - Maladies infectieuses.* 2007;2(2):1-20.