Dicle Tıp Dergisi / Dicle Med J (2023) 50 (4) : 439-446

www.diclemedj.org

Original Article / Özgün Araştırma

Comparison of Perinatal Complications in Macrosomic İnfants of Diabetic and Nondiabetic Mothers

Akan Yaman[1], Ibrahim Kandemir[2], Zeynep Alp Unkar[3], Sinem Gulcan Kersin[4], Mehmet Tolga Kole[5], Hulya Bilgen[6], Eren Ozek[7]

1 Nisantasi University, Faculty of Medicine, Department of Pediatrics, Division of Neonatalogy, Istanbul, Turkey

2 Biruni University, Faculty of Medicine, Department of Pediatrics, Istanbul, Turkey

3 Istanbul University, Cerrahpasa Faculty of Medicine, Department of Pediatrics, Division of Neonatology, Istanbul Turkey

4 Marmara University, Faculty of Medicine, Department of pediatrics, Division of Neonatalogy, Istanbul, Turkey

5 University of Health Science, Kartal Dr. Lutfi Kirdar City Hospital, Department of Pediatrics, Istanbul, Turkey

6 Marmara University, Faculty of Medicine, Department of pediatrics, Division of Neonatalogy, Istanbul, Turkey

7 Marmara University, Faculty of Medicine, Department of pediatrics, Division of Neonatalogy, Istanbul, Turkey

Received: 11.05.2023; Revised: 03.11.2023; Accepted: 13.11.2023

Abstract

Introduction: Metabolic, congenital disorders, and complications seen in infants of diabetic mothers (IDM) are well defined in the literature. We aimed to compare perinatal problems in macrosomic IDM and infants of mothers without diabetes.

Methods: We included all macrosomic infants admitted to neonatal intensive care unit (NICU) at two centers between 2017-2020. Birth history, anthropometric measurements, gestational age, metabolic and cardiac problems were compared between macrosomic IDMs and infants of non-DMs. The p-value less than 0.05 was considered statistically significant.

Results: 156 (37 IDM, and 119 non-IDM) macrosomic newborns were included in the study. While the incidence of hypoglycemia, need for mechanical ventilation, respiratory distress syndrome, ventricular septal defect (VSD) and persistent pulmonary hypertension (PPH) were statistically similar, the incidence of cesarean section (p=0.002), myocardial hypertrophy (p=0.001), and polycythemia (p=0.019) was higher in the IDM group. While the incidence of respiratory problems and VSD was similar in both groups, myocardial hypertrophy was found in approximately in one fourth (22.2%) of the non-diabetic group.

Conclusion: Macrosomic non-IDMs have a similar risk for perinatal-postnatal complications as macrosomic IDMs and should be evaluated accordingly.

Keywords: Infant of diabetic mother; Macrosomia; Macrosomic infant; Newborn; Persistent Pulmonary Hypertension

DOI: 10.5798/dicletip.1411481

Correspondence / Yazışma Adresi: *Mehmet Tolga Kole, 5 University of Health Science, Kartal Dr. Lutfi Kirdar City Hospital, Department of Pediatrics, Istanbul, Turkey e-mail: mehmet_tolga@hotmail.com*

Diyabetik ve diyabetik olmayan annelerin makrozomik bebeklerinde perinatal komplikasyonların karşılaştırılması

Öz

Giriş ve Amaç: Diyabetik annelerin bebeklerinde (DAB) görülen metabolik, konjenital bozukluklar ve komplikasyonlar literatürde iyi tanımlanmıştır. Diyabetik ve non-diyabetik annelerden doğan makrozomik bebeklerde görülen perinatal komplikasyonların karşılaştırılması amaçlanmıştır.

Yöntemler: Yenidoğan yoğun bakım ünitesine (YYBÜ) 2017-2020 yılları arasında iki merkezde başvuran tüm makrozomik bebekleri dahil ettik. Makrozomik DAB' ler ile DAB olmayan bebekler arasında doğum öyküsü, antropometrik ölçümler, gebelik yaşı, metabolik ve kardiyak problemler karşılaştırıldı. 0.05'in altındaki p değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular: Çalışmaya 156 (37 DAB ve 119 DAB dışı) makrozomik yenidoğan dahil edildi. Hipoglisemi, mekanik ventilasyon ihtiyacı, solunum sıkıntısı sendromu, ventriküler septal defekt (VSD) ve persistan pulmoner hipertansiyon insidansı istatistiksel olarak benzer iken, DAB'de sezaryen (p=0.002), miyokardial hipertrofi (p=0.001) ve polisitemi (p=0.019) insidansı daha yüksekti. Solunum problemleri ve VSD insidansı her iki grupta da benzer iken, hipertrofik kardiyomiyopati diyabetik olmayan grubun yaklaşık dörtte birinde (% 22.2) bulundu.

Sonuç: Makrozomik non-IDM'ler, makrozomik IDM'ler ile benzer perinatal-postnatal komplikasyon riskine sahiptir ve buna göre değerlendirilmelidir.

Anahtar kelimeler: Diyabetik anne bebeği; Makrozomi; Makrozomik bebek; Yenidoğan; Persistan Pulmoner Hipertansiyon.

INTRODUCTION

Fetal macrosomia is a clinical condition defined for babies born more than 4000 grams and is not the same for the terminology of large for gestational age (LGA), which represents babies with a birth weight of more than 90 percent[1]. Incidence of fetal macrosomia is reported to be 9% worldwide, 6% in Turkey and 1-5% in developing countries[2,3].

Fetal macrosomia increases the risk of complications such as shoulder dystocia, brachial plexus injury, and clavicle fracture in newborns, as well as high cesarean section rate[4-6]. In addition, respiratory distress, need for mechanical ventilation, meconium aspiration syndrome, neonatal mortality and 5th minute low APGAR score are more common in macrosomic newborns[5].

Gestational diabetes occurs as a result of insulin resistance during the pregnancy of a non-diabetic woman 7, and gestational diabetes increases with advanced age and body mass index[8]. Complications and outcomes of infants of diabetic mothers (IDM) are well described in the literature. Cardiovascular system (ventricular septal defect, myocardial hypertrophy, transposition of great vessels, patent ductus arteriosus, coarctation of aorta), central nervous system (neural tube defects, anencephaly), gastrointestinal system (anal atresia, duodenal atresia, small left colon), genitourinary system (renal agenesis, pelviectasis, ureteral duplication) defects may occur[9,10]. 15-45% of pregnancies of diabetic mothers may result in fetal macrosomia[11]. In non-diabetic pregnants, ethnic origin of the mother, birth weight of the mother above 4000 g, mother's height above the 80th percentile, maternal obesity, hypertriglyceridemia, excessive weight gain during pregnancy, multiparity are risk factors for fetal macrosomia. In addition, male gender, syndromes such as Beckwith-Wiedemann, Weaver or Sotos have been identified as risk factors for fetal macrosomia[12].

In this study, we aimed to compare perinatal, postnatal and metabolic outcomes in macrosomic IDMs and non-IDMs treated in the neonatal intensive care unit (NICU).

METHODS

We included all macrosomic-born infants treated in the NICU at two centers between 2017-2020. This study was approved by the Marmara University Faculty of Medicine ethics committee on 11.02.2022 with the decision number 09.2022.274. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Healthy macrosomic newborns followed up with the mothers after delivery were excluded in both centers. Diabetes was defined as an HbA1C level of 6.5% or higher that the mother had during her pregnancy. Demographic characteristics, anthropometric measurements (length, weight, head circumference, and standard deviations according to Fenton intrauterine growth curve), weight, length and head circumference Z-scores and antepartum medical history were all recorded. Respiratory status (any respiratory problem; need for invasive ventilation, respiratory distress syndrome), echo-cardiographic features (ventricular septal defect, myocardial hypertrophy, pulmonary hypertension, patent ductus arteriosus), metabolic problems (hypoglycemia, hypocalcemia, polycythemia), birth injury (Erb-Duchenne paralysis, clavicle and vertebral fracture, cephalohematoma, caput succedaneum) and perinatal asphyxia were evaluated.

Statistics

We used the open-source R-based JAMOVI 1.6.1 statistical package program for statistical calculations. Descriptive results for continuous data were presented as median (25-75th percentile) and mean±standard deviation for non-normal and normal distributed data. We used the Mann-Whitney U test and Student's t-test to compare two non-normal distributed and normally distributed independent groups, the Chi-square test and Fisher's exact test for comparing categorical variables. A p-value less than 0.05 was considered statistically significant.

RESULTS

We included 108 male (69.2%) and 48 female (30.8%) infants in our study. Median gestational week at birth was 39 (38-40) weeks, and the delivery route of the 64.5% (n=100) of the study population was a cesarean section. 23.7% (n=37) of the patients were IDMs, and 76.3% of them (n=119) did not have diabetes mellitus. We assessed all the newborns for anthropometric measurements (birth length, weight, head circumference, and standard deviations according to Fenton intrauterine growth curve), birth injuries (Erb-Duchenne, clavicle and vertebral fracture, cephalohematoma), and history of perinatal asphyxia. The descriptive characteristics of the patients were shown in Table I.

Table I: Perinatal features of macrosomic infants comparing IDM and non-IDM in NICU

	Total	IDM	Non-IDM	p
Gender	69.2% (n=108) male 30.8% (n=48) female	59,5% (n=22) male 40,5% (n=15) female	72.3% (n=86) male 27.7% (n=33) female	0,14**
Gestational week at birth	39(38-40)	38.3±1.22	39.4(38.1-40)	**<0,001***
Delivery type	63.6% (n=100) C/S 36.4% (n=55) NSD	86.1% (n=31) C/S 13.9% (n=5) NSD	58.0% (n=69) C/S 42.0% (n=50) NSD	0,002**
Birth weight	4200 (4070-4433)	4250 (410-4540)	4180 (4065-4390)	0,068*
Birth weight z-score	1.82 (1.36-2.26)	2.36±0.82	1.67±0.642	**0,018****
Birth length	53 (52-54)	52.9±1.53	53 (52-54)	0,664*
Birth length z-score	1.21±0.848	1.49±0.804	1.12±0.845	**0.018****
Head circumference	37 (36-37)	37(36-37)	37 (36-37)	0.312*
Head circumference z-score	1.41 (1-2.03)	1.85±1.06	1.38 (0.93-1.99)	**0.032***
Meconium stained amniotic fluid	12.2% (n=19)	8.1% (n=3)	13.4% (n=16)	0.386**

**Mann-Whitney U test, **Chi-square test, ***Fisher's exact test, ****Student's t test*

C/S: cesarean section, NSD: normal spontaneous delivery

We evaluated all patients for maternal diabetes history, respiratory problems (respiratory failure, need for invasive ventilation, respiratory distress syndrome), echo-cardiographic features (ventricular septal defect, myocardial hypertrophy, pulmonary hypertension), and metabolic problems (hypoglycemia, hypocalcemia, polycythemia). The IDMs were born significantly at a lower gestational week than the non-IDMs. Birth height and head circumference z-scores, the incidences of cesarean section, hypoglycemia, polycythemia, myocardial hypertrophy were significantly higher in the IDMs (Table 2).

Table II: Postnatal traumatic, metabolic, cardiac and congenital problems of macrosomic infants comparing IDM and non-IDM in NICU.

	Total	IDM	Non-IDM	p
Birth injury	10.9% (n=17)	8.1% (n=3)	11.8% (n=14)	**0.533***
Erb-Duchenne	3.8% (n=6)	5.4%(n=2)	3.4%(n=4)	0.628**
Clavicle fracture	3.8% (n=6)	5.4% (n=2)	3.4% (n=4)	0.572**
Vertebral fracture	0.6% (n=1)	2.7% (n=1)	0%	0.237**
Humerus fracture	0.6% (n=1)	0%	0.8% (n=1)	1**
Cephalohematoma	2.6% (n=4)	5.4% (n=2)	1.7% (n=2)	0.239**
Perinatal asphyxia	4.5% (n=7)	%0	%5,9 (n=7)	0.131***
Hypoglycemia	13.5% (n=21)	21.6% (n=8)	10.9% (n=13)	**0.049***
Polycythemia	5.1% (n=8)	13.5% (n=5)	2.5% (n=3)	**0.019****
Hypocalcemia	2.6% (n=4)	5.4% (n=2)	1.7%(n=2)	0.239**
Respiratory problems				
Invasive MV	22.6% (n=35)	27% (n=10)	21.2% (n=25)	0.501*
RDS	4.5% (n=7)	8.1% (n=3)	3.4% (n=4)	0.358**
Myocardial hypertrophy	34.5% (n=29)	56.7% (n=17)	22.2% (n=12)	**0.001***
Ventricular septal defect	9.5% (n=8)	13.3% (n=4)	7.4% (n=4)	0.375*
Pulmonary hypertension	7.1% (n=6)	3.3% (n=1)	9.3% (n=5)	0.414**
Anal atresia	1.9% (n=3)	2.7% (n=1)	1.7% (n=2)	0.559**
CNS anomaly	1.9% (n=3)	2.7% (n=1)	1.7% (n=2)	0.559**

** Chi-square test, ** Fisher's exact test,*

DISCUSSION

Although genetic, ethnic and racial factors determine birth weight, male infants are heavier and have a higher incidence of macrosomic than female infants[13]. In the literature, the incidence of macrosomic male infants has been reported 2.12-2.15 times more than females[14-16]. Although macrosomic male infants were more common in our study, no statistical significance was found between the IDMs and non-IDMs according to gender. We think that this result indicates male predominance in infants born macrosomic, regardless of maternal diabetes status.

The mean gestational week at the birth of the IDMs was 1.1 weeks earlier than the non-IDMs. Studies reported that IDMs were born 1.5-2 weeks earlier than non-IDMs.14-16 86.1% of the IDMs and 58% of the non-IDMs were delivered by cesarean section (p=0.002). Studies have reported that cesarean delivery was statistically higher in IDMs compared with non-IDMs[16,17]. Elective deliveries may be performed at earlier weeks, as maternal diabetes causes more weight in newborns. Since

some of the patients were referred to our unit from different centers, we could not evaluate whether the high cesarean section rate in the IDMs was an emergency cesarean delivery due to fetal distress or whether it was preferred by gynecologists because of the lower risk of birth trauma.

Macrosomic babies have a higher risk of birth injury, such as shoulder dystocia, Erb-Duchenne paralysis, clavicle or vertebral fracture, cephalohematoma. Although shoulder dystocia was reported to be associated with gestational diabetes, brachial plexus injury was reported in 2.4% of all macrosomic non-IDMs in a study.3 In a meta-analysis, the incidence of Erb-Duchenne in macrosomic neonates was reported as 0.7%.6 In our study, Erb-Duchenne paralysis was seen 3.8% of all macrosomic patients, 3.4% of the non-IDMs and 5.4% of the IDMs. Compared to the literature, the reason why it was more common in our study may be because it included complicated patients who required intensive care. Studies have also reported statistically insignificant differences for brachial plexus injury between IDMs and non-IDMs, similar to our results (p=0.628)[16,18]. All macrosomic patients should be evaluated for shoulder dystocia,and clavicle fracture[18]. Similar to shoulder dystocia, the incidence of clavicle fracture in our study was the same and there was no statistical difference between groups (p=0.572). In a study, the incidence of clavicle fracture was reported as 6.5% in non-IDMs and 2.4% in IDMs, which was statistically insignificant[16]. In another study the overall incidence of clavicle fracture was reported as 1.8%[19]. In our study, 5.4% of the IDMs and 1.7% of the non-IDMs had cephalohematoma (p=0.239). In a study, this incidence was reported as 5.3% in non-IDMs and 2.4% in IDMs, and no statistical difference was found[16].

Although the cesarean rate was higher in IDMs, the incidence of birth injuries was not statistically significantly different between the two groups. In the literature, the incidence of perinatal asphyxia in macrosomic newborns has been reported as 0.8-2.9%[4,6,17]. Seven babies with perinatal asphyxia (%4.5) in our study were born from non-diabetic mother, however no statistical difference was found between the groups (p=0.131). Although perinatal asphyxia was not found in the IDMs in our study, the rate of perinatal asphyxia up to 25% was reported in the literature[20]. We think that the reason why our study result is different from the literature may be related to the referral of such patients, who constitute the study population, from other centers.

As it is known, hypoglycemia is one of the most important metabolic conditions for all newborns. Risk groups, including macrosomic babies, are screened for asymptomatic hypoglycemia on the first day of life. In two studies in the literature, the incidence of hypoglycemia was reported as 6.1% vs. 2.9% and 7.8% vs. 1% in macrosomic and non-macrosomic infants, respectively[15,17]. In another study, the incidence of hypoglycemia in macrosomic infants was as high as 22.7%[21]. In our study, 13.5% of all macrosomic infants (21.6% of the IDMs and 10.9% of the non-IDMs) had hypoglycemia (p=0.049). In one study, hypoglycemia was reported in 5.3% of all healthy and sick IDMs[22]. One study reported that LGA infants born to diabetic mothers were more likely to have hypoglycemia than those born to nondiabetic mothers (12.8% vs. 5.3%, respectively)[23]. In our study, hypoglycemia was more common in the IDMs than the non-IDMs. In a study, it was reported that the incidence of hypoglycemia was higher in the macrosomic non-IDMs, without a significant difference between the groups (14.3% vs 16.3%)[14]. There are conflicting results in the literature, but we think that the tendency to hypoglycemia in IDMs is a result of fetal hyperinsulinemia. In addition, hypoglycemia is not uncommon in macrosomic non-IDMs treated in the NICU, and

we think that clinicians should be aware of hypoglycemia.

Polycythemia, another metabolic condition, is screened between postnatal 2-4th hours in IDMs and other risk groups[20,24,25]. In a study comparing IDMs and healthy babies, the incidence of polycythemia was reported as 8% and it was reported to be statistically higher in IDMs than control group[26]. In a study that included all LGA newborns, it was reported that polycythemia was more frequently in IDMs than in non-IDMs (9.3% vs 3.0%; p=0.010)[23]. In our study, similar to this study, polycythemia was more common in IDMs and there was a significant difference between the groups (13.5% and 2.5%, respectively, p=0.019). As it is known, hypocalcemia is more common in IDMs, its incidence has been reported as 4-14% in the literature[18,20,25,26]. In our study, 5.4% of the IDMs and 1.7% of the non-IDMs had hypocalcemia, and there was no statistically significant difference between groups.

In the literature, respiratory problems in IDMs are reported in a wide range, such as 10-74.8%[18,20,25,27]. In our study, 22.6% of all macrosomic infants (27% of the IDMs and 21.2% of the non-IDMs) required invasive mechanical ventilation. While there was no significant difference between the groups in the need for invasive ventilation in our study, we think that the reason may be elective cesarean delivery. Das et al. reported that respiratory problems were significantly more common in IDMs than non-IDMs (29.2% vs. 9.2%)[16]. In a study, the incidence of RDS was reported as 4% in IDMs and 1.7% in non-IDMs.22 4.5% of all macrosomic infants in our study, 8.1% of the IDMs and 3.4% of the non-IDMs, had RDS and although they required intratracheal surfactant treatment, there was no statistical difference between the groups.

Genetic and environmental factors are involved in the etiology of congenital heart defects; and one of them is maternal diabetes[18,20,25]. It is known that the risk of congenital heart disorders is associated with poorly controlled maternal glucose levels in early pregnancy[27,28]. The incidence of myocardial hypertrophy is 12.1% in symptomatic newborns and 30% in all newborns[28]. In the literature, heart affection has been stated in a very wide range between 25%-75% in IDMs[20,27,29]. In our study, myocardial hypertrophy was seen in 56.7% of the IDMs and 22.2% of the non-IDMs, and this was statistically significant (p=0.001). Although we know that antenatal hyperinsulinemia is involved in the etiopathogenesis of myocardial hypertrophy in the IDMs, the incidence of 22.2% in non-IDMs should not be underestimated and it is quite remarkable.

In our study, the incidence of VSD was 13.3% in the IDMs and 7.4% in the non-IDMs, which was not statistically significant. We know that the reason for the higher incidence of VSD, which has been reported as 3.5% in the literatüre[27], is due to the inclusion of sick infants in the NICU. In our study, the incidence of PPH was 3.3% in the IDMs and 9.3% in the non-IDMs, without a statistically significant difference. But the higher incidence in non-IDMs is remarkable. It has been reported in the literature that the odds ratio of PPH in IDMs increases 1.91 times[30].

CONCLUSION

While polycythemia and myocardial hypertrophy are more common in the IDMs due to hyperinsulinemia. Hypoglycemia, perinatal asphyxia, need for mechanical ventilation, RDS, VSD, PPH can be detected in macrosomic newborns independent of maternal diabetes. Macrosomic infants should be closely observed for respiratory problems, birth injuries, hypoglycemia, polycythemia. All sick infants with respiratory distress in the NICU, whether with or without IDM, should be evaluated for congenital heart disease.

Ethics Committee Approval: This study was approved by the Marmara University Faculty of

Medicine ethics committee on 11.02.2022 with the decision number 09.2022.274. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Beta J, Khan N, Khalil A, et al. Maternal and neonatal complications of fetal macrosomia: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2019;54:308-18.

2. Chauhan SP, Grobman WA, Gherman RA, et al. Suspicion and treatment of the macrosomic fetus: a review. Am J Obstet Gynecol 2005;193:332-46.

3. Oral E, Cağdaş A, Gezer A,et al. Perinatal and maternal outcomes of fetal macrosomia. Eur J Obstet Gynecol Reprod Biol 2001;99:167-71.

4. Konje JC, Ladipo OA. Nutrition and obstructed labor. Am J Clin Nutr 2000;72:291S-297S.

5. Boulet SL, Alexander GR, Salihu HM, Pass M. Macrosomic births in the united states: determinants, outcomes, and proposed grades of risk. Am J Obstet Gynecol 2003;188:1372-78.

6. Ju H, Chadha Y, Donovan T, O'Rourke P. Fetal macrosomia and pregnancy outcomes. Aust N Z J Obstet Gynaecol 2009;49:504-09.

7. Creasy and Resnik's maternal-fetal medicine: principles and practice. 7th ed. Philadelphia, PA: Saunders-Elsevier; 2014:978–81.

8. Güdücü N, Gönenç G, İşçi H, Yiğiter AB, Dünder İ. Gestasyonel diabetes mellitus riskinin maternal yaş ve gebeliğin başlangıcındaki vücut kitle indeksi ile ilişkisi. Dicle Tıp Dergisi 2013;40:406-9.

9. Kallem VR, Pandita A, Pillai A. Infant of diabetic mother: what one needs to know?. J Matern Fetal Neonatal Med 2020;33:482-92.

10. Veille JC, Sivakoff M, Hanson R, Fanaroff AA. Interventricular septal thickness in fetuses of diabetic mothers. Obstet Gynecol 1992;79:51-4.

11. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. Ann Nutr Metab 2015;66:14-20.

12. Nguyen MT, Ouzounian JG. Evaluation and Management of Fetal Macrosomia. Obstet Gynecol Clin North Am 2021;48:387-99.

13. Najafian M, Cheraghi M. Occurrence of fetal macrosomia rate and its maternal and neonatal complications: a 5-year cohort study. ISRN Obstet Gynecol 2012;2012:353791.

14. Kleiner I, Ram S, Kovo M, et al. Pregnancy outcomes in association with placental histopathology in pregnancies complicated by macrosomia in diabetic vs. non-diabetic women. Eur J Obstet Gynecol Reprod Biol 2020;248:24-29.

15. Gyurkovits Z, Kálló K, Bakki J, et al. Neonatal outcome of macrosomic infants: an analysis of a two-year period. Eur J Obstet Gynecol Reprod Biol 2011;159:289-92.

16. Das S, Irigoyen M, Patterson MB, Salvador A, Schutzman DL. Neonatal outcomes of macrosomic births in diabetic and non-diabetic women. Arch Dis Child Fetal Neonatal Ed 2009;94:419-22.

17. Lloreda-García JM, Sevilla-Denia S, Rodríguez-Sánchez A, Muñoz-Martínez P, Díaz-Ruiz M. Perinatal outcome of macrosomic infants born to diabetic versus non-diabetic mothers. Resultados perinatales entre macrosomas hijos de madre diabética y macrosomas hijos de madre no diabética. Endocrinol Nutr 2016;63:409-13.

18. Hatfield L, Schwoebel A, Lynyak C. Caring for the infant of a diabetic mother. MCN Am J Matern Child Nurs 2011;36:10-16.

19. Linder N, Lahat Y, Kogan A, et al. Macrosomic newborns of non-diabetic mothers: anthropometric measurements and neonatal complications. Arch Dis Child Fetal Neonatal Ed 2014;99:353-58.

20. Hay WW Jr. Care of the infant of the diabetic mother. Curr Diab Rep 2012;12:4-15.

21. Said AS, Manji KP. Risk factors and outcomes of fetal macrosomia in a tertiary centre in Tanzania: a case-control study. BMC Pregnancy Childbirth 2016;16:243.

22. Esakoff TF, Cheng YW, Sparks TN, Caughey AB. The association between birthweight 4000 g or greater and perinatal outcomes in patients with and without gestational diabetes mellitus. Am J Obstet Gynecol 2009;200:672.e1-672.e6724.

23. Onal EE, Hirfanoglu IM, Beken S, et al. Are the neonatal outcomes similar in large-for-gestational age infants delivered by women with or without gestational diabetes mellitus?. World J Pediatr 2012;8:136-39.

24. Negrato CA, Gomes MB. Historical facts of screening and diagnosing diabetes in pregnancy [retracted in: Diabetol Metab Syndr. 2014;6:59]. Diabetol Metab Syndr 2013;5:22.

25. Kitzmiller JL, Ferrara A, Peng T, et al. Preexisting Diabetes and Pregnancy. In: Cowie CC, Casagrande SS, Menke A, et al., eds. Diabetes in America. 3rd ed. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); August 2018.

26. Saxena P, Tyagi S, Prakash A, Nigam A, Trivedi SS. Pregnancy outcome of women with gestational diabetes in a tertiary level hospital of north India. Indian J Community Med 2011;36:120-23.

27. Ferdousi SA, Sarker FR, Jahan N, Fatema N. Pattern of congenital heart disease in infants of diabetic mother. Bangladesh Journal of Child Health 2014;38:79-85.

28. Vural M, Leke L, Mahomedaly H, et al. Should an echocardiographic scan be done routinely for infants of diabetic mothers?. Turk J Pediatr 1995;37:351-56.

29. El-Ganzoury MM, El-Masry SA, El-Farrash RA, Anwar M, Abd Ellatife RZ. Infants of diabetic mothers: echocardiographic measurements and cord blood IGF-I and IGFBP-1. Pediatr Diabetes 2012;13:189-96.

30. Shu LP, Zhang RH, Cai YH, et al. Maternal Diabetes Mellitus and Persistent Pulmonary Hypertension of the Newborn: Accumulated Evidence From Observational Studies. Can J Diabetes 2020;44:327-34.e3.