Original Article

Short Term Outcome Of Macrosomic Neonates Of Diabetic & Non-Diabetic Mothers

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Summary:

Background: Big birth weight is one of the important factors affecting the perinatal morbidity & mortality. It may result in an irreversible squeal because of birth trauma & fetal asphyxia.
Objectives: to compare the short term outcomes of macrosomic infants born to diabetic and non-diabetic mothers.

Patients & Methods: This is a prospective study of 50 singleton macrosomic newborns weighting 4000 g & more aged 1-3 days admitted in the neonatal care unit of Children Welfare Teaching Hospital & Baghdad Teaching Hospital during a 6 months period from 1st of March to 1st of September 2010. The maternal & neonatal records were reviewed & infant morbidities including hypoglycemia, respiratory distress, feeding intolerance, birth injury & associated anomalies were discussed. All the infants were followed until they were discharged from the hospital.

Results: Infants of diabetic mothers (52%) were more likely to develop neonatal morbidity compared to infants of non diabetic mothers (48%), these include hypoglycemia (76.9% vs. 8.3%), Respiratory distress (61.5% vs. 37.5%), and birth injury (7.7% vs. 4.2%) & nearly equal incidence of feeding intolerance (11.5% vs. 12.5%). Associated anomalies especially congenital heart disease (10%) found in infant of diabetic mothers only.

Conclusions: Most of birth weight variation remains unexplained & most non-IDM macrosomic infants do not have identifiable risk factors. Macrosomia is generally associated with neonatal morbidity & neonatal injury. The potential dangers of birth injury in vaginal delivery have increased the rates of cesarean section to (68%). Infants of diabetic mothers have a higher rate of neonatal morbidity overall including hypoglycemia, respiratory distress, birth injury & congenital heart disease.

Keywords: Outcome, Infants, Macrosomic neonates, Diabetic mothers, non-Diabetics mothers.

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Introduction:

Birth weight is one of the important factors affecting perinatal morbidity & mortality. It is the main criterion for macrosomia.(1) Fetal macrosomia is defined as birth weight of 4000-4500 g or greater than 90% for the newborn adjusted for race, sex & gestational age. (2) Common causes of macrosomia can be divided into maternal & fetal causes:

A. Maternal causes: a. Gestational diabetes is one of the strongest risk factors associated with giving birth to infant that is considered large for gestational age (2). Pregestational & gestational diabetes result in fetal macrosomia (3). b. Maternal weight prior to pregnancy can affect the weight of the fetus (4). c. Excessive weight gain (more than 20 Kg) in pregnancy is a risk factor for macrosomia (5). d. Postmaturity (11,5). e. Multiparity & grandmultiparity increases the risk of macrosomia (4). f. Previous macrosomic infants (2). g.Variation in the percentage of macrosomia in different ethnic groups has been observed independent of
diabetes. h. Parental stature: Taller & heavier parents typically produce larger offspring (4).

B. Fetal causes: 1. Fetal sex: male infants are more likely to be considered large for gestational age because they are an average of 150 g heavier than matched female fetuses at each gestational age.(6) 2. Eryhtroblastosis fetalis. (7) 3.Nesidioblastosis: diffuse or microadenomatous forms of islet cell hyperplasia.(2) 4. Hydrocephalus. (2) 5. Genetic disorders of overgrowth e.g. Beckwith-Wiedemann syndrome (hypoplasia of pancreatic islets, gigantism & exomphalos), cerebral gigantism (Sotos syndrome) & transposition of great vessels.(7)

Despite causes of macrosomia, much of the variation in birth weights remains unexplained. Most infants whose weight > 4500 g have no identifiable risk factors. (8) Symptoms & complications: Macrosomia may place the mother & fetus or neonate at high risk for adverse

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outcomes & identification of these at risk pregnancies may allow intervention to reduce the risk, to provide appropriate counseling & plans for monitoring & follow up care during pregnancy & after delivery.(9). Symptoms depend on which complications occur. Common complications include the following: * Hypoglycemia: Often hypoglycemia causes no symptoms. Sometimes, newborns are listless, limp or jittery. Even in macrosomic newborns from non-diabetic mothers, insulin C-peptide concentrations in the cord blood have been found to be elevated compared with normosomic infants (8).*Feeding intolerance:

Despite their large size , Infants of diabetic mothers (IDM) often do not feed well for the first few days .(10) *Hypocalcemia: IDM tend to be jumpy ,tremulous & hyperexcitable. Later appearance of these signs is often related to hypocalcemia. Hypomagnesemia may be associated with hypocalcemia.(11)* Lung problems: It is generally accepted that respiratory distress syndrome (RDS) is seen more commonly in IDM than in normal infants born between 30 & 38 weeks gestation (10). This higher incidence observed in those born by cesarean section as well as by vaginal route (although more so in the former group) & is independent of maternal parity or presence or absence of birth depression and/or asphyxia, but may suffer from meconium aspiration if depressed or overly stressed before or during the birth process.(12)* Birth injuries: Macrosomic newborns are at increased risk of birth injuries such as brachial plexus injuries &clavicle fractures.(11). Difficulties occur with delivery of unexpected large shoulders , sometimes after using forceps , but often after an unprolonged spontaneous delivery, usually with a prolonged second stage (13).* polycythemia: Large-for-gestational age newborns may have a ruddy complexion because too many red blood cells are produced, as the excess RBC are broken down, bilirubin is formed which along with poor feeding results in jaundice.(14)* congenital anomalies: IDM as a total group will have approximately 3-times the usual incidence of congenital anomalies compared to infants from non-diabetic general population. Congenital heart disease occurs approximately 3 to 4 times more frequently in IDM than in the general population and neural tube defects (e.g. meningomyelocele) are more common also.(15).This study aimed to compare the short term outcomes of macrosomic infants born to Diabetic mothers (IDM) and non-diabetic mothers (non-IDM).

Patients and Methods:

This is a prospective study of 50 live born singleton neonates with a birth weight of 4000 g & more, aged 1-3 days admitted to neonatal care unit of Children Welfare Teaching Hospital & Baghdad Teaching Hospital during a 6-months period from 1st of March to the 1st of September 2010. Clinical information was extracted from medical records of the mothers and the infants. All infants were managed and followed until they were discharged according to guidelines of these hospitals. Macorosmia was defined as a birth weight of > 4000 g irrespective of gestational age & maternal diabetic status. Infants born to diabetic women were termed infants of diabetic mothers (IDM) & the rest were identified as (non-IDM).Data about parity, mode of delivery and maternal diabetes status were obtained from personal records of the mother. History of previous big baby (body weight > 4000 g) were obtained from the mother directly or a relative.Neonatal outcomes included hypoglycemia, respiratory distress, feeding intolerance, birth injuries and associated anomalies. Hypoglycemia was defined as blood glucose < 50 mg/dl occurring at any time during first 24 hours of life. Blood sugars were routinely checked in all macrosomic infants at birth & monitored periodically during the first 3 days of life.(16) Respiratory distress consists of tachypnoea and/or other signs of respiratory distress. Feeding intolerance was defined as abdominal distension and/or vomiting requiring management in the neonatal intensive care unit with intravenous fluid. Birth injuries detected by examination of newborn looking for cephalhematoma, facial palsies and asymmetric moro reflex. Associated anomalies especially congenital heart defects were detected by heart examination looking for abnormal heart sounds and murmurs & proved by doing echocardiography study.

The outcomes were compared between the infants of diabetic and non-diabetic mothers using X2 test and statistical significance was set at $p < 0.05$.

Results:

A total of 50 singleton newborns with body weight 4000 g and more were admitted to the neonatal care unit during the study period,

Table (1) show difference in the sex of the newborn between males 32 (64%) and females 18 (36%), with male: female ratio of 1.7:1, which show significant p-value of 0.048. Term infants show higher percentage 41 (82%), post-terms 7(14%) and only 2 (4%) infants

born prematurely. Thirty three (66%) of infants have birth weights 4-4.49 Kg, 13 (26%) with birth weight 4.5-4.99 Kg and 4 (8%) with birth weight 5 Kg and more.

Table (1): Distribution of study sample according to the infant gender,Gestational age & birth weight

Variables	N=50 (%)	X2	p-value
Sex Male Female	32 (64.0) 18 (36.0)	3.92	0.048
Gestational age at birth Preterm Term Post-term	2 (4.0) 41 (82.0) 7 (14.0)	54.04	0.000
Birth weight (Kg) 4.00-4.49 4.50-4.99 > 5.00	33 (66.0) 13 (26.0) 4 (8.0)	26.44	0.000

Table (2) show that multipara women with history of parity of more than three accounting for majority of cases 36 (72%) compared to those with parity of three & less than three 14 (28%) with p-value of 0.02. Thirty four (68%) delivered by cesarean section and the remaining 16 (32%) delivered by normal vaginal delivery. Maternal history of previous big baby (4000 g and more) found only in 5 (10%) of cases, all of them born to mothers without history of diabetes during pregnancy.

Twenty six (52%) of macrosomic infants were IDM whereas 24 (48%) were non-IDM.

Table (2): Distribution of study sample according to the obstetric characteristics

Variables	N=50 (%)	X2	p-value
Parity 1-3 > 3	14 (28.0) 36 (72.0)	9.68	0.002
Type of delivery Normal vaginal delivery Caesarean section	16 (32.0) 34 (68.0)	22.84	0.02
History of previous big baby Positive Negative	10.0))5 90.0))45	32.00	0.000
Maternal diabetes (during pregnancy) Yes No	52.0))26 48.0))24	0.08	0.777

Table (3) show that the birth weight range of 4.00-4.49 Kg account for majority of cases 33 (66%) with higher percentage 18 (75%) occur among non-IDM compared to 15 (57.7%) in IDM.

There was no significant difference in the gender of macrosomic IDM & non-IDM {male: 17 (65.4%) vs. 15 (62.5%)} respectively &{female: 9 (34.6%) vs. 9 (37.5%)} respectively.

Regarding gestational age, most macrosomic infants born at term 41 (82%) with no significant p-value(0.86) between IDM 22 (84.6%) and non-IDM 19 (79.2%). The type of delivery show p-value of (0.04) with IDM delivered by cesarean section 20 (76.9%) occur more than non-IDM 14 (58.3%) whereas non-IDM delivered by normal vaginal delivery 10 (41.7%) occur more than IDM 6 (23.1%).

Table (3): Distribution of study sample according to maternal diabetes during pregnancy and to some infant and obstetric characteristics

Variables	Maternal diabetes Yes N=26 (%)	Maternal diabetes No N=24 (%)	Total N=50 (%)	X2	p-value
Birth weight (Kg) 4.00-4.49 4.50-4.99 > 5.00	15 (57.7) 8 (30.8) 3 (11.5)	18 (75.0) 5 (20.8) 1 (4.2)	33 (66.0) 13 (26.0) 4 (8.0)	1.888	0.389
Sex Male Female	17 (65.4) 9 (34.6)	15 (62.5) 9 (37.5)	32 (64.0) 18 (36.0)	0.045	0.832
Gestational age Preterm Term Post-term	1 (3.8) 22 (84.6) 3 (11.5)	1 (4.2) 19 (79.2) 4 (16.7)	2 (4.0) 41 (82.0) 7 (14.0)	0.283	0.868
Type of delivery Normal vaginal delivery Caesarean section	6 (23.1) 20 (76.9)	10 (41.7) 14 (58.3)	16 (32.0) 34 (68.0)	9.963	0.04

Table (4) show that birth injury occurred in 3 cases (6%) of macrosomic neonates, with 2 cases (7.7%) presented with Erb's palsy found in IDM & one case (4.2%) of clavicle fracture occurred in non-IDM. Hypoglycemia was noted in 22 (44%) of cases with majority 20 (76.9%) seen in IDM & only 2 cases (8.3%) in non-IDM.

Table(4): Distribution of study sample according to maternal diabetes during pregnancy and to some infant outcome.

Variables	Maternal diabetes Yes N=26 (%)	Maternal diabetes No N=24 (%)	Total N=50 (%)	X2	p-value
Birth injury Yes No	 2 (7.7) 24 (92.3)	 1 (4.2) 23 (95.8)	 3 (6.0) 47 (94.0)	0.275	0.600
Hypoglycemia Yes No	 20 (76.9) 6 (23.1)	 2 (8.3) 22 (91.7)	 22 (44.0) 28 (56.0)	30.769	0.01
Respiratory distress Yes No	 16 (61.5) 10 (38.5)	 9 (37.5) 15 (62.5)	 25 (50.0) 25 (50.0)	2.885	0.089
Feeding intolerance Yes No	 3 (11.5) 23 (88.5)	 3 (12.5) 21 (87.5)	 6 (12.0) 44 (88.0)	0.011	0.917
Anomalies Positive for anomaly Type of anomaly - Congenital heart disease - Other anomalies Normal baby	 5 (19.2) 4 (15.4) 1 (3.8) 21 (80.8)	 0 (0.0) 0 (0.0) 0 (0.0) 24 (100.0)	 5 (10.0) 4 (8.0) 1 (2.0) 45 (90.0)	5.128	0.024

Respiratory distress occurred in 25 (50%), 16 (61.5%) of them seen in IDM compared to 9 (37.5%) in non-IDM.
Feeding intolerance seen in 6 cases (12%) of the total, 3 of them (11.5%) occurred in IDM & other 3 (12.5%) in non-IDM.Anomalies found in 5 cases (10%), all of them occurred in IDM,4 cases (15.4%) presented with congenital heart disease (3 cases of VSD & one case TGA) proved by echo study; other anomalies was one case(3.8%) of club foot, the remaining 45 (90%) infants were normal babies.

Discussion:

The birth weight is one of the important factors affecting the perinatal morbidity & mortality. It may result in an irreversible sequel because of fetal asphyxia and birth trauma. (1)Recently, developing obstetric techniques and neonatal intensive care have reduced the rate of perinatal morbidity and mortality. (17).

In this study, IDM have a higher rate of neonatal morbidity overall, the incidence of hypoglycemia among IDM was (76.9%) not surprising & goes with Smith et al study (70.2%) (18) & Das S study (76.1%) (19), this would suggest that diabetic mothers during pregnancy require close monitoring for diabetes.

Macrosomic infants whose mothers do not have diabetes have been claimed to be at risk for transient hypoglycemia, despite the lack of studies that support this assumption. Our study showed only 2 cases
(8.3%) developed asymptomatic hypoglycemia, both of them in the 1st hour of life & this percentage is far below (16%) that found in Das S study (19) & (28.6%) in Schaefer – Graf et al (20) the largest published study to our knowledge. This difference may be related to a smaller population of macrosomic non-IDM 24 (48%) in our study.

The higher rate of respiratory distress syndrome that was found in our IDM group (61.5%) agrees with Oral et al study (58%) (21) & Sermer et al study (64.2%) (22) & this may be due to the influence of maternal diabetes on lung maturity & a higher number of cesarean section.

Feeding intolerance & vomiting in the first 24 hours of life in the absence of RDS that required hospital admission was found in (11.5%)of IDM &(12.5%)of non-IDM, a finding that is not present in Oral et al study (21)which revealed(6.5%)of IDM developed feeding intolerance and this may be due to hypoglycemia, being restless or jittery or due to swallowing large amount of amniotic fluid that require frequent suctioning especially

those delivered by cesarean section.

The major focus of most reports on the neonatal outcomes of macrosomia was around the incidence of birth related injuries. This study showed that (6%) had brachial plexus plus fracture injuries which are considerably close to(7.3%)in Das S study(19), but also our overall rate of birth related injuries was higher than that of Wollschaeger et al (23) which was(2.4%). This higher rate of macrosomia-related

Injuries may be due to increased rates of birth weight > 4.5 Kg & failure of prediction of macrosomia.

Birth injuries in IDM were (7.7%) in our study, which agree with (6.8%) found in Sheiner E study. (24) This results is considered high compared to (4.2%) in non-IDM of our study &(3%) in Sheiner E study. This difference is probably because of the disproportionate growth of IDM leading to larger shoulder and extremity circumference compared to fetal head and increased body fat which increase risk of birth injuries.

It is well known that IDM have increased risk of congenital heart disease than general population (15) and this is quite true as all cases of macrosomia with CHD were (8%) found in IDM (15.4%) & this result in somewhat close to that observed in Mark A study (25)(18.2%)& this is because congenital anomalies correlate with poor metabolic control during the periconception & organogenesis periods and may be due to hyperglycemia. (25)

There is a major difference between our IDM and non-IDM regarding type of delivery. IDM group had a significantly higher percentage of cesarean deliveries (76.9% vs. 58.3%). This is much higher than the results of Ecker's study (26) whose cesarean rate was (59.6%) among diabetes versus (28.5%) in non-diabetics & much higher than that of Kolderup et al (27) (45.5%) cesarean section rate among their diabetic mothers. This most likely because of elective cesarean section for suspected macrosomia results in a high number of unnecessary procedures, high number of mothers who have previous cesarean section & early induction of labor may result in a substantial increase in caesarean rate because of failed inductions.

Conclusions:

Most of birth weight variation remains unexplained & most non-IDM macrosomic infants do not have identifiable risk factors. Macrosomia is generally associated with neonatal morbidity & neonatal injury. The potential dangers of birth injury in vaginal delivery have increased the rates of cesarean section (68%). IDM have a higher rate of neonatal morbidity overall including hypoglycemia, respiratory distress, birth injury & congenital heart disease. We recommend early diagnosis of macrosomic fetuses especially in IDM, and prepare for safer delivery and neonatal care.

References:

1. Allahyar J, Mariam Katz & Moshe Mazar. An increasing proportion of infants weight more than 4000 g at birth. European Journal of Obstetrics & Gynecology & Reproductive Biology 2010 Feb; 40: 931-6.

2. Seidman DS, Ever-Hadani P, Gale R.The effect of maternal weight gain in pregnancy & birth weight. Obstet Gynecol 2008; 74: 240-6.

3. Bennett PH, Burch TA, Miller M et al. Diabetes mellitus in American (pima) Indians. Lancet II; 2007: 125-28.

4. Tallarigo L, Giampetro O, Penno G, Miccoli R et al. Relation of glucose tolerance to complications of pregnancy in non-diabetic women. N Engl J Med, 2002; 315: 989-92.

5. Edwards LE, Hellerstedt WL, Altan IR, Story M et al. Effects of gestational weight change. Obstet Gynecol, 2006; 87: 389-99.

6. Mimouni F, Porat S, Merlob P, Zaizov R et al. Perinatal asphyxia in infants of insulin-dependent diabetic mothers. JAMA 2003; 25: 405-11.

7. Essel J, Opai-Tetteh E. Macrosomia: maternal & fetal risk factors. SAfr. Med J; 2005; 85: 41-51.

8. Lazer S, Biale Y, Mazor M, Lewenthal H, Insler V. et al. Complications associated with macrosomic fetus. J Reprod Med 2008; 31: 501-05.

9. Susser M, Marolla FA, Fleiss J et al. Birth weight, fetal age & perinatal mortality. Am J Epidemiol, 2000; 96: 194-7.

10. American College of Obstetricians & Gynecologists. Fetal macrosomia. Washington (DC): The College; 2000. Practice Bulletin No. 22.

11. Barbara J. Stoll. Infant of diabetic mothers. Nelson Textbook of pediatric by Behrman, Kliegman, Jenson, 18th edition, Ch 107, USA, 2007: 783-84.

12. Gregory KD, Henry OA, Ramicone E, Chan R et al. Maternal & infant complications in high and normal weight infants by method of delivery. Obstet Gynecol 1999; 92: 507-13.

13. O'Leary JA, Lenetti HB. Shoulder dystocia:

prevention & treatment. Am J Obstet Gynecol 2010; 162: 5-9.
14. Yeruchimovich M, Mimouni FB, Green DW, Dollbery S. Nucleated red blood cells in healthy infants of women with gestational diabetes. Pediatrics 2000; 95: 84-6.
15. Dunn PM: Infant of diabetic mother. Acta Paediatr Scand Suppl 2001; 319: 7-16.
16. Kaur S, Mathew M. Outcome of pregnancy with abnormal glucose metabolism. Oman Medical Journal, 2000; 2: 19-23.
17. Boney CM, Verma A, Tucker R, Vohr BR et al. Association of birth weight with maternal obesity & gestational diabetes mellitus. Pediatrics, 2005; 115: 290-6.
18. Smith GC, Smith MF, McNay MB, Fleming JE. Hypoglycemia in infants of diabetic mothers. BJOG 2007; 104: 186-90.
19. Das S, Irigoyen M, Patterson MB, Salvador A et al. Neonatal outcomes of macrosomic births in diabetic & non diabetic women. Archives of Disease in Childhood – Fetal & Neonatal Edition 2009; 94: 419-22.
20. Scchaefer – Coraf, Rainer Rossi, Christoph Buhrer, Greda Siebert et al. Rate & risk factors of hypoglycemia in large for gestational age infants of non diabetic mothers. Am J Obstet Gynecol; 2002; 187(4): 913-17.
21. Oral E, Cagdas A, Gezer A, Kaleli S et al. Perinatal maternal outcomes of fetal macrosomia. Eur J Obstet Gynecol Reprod Biol 2001; 99: 167-71.
22. 27. Sermer M, Naylor CD, Farine D, Kenshole AB et al. The Toronto Tri-Hospital Gestational Diabetes Project: a preliminary review. Diabetes Care 2008; 21: 33-42.
23. Wollschlaeger K, Nieder J, Koppe I et al. A study of fetal macrosomia. Arch Gynecol Obstet 1999; 263: 51-55.
24. Sheiner E, Amalia Levy, Reli H, Rachel D et al. Determining factors associated with shoulder dystocia: a population based study. Eur J of Obstet & Gynecol & Reprod. Biology 2006; 126: 11-15.
25. Mark A, Zamorski & Wendy S. Management of suspected fetal macrosomia. A peer reviewed journal of the American Academy of family Physicians; 2001; 15: 1-4.
26. Ecker JL, Greenbery JA, Norwitz et al. Birth weight as a predictor of brachial plexus injury. Obstet Gynecol Journal 2004; 89: 643-7.
27. Kolderup LB, Laros RK, Musci J. Incidence of persistent birth injury in macorsomic infants: Association with mode of delivery. Am J Obstet Gynecol 2007; 177: 37-41?.