Prevalence and outcomes of macrosomic infants born to non-diabetic mothers: A ten years' experience at tertiary care center

Fahad Al-Qashar[1], Mohamed Al-Ghamdi[2], Wahid Agab[1], Mohamed Al-Sayed[3], Mosleh Jabari[4], Hassan Al-Shehri[4], Bader Hassan Sobaih[5]

[1]Department of Pediatrics, Bahrain defense force Hospital, Royal Medical Services, Kingdom Of Bahrain
[2]Department of Pediatrics, Division of Neonatology, King Fahd University Hospital, University of Dammam, Eastern Province, Kingdom of Saudi Arabia.
[3]Department of Pediatrics, Security Forces Hospital, Riyadh, Saudi Arabia
[4]Department of Pediatrics, College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University, Riyadh, Saudi Arabia.
[5]Department of Pediatrics, College of Medicine, King Saudi University, Riyadh, Saudi Arabia.
dr.h.alshehri@hotmail.com

Abstract: Objective: To investigate the prevalence of macrosomic births, it's neonatal outcome as well as it's obstetric outcome in diabetic, gestational diabetic and non-diabetic maternities in people with Saudi and non-Saudiethinicity of Riyadh. **Material and Methods:** This retrospective study was carried out from in Department of Paediatrics at Al-Imam Muhammad Ibn Saud Islamic University, Riyadh. Information of the term infants (within 37 to 42 weeks of gestational age) and birth weight of more than 4000 grams were extracted from the medical records. Newborn data consisted of birth weight, gender and admission to newborn care where as maternal data consisted of nationality, mode of delivery, diabetic status, and duration of hospitalization. All the data were analyzed using SPSS version 21. **Results:** Out of 14661 singletons, the frequency of macrosomia was 3.58%. Among the macrosomic infants, 89.9% were born to non-diabetic mother, 7.8% to mothers having gestational diabetes while only 2.3% were born to diabetic mothers. Incidence of macrosomia was higher in mother of Saudi origin (61.5%). The percentage of female infants was remarkably higher than male (63.4% vs. 36.4%). The duration of hospitalization was lower in infants born within weight range of 4000-4500g while it was higher in infants with weight >5000g ($p< 0.01$). Nationality, diabetic status of mother, and mode of delivery was comparable between different weight groups. Overall, the non-diabetic mother showed lower level of complications in mode of delivery (i.e. caesarean section), admission to newborn care (i.e. well baby nursery), and duration of hospitalization (≥3 days) as compared to diabetic mothers ($p <0.001$). **Conclusions:** There an increase in macrosomia in non-diabetic women. Although maternal and foetal complications are low in non-diabetic mothers, the infants are not completely healthy. However, the complication increases in diabetes.

[Fahad Al-Qashar, Mohamed Al-Ghamdi, Wahid Agab, Mohamed Al-Sayed, Mosleh Jabar, Hassan Al-Shehri, Bader Sobaih. **Prevalence and outcomes of macrosomic infants born to non-diabetic mothers: - A ten years' experience at tertiary care center.** *J Am Sci* 2016;12(12):89-94]. ISSN 1545-1003 (print); ISSN 2375-7264 (online). http://www.jofamericanscience.org. 12. doi:10.7537/marsjas121216.12.

Keywords: Prevalence; outcome; macrosomic infant; born; diabetic; mother; tertiary care

1. Introduction

Large birth weight (>4000 g) is one of the important factors affecting the prenatal morbidity and mortality worldwide [1]. The incidence of macrosomia has increased in the past 50 years and varies widely from 0.5% to 25% with an average incidence of 9% in general hospital population[1-3]. Preventing macrosomia has long been acknowledged as an important objective for reducing morbidity for infants.

Macrosomianegatively affects the health of both mothers and infants. The adverse neonatal short-term outcomes includes neonatal mortality caused by either birth asphyxia or somemetabolic disorders (hypoglycemia, hyperbilirubinemia, hypomagnesia), shoulder dystocia, meconium aspiration and birth trauma such as brachial plexus injuries and clavicle fractures[4-6]. The long-termconsequences include a higher predisposition to develop obesity and type 2 diabetes later in life [7-9]. The maternal complications associated with the delivery of macrosomic infants include postpartum hemorrhage due to prolonged labor, postpartum infection, laceration of the anal sphincter and the incidence of acute cesarean section (C-section) or vaginal operative delivery[2, 10].

The causes of macrosomia are multifactorial, and can be broadly divided into non-modifiable and modifiable factors. The non-modifiable risk factors include genetic, maternal age, parity, gestational age and gender of child [11]. The modifiable risk factors include maternal anthropometry such as pre-

gestational weight, BMI, gestational weight gain, physical activity, nutrient intake (both macro-and micronutrients), obesity and diabetes [12-14]. Nevertheless, 34% of macrosomic infants are born to mothers without any risk factors[15].

Different studies from Saudi Arabia have shown the rise in prevalence of diabetes mellitus in the population. Al-Nozha et al. specified that one in every four people above the age of 30 is reported to have diabetes in Saudi Arabia[16]. Further, abnormal glycemic control affects 8.9-12.5% of all pregnancies based on the regionof Saudi Arabia, and the diagnostic criteria used [17, 18]. In recent years, macrosomic infants born to non-diabetic mothers are increasingly reported. Nadir et al. studied the prevalence of macrosomia in Saudi diabetic and non-diabetic mothers in Al-Jouf region [19]. However, there is a lack of information on the prevalence of macrosomic infants born to non-diabetic mothers in the Eastern Province of Saudi Arabia. In this retrospective study, we therefore, aim to report the prevalence and outcomes of macrosomic infants born to diabetic, gestational diabetic and non-diabetic mothers in a tertiary care center of Riyadh and identify the risk factors which might contribute to the complication related to macrosomia.

2. Methods

A retrospective investigation of all the live births with singleton neonates was conducted at the Department of Pediatrics, College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University, Riyadh, Saudi Arabia, for a period of 6 months from. For reviewing, we collected relevant neonatal and maternal data from the archived medical records of the infants and their mothers. This study was approved by the Research Ethics Committee.

Macrosomia was defined as a birth weight ofequal to or more than 4000 g. Term infants within 37 to 42 weeks of gestational age and birth weight of more than 4000 grams were included in the study. Infants were excluded if they were Preterm infants less than 37 weeks gestational age, birth weight less than 4000 g, diagnosed with major congenital anomalies and without any antenatal follow up.

Maternal diabetic status was determined from prenatal records of a 1 h glucose challenge test and/or a 3 h glucose tolerance test in accordance with protocol. Prolonged hospital stay in the well newborn nursery was defined as a stay of >72 hdue to infant related complications. In our centre, macrosomic infants of diabetic women receiving insulin during pregnancy are admitted to the neonatal intensive care unit (NICU) after delivery. Neonatal outcome included admission into well baby nursery (WBN) or NICU and period of hospitalization, while maternal outcome included mode of delivery (Normal spontaneous delivery (NSD), C-section or other methods).

All the data were analyzed using SPSS 21.0. Descriptive statistic such as frequency and percentages were used to describe the data. Non-parametric Chi-square test was used to describe the significance level in each group. Associations between various parameters were tested using Fischer's exact test. A p value less than 0.05 was considered statistically significant.

3. Results

Of the14661 live births occurred at our medical centre during the 10-year study period, 525 (3.6%) infants were macrosomic with a birth weight of ≥4000 g. All the macrosomic infants were singleton births. They included 89.9% newborns to non-diabetic mother, 7.8% to mothers having gestational diabetes while only 2.3% were born to diabetic mothers. The clinical characteristics of the study groups are described in Table 1. The majority of newborns had a birth weight between 4000 and 4500 g (80%). The percentage of female infants was remarkably higher that male (63.4% vs. 36.4%, $p<0.001$). A greater number of the neonates were of Saudi origin (61.5%). Interestingly, most of the macrosomic infants were born to non-diabetic mother (89.9%) than diabetic or GDM irrespective of their ethnic background.

The duration of hospitalization was lower in infants born within weight range of 4000-4500g while it was higher in infants with weight >5000g. This difference was statistically significant ($p< 0.01$). Within the weight range of 4000g - 5000g a strong tendency for macrosomic infants to be female was observed while with birth weight >5000g a strong tendency for male child was observed ($p = 0.073$). Further, a trend towards increased infant admission to WBN was observed in all the weight groups ($p =0.095$). However, nationality, diabetic status of mother, and mode of delivery was comparable between different weight groups (Table 2).

Overall, the non-diabetic mother showed lower level of complications in mode of delivery ($p <0.01$), admission to newborn care, and duration of hospitalization as compared to diabetic mothers ($p <0.001$). No variation was observed for gender and nationality within the groups. In GDM group, all the factors were comparable except for neonatal admission where more number of admissions to WBN was observed (Table 3).

Table 1. Clinical characteristics of the studypopulation

Clinical characteristics	N (%)	p value
Birth weight (g) *4000- 4500* *4501 - 5000* *>5000*	 454 (86.5%) 67 (12.8%) 4 (0.8%)	<0.001
Gender *Male* *Female*	 191 (36.4%) 333 (63.4%)	<0.001
Nationality *Saudi* *Non-Saudi*	 323 (61.5%) 202 (38.5%)	<0.001
Mother's diabetic status *Diabetic* *GDM* *Non-diabetic*	 12 (2.3%) 41 (7.8%) 472 (89.9%)	<0.001
Mode of delivery *NSD* *C/S* *Others*	 352 (67%) 158 (30.1%) 15 (2.9%)	<0.001
Neonatal admission *WBN* *NICU*	 478 (91%) 47 (9%)	<0.001
Period of hospitalization *≤ 3 days* *>3 days*	 342 (65.1%) 183 (34.9%)	<0.001

Table 2. Comparison ofoutcome by weight

Characteristic	Weight (4000 - 4500 g) (N= 454)	Weight (4501 - 5000 g) (N= 67)	Weight (>5000 g) (N= 4)	p value
Gender *Male* *Female*	 163 (35.9%) 291 (64.1%)	 25 (37.3%) 41 (61.2%)	 3 (75%) 1 (25%)	0.073
Nationality *Saudi* *Non-Saudi*	 283 (62.3%) 171 (37.7%)	 39 (58.2%) 28 (41.8%)	 1 (25%) 3 (75%)	0.272
Mother's diabetic status *Diabetic* *GDM* *Non-diabetic*	 10 (2.2%) 32 (7%) 412 (90.7%)	 2(3%) 8(11.9%) 57(85.1%)	 0(0%) 1(25%) 3(75%)	0.224
Mode of delivery *NSD* *C/S* *Others*	 307 (67.6%) 132 (29.1%) 15 (3.3%)	 41(61.2%) 26 (38.8%) 0 (0%)	 4 (100%) 0 (0%) 0 (0%)	0.188
Neonatal admission *WBN* *NICU*	 418 (92.1%) 36 (7.9%)	 56 (83.6%) 11 (16.4%)	 4 (100%) 0 (0%)	0.095
Period of hospitalization *≤ 3 days* *>3 days*	 308 (67.8%) 146 (32.2%)	 33 (49.3%) 34 (50.7%)	 1 (25%) 3 (75%)	0.002

% are calculated within the given weight range.

Table 3: Comparison of outcome by maternal diabetic status

Characteristic	Diabetic (N= 454)	GDM (N= 67)	Non-diabetic (N= 4)	p value
Mode of delivery				
NSD	3 (25%)	22 (53.7%)	327 (69.3%)	
C/S	9 (75%)	19 (46.3%)	130 (27.5%)	<0.01
Others	0 (3.3%)	0 (0%)	15 (3.2%)	
Neonatal admission				
WBN	2 (16.7%)	38 (92.7%)	438 (92.8%)	<0.001
NICU	10 (83.3%)	3 (7.3%)	34 (7.2%)	
Period of hospitalization				
≤ 3 days	3 (25%)	17 (41.5%)	322 (68.2%)	<0.001
>3 days	9 (75%)	24 (58.5%)	150 (31.8%)	

% are calculated within the maternal diabetic status.

4. Discussion

The study presents that incidences of macrosomias are more common in non-diabetic mothers irrespective of their ethnicity (Saudi or non-Saudi). Interestingly, macrosomic infants were predominantly females. Macrosomias with weight <5000g had increased hospital stay irrespective of the diabetic status of their mother. Nonetheless, large for gestational age baby born to diabetic mothers were associated with increased complications such as delivery by C-section, admission in NICU, and the span of hospital stay.

The global prevalence of neonatal macrosomia has a wide range which varies between 0.5-25%[2, 3]. A lack of consensus in the definition of macrosomia and anthropometric variations in different race are the two major factors contributing to the wide range of prevalence. Our study showed a predominance of 3.58%. Nadir et al. reported a prevalence of macrosomia to be about 8.1% in the Al-Jouf region of Saudi Arabia[19] which is much higher than our study. This could be due to the differences in the study, while Nadir et al. studied only people of Saudi origin, our study had people of both Saudi as well as non-Saudi.

In our study large for gestational age babies were increasingly born to non-diabetic mother. Although macrosomic baby being born to non-diabetic mother are also reported by other studies, the reason behind it is not known [20-23]. In their study, Hoegsberg et al. found significantly elevated insulin levels in the cord blood and speculated that subtle hyperglycemia, undetected with routine diabetic screening tests, may have been the cause of the macrosomia in infants of presumed non-diabetic mothers [24]. Further, in an animal study, Eriksson et al. showed that a protein-deficient diet during pregnancy decreases insulin production resulting in excess glucose and other nutrients which are transferred to the fetus thus leading to macrosomia [25]. Contrary to the above study, Cuco et al., reported that in well nourished females a protein rich diet, especially meat, in preconception period as well as during pregnancy increases birth weight [26]. People of Saudi Arabia are well nourished, consume meat predominantly in their daily diet as well as perform less physical activities due to extensive urbanization. All these factors might have contributed to the increased incidence of macrosomia in non-diabetic mother.

Weight was not associated with any of the risk factors studied except for period of hospitalization (>3 days). It was lower for infants born within weight range 4000 - 4500 g and increased >5000 g weight. Excessive weight of child induced trauma to the birth canal while delivering may increase the duration of hospitalization [2, 10].

Diabetes as well as gestational diabetes are the strongest predictors of macrosomia. Increased awareness diabetes related complications during pregnancies have controlled the incidences of diabetes-related marosomia [17, 18]. Similar effect is also observed in our study. However, diabetes was associated with maternal and neonatal complications such as increased C-section in mother and number admission to NICU and duration of hospital stay in newborns. Diabetes-related maternal and neonatal complications are also been reported many studies [2, 5, 10]. None of the babies in this study were healthy enough to be with their mother immediately. Newborns are admitted to WBN due to infant-related problems. We observed an association of non-diabetic mother with increased admission to WBN indicating that certain complications do persist in infants born to non-diabetic mother. Identifying those complications and studying their long and short-term effects of the health of child is necessary.

Various studies have reported that macrosomia is influenced by the sex of the infant. Male infants tend to have higher weight [27, 28]. However, we observed contradictory results. In our study, macrosomic newborns were predominantly females. The reason for this discrepancy is not known and needs to be investigated.

The prime limitation of our study is its retrospective design. As a consequence the data set available for both mother and infant was rather limited. Data on maternal age, weight, glycemic status of infants, and other risk factors governing macrosomia were unavailable. Moreover, we were unable to control for all the possible maternal risk factors. Further prospective study is necessary where all the risk factors associated with macrosomia would be assessed to delineate the predictive risk parameters for various morbidities in macrosomic infants.

Conclusions

This study highlights that most macrosomic neonates are born to non-diabetic mothers. Although the maternal and neonatal complications are less macrosomic infants are not completely healthy. Diabetes complicates the maternal and neonatal outcome. However, further investigations into the complications of non-diabetic infants are required and its short and long term effects on infants health should be studied.

Corresponding author
Hassan Al-Shehri
Department of Pediatrics, College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University, Riyadh, Saudi Arabia, P.O. Box: 7544, Riyadh 13317-4233, Kingdom of Saudi Arabia.
E-mail: dr.h.alshehri@hotmail.com

References

1. Allahyar J MKaMM: An increasing proportion of infants weight more than 4000g at birth. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 2010, 40:931-936.
2. Henriksen T: The macrosomic fetus: a challenge in current obstetrics. *Acta obstetricia et gynecologica Scandinavica* 2008, 87(2):134-145.
3. Koyanagi A, Zhang J, Dagvadorj A, Hirayama F, Shibuya K, Souza JP, Gulmezoglu AM: Macrosomia in 23 developing countries: an analysis of a multicountry, facility-based, cross-sectional survey. *Lancet* 2013, 381(9865):476-483.
4. Gregory KD, Henry OA, Ramicone E, Chan LS, Platt LD: Maternal and infant complications in high and normal weight infants by method of delivery. *Obstetrics and gynecology* 1998, 92(4 Pt 1):507-513.
5. Oral E, Cagdas A, Gezer A, Kaleli S, Aydinli K, Ocer F: Perinatal and maternal outcomes of fetal macrosomia. *European journal of obstetrics, gynecology, and reproductive biology* 2001, 99(2):167-171.
6. Wollschlaeger K, Nieder J, Koppe I, Hartlein K: A study of fetal macrosomia. *Archives of gynecology and obstetrics* 1999, 263(1-2):51-55.
7. A. O: Prenatal origin of obesity and their complications: gestational diabetes, maternal overweight and the paradoxical effects of fetal growth restriction and macrosomia. *Reprod Toxicol* 2011, 32(2):205-212.
8. Boney CM, Verma A, Tucker R, Vohr BR: Metabolic syndrome in childhood: association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics* 2005, 115(3): e290-296.
9. Hermann GM DL, Haskell SE, Roghair RD: Neonatal macrosomia is an independent risk factor for adult metabolic syndrome. *Neonatology* 2010, 98(3):238-244.
10. Boulet SL, Salihu HM, Alexander GR: Mode of delivery and birth outcomes of macrosomic infants. *Journal of obstetrics and gynaecology: the journal of the Institute of Obstetrics and Gynaecology* 2004, 24(6):622-629.
11. Heiskanen N, Raatikainen K, Heinonen S: Fetal macrosomia--a continuing obstetric challenge. *Biology of the neonate* 2006, 90(2):98-103.
12. Mathew M, Machado L, Al-Ghabshi R, Al-Haddabi R: Fetal macrosomia. Risk factor and outcome. *Saudi medical journal* 2005, 26(1):96-100.
13. Ouzounian JG, Hernandez GD, Korst LM, Montoro MM, Battista LR, Walden CL, Lee RH: Pre-pregnancy weight and excess weight gain are risk factors for macrosomia in women with gestational diabetes. *Journal of perinatology: official journal of the California Perinatal Association* 2011, 31(11):717-721.
14. Yajnik CS, Deshmukh US: Maternal nutrition, intrauterine programming and consequential risks in the offspring. *Reviews in endocrine & metabolic disorders* 2008, 9(3):203-211.
15. Zamorski MA, Biggs WS: Management of suspected fetal macrosomia. *American family physician* 2001, 63(2):302-306.
16. Al-Nozha MM, Al-Maatouq MA, Al-Mazrou YY, Al-Harthi SS, Arafah MR, Khalil MZ, Khan NB, Al-Khadra A, Al-Marzouki K, Nouh MS *et al*: Diabetes mellitus in Saudi Arabia. *Saudi medical journal* 2004, 25(11):1603-1610.

17. Ardawi MS, Nasrat HA, Jamal HS, Al-Sagaaf HM, Mustafa BE: Screening for gestational diabetes mellitus in pregnant females. *Saudi medical journal* 2000, 21(2):155-160.
18. Khwaja SS, al-Suleiman SA, al-Sibai MH: Screening for gestational diabetes in a teaching hospital in Saudi Arabia. *The Australian & New Zealand journal of obstetrics & gynaecology* 1989, 29(3 Pt 1):209-211.
19. Shahnaz Nadir SJ, Mohammed Hamid: The prevalence of macrosomia in newborns and its association with maternal diabetes. *J Med Sci* 2015, 23(1):3-6.
20. McFarland MB, Trylovich CG, Langer O: Anthropometric differences in macrosomic infants of diabetic and nondiabetic mothers. *The Journal of maternal-fetal medicine* 1998, 7(6):292-295.
21. Linder N LY, Kogan A, Fridman E, Kouadio F, Melamed N, Yogev Y, Klinger G: Macrosomic newborns of non-diabetic mothers: anthropometric measurements and neonatal complications. *Arch Dis Child Fetal Neonatal Ed* 2014, 99(5): F353-358.
22. Das S, Irigoyen M, Patterson MB, Salvador A, Schutzman DL: Neonatal outcomes of macrosomic births in diabetic and non-diabetic women. *Archives of disease in childhood Fetal and neonatal edition* 2009, 94(6): F419-422.
23. Tala Anwar Al-Awqati FJA-I: Maternal and Neonatal Outcomes in Diabetic and Non-Diabetic Women with Macrosomic Births. *Iraqi J Comm Med* 2012, 1.
24. other Ttodamfpa, senior health workers. Geneva SWHO, http://whqlibdoc.who.int/hq/2003/ Fr, WHO_FCH_CAH_03.7.pdf.
25. Ulf J. Eriksson IS: Diabetes in Pregnancy: Fetal Macrosomia, Hyperinsulinism, and 1slet Hyperplasia in the Offspring of Rats Subjected to Temporary Protein-Energy Malnutrition Early in Life *Pediatric Reseach* 1993, 34(6):791-795.
26. Cucó G1 AV, Iranzo R, Vilà J, Prieto MT, Fernández-Ballart J.: Association of maternal protein intake before conception and throughout pregnancy with birth weight. *Acta Obstet Gynecol Scand* 2006, 85(4):413-421.
27. Linder N, Lahat Y, Kogan A, Fridman E, Kouadio F, Melamed N, Yogev Y, Klinger G: Macrosomic newborns of non-diabetic mothers: anthropometric measurements and neonatal complications. *Archives of disease in childhood Fetal and neonatal edition* 2014, 99(5): F353-358.
28. Laura E. Caulfielda SBH, Elaine A. Whalenc, Mark E. Sugamori: Maternal nutritional status, diabetes and risk of macrosomia among Native Canadian women. *Early Human Development* 1998, 50:293-303.

12/13/2016