The Professional Medical Journal
www.theprofesional.com

https://doi.org/10.29309/TPMJ/2021.28.11.5627

ORIGINAL PROF-0-5627

Glycemic status of infants of Diabetic mothers; a study at the Children's Hospital and Institute of Child Health, Multan.

Abdur Rehman[1], Waqas Imran Khan[2], Ahmad Iqbal Quddusi[3], Aashee Nadeem[4], Nazia Fatima[5], Mubarak Ali Chaudary[6], Imran Iqbal[7]

1. MBBS, DCH, FCPS (Pediatrics), FCPS (Neonatology)
   Assistant Professor Neonatology
   Children Hospital and Institute of Child Health, Multan.
2. MBBS, FCPS (Pediatrics)
   Fellowship in Endocrinology (UK)
   Associate Professor and Head of Endocrinology
   Children Hospital and Institute of Child Health, Multan
3. MBBS, FCPS (Pediatrics)
   Assistant Professor
   Bakhtawar Ameen Medical and Dental College Multan.
4. MBBS, MCPS (Pediatrics)
   Admin Registrar Neonatology
   Children Hospital and Institute of Child Health, Multan.
5. MBBS, FCPS (Pediatrics), FCPS (neonatology)
   Senior Registrar Neonatology
   Children Hospital and Institute of Child Health, Multan.
6. MBBS, FCPS (Pediatrics)
   Head of Pediatrics
   Children Hospital and Institute of Child Health, Multan.
7. MBBS, FCPS (Pediatrics)
   Professor Emeritus
   Children Hospital and Institute of Child Health, Multan.

Correspondence Address:
Dr. Abdur Rehman
Al-Rahim Colony Prince Hotel Street
Nishtar Road Near Nishtar Flyover
Multan.
dr.armalik@outlook.com

Article received on:
15/07/2020
Accepted for publication:
21/09/2020

ABSTRACT… Objective: To find out the frequency of hypoglycemia among infants of diabetic mothers (IDMs) and factors affecting it. **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Neonatology, The Children's Hospital and Institute of Child Health, Multan, Pakistan. **Period:** September 2019 t0 June 2020. **Material & Methods:** A total of 186 IDMs admitted to department of neonatology during the study period were enrolled. Bed side blood glucose (BG) was measured using "Accu Chek Performa Blood Glucose Meter" at 0, 2, 4, 6, 8, 12, 18 and 24 hours of life. All IDMs (Infants of Diabetic Mothers) were labeled either gestational diabetes mellitus (GDM) or pre GDM (pre-GDM). IDMs noted to have hypoglycemia during 1st 24 hours of life were described as hypoglycemic and others were labeled as normoglycemic IDMs. **Results:** Hypoglycemia was noted among 77 (41.4%) IDMs. Duration of disease was significantly more among mothers of hypoglycemic infants (27.62+28.8months vs. 19.69+24.41 months, p=0.0444). Significantly more large for gestational age (LGA) IDMs were found to be hypoglycemic in comparison to normoglycaemic ones (32.5% vs. 16.5%, p=0.0110). Among a total of 77 IDMs noted to have hypoglycemia, 34 (44.1%) were born to mothers who had GDM while remaining 43 (55.9%) were born to pre-GDM mothers. Significantly more IDMs were preterm among pre-GDM mothers when compared to GDM mothers (53.5% vs. 23.5%, p=0.0077). **Conclusion:** Hypoglycemia is frequent problem among IDMs. Increased duration of diabetes among mothers, LGA as well as preterm IDMs are found to have significantly increased risk of developing hypoglycemia.

Key words: Duration of Diabetes, Gestational Diabetes Mellitus, Hypoglycemia, Normoglycaemic, Preterm.

Article Citation: Rehman A, Khan WI, Quddusi AI, Nadeem A, Fatima N, Chaudary MA, Iqbal I. Glycemic status of infants of Diabetic mothers; a study at the Children's Hospital and Institute of Child Health, Multan. Professional Med J 2021; 28(11):1626-1632. https://doi.org/10.29309/TPMJ/2021.28.11.5627

INTRODUCTION

Diabetes mellitus is considered a frequent medical condition during pregnancy.[1] Prevalence of DM during pregnancy is estimated to be between 1-14%.2 DM during pregnancy can be either pre-gestational DM (pre-GDM) or gestational DM (GDM).[3] Incidence of DM is increasing globally and an increase of about 35% was estimated by WHO in the total number of individuals affected by DM from 1995 to 2025.[4] Asian women are noted to have the highest risk of GDM, accounting around 17%.[5,6] As incidence of DM is increasing every minute across all age groups, women of childbearing age are found to have increased chances of DM during pregnancy.

Glucose is vital for normal functions of the brain cells. In newborns, normal blood glucose (BG) level ensures appropriate neurological development.[7] Timely identification of hypoglycemia among neonates at increased risk is essential to avoid complications linked to neonatal hypoglycemia. Factors like birth-weight, gestational age, perinatal complications, mode of delivery as well as feeding behavior are considered important influencing newborn's BG concentration.[8] Most infants of diabetic mothers (IDMs) are thought to have increased chances of hypoglycemia in the 1st post-natal hours.[6] Following stoppage of maternal glucose infusion, chances of hypoglycemia are highest during 1 to 4 hours of age when plasma glucose levels fall.[9,10]

Uncontrolled maternal glycaemia is found to cause neonatal hypoglycemia and/or transient hyperinsulinemia. In utero, maternal hyperglycemia is noted to raise levels of placental glucose transportation and might result in fetal hyperglycemia, which in turn, can stimulate fetal pancreatic insulin synthesis.[11] Following delivery, maternal glucose provision stops but insulin production carries on which might result in to hypoglycemia. Hypoglycemia usually carries on for about 24 to 72 hours up till when insulin secretions turn normal.[12]

Newborns of IDMs need to be screened in the 1st few hours following delivery for the early identification of possible complications.[13] High levels of insulin, low levels of glucagon as well as epinephrine are frequently seen in IDMs. Newborn's glucose production is diminished significantly when compared to normal infants that make them more prone to hypoglycemia.[14]

As timely diagnosis and prompt management in newborns having hypoglycemia is vital to avoid brain damage, the exact burden of hypoglycemia among IDMs needs to be calculated. Regarding this, no recent work is seen locally so we conducted this research to find out frequency of hypoglycemia among IDMs and factors affecting it. Findings of this research will further enlighten our understanding about BG evaluation and risk factors related to IDMs.

MATERIAL & METHODS

This descriptive cross sectional study was conducted at Department of Neonatology, The Children's Hospital and Institute of Child Health, Multan, Pakistan from September 2019 to June 2010 Approval from Institute's Ethical Committee was taken for this research.

A total of 186 IDMs admitted to department of neonatology during the study period were enrolled. IDMs having very low birth weight or extremely low birth weight, with asphyxia, respiratory distress, sepsis, congenital abnormalities and those admitted to intensive care unit (ICU) were not included. Informed consent from parents/ guardians of each study participant was sought. Hypoglycemia was defined as blood sugar < 47 mg/dl (2.6 mmol/l). Bed side BG was measured using "Accu Chek Performa Blood Glucose Meter" at 0, 2, 4, 6, 8, 12, 18 and 24 hours of life. Whole BG concentrations were measured using quantitative amperometric assay.

All study participants were fed with milk initially. IDMs developing hypoglycemia were handled adopting institutional protocol. All IDMs were labeled either GDM or pre-GDM. GDM was described as onset of glucose intolerance during pregnancy while pre-GDM was described as onset of glucose intolerance prior to pregnancy. As per World Health Organization, GDM is defined as at least one abnormal value following 75 gram oral glucose tolerance test. Abnormal values for GDM were described as 92 mg/dl (5.1 mmol/l), 180 mg/dl (10 mmol/l) or 153 mg/dl (8.5 mmol/l) at fasting, 1 hour or 2 hours respectively.[15] IDMs noted to have hypoglycemia during 1st 24 hours of life were described as hypoglycemic and others were labeled as normoglycaemic IDMs.

All the study data was entered on a specially made proforma. SPSS version 24.0 was used for data analysis. Hypoglycemic IDMs and normoglycaemic IDMs were compared. Comparison was also made between GDM and pre-GDM IDMs. Chi square test was employed to compare qualitative variables while independent sample t-test was used to compare quantitative variables. P value less than 0.05 was considered as statistically significant.

RESULTS

In a total of 186 IDMs, hypoglycemia was noted among 77 (41.4%) whereas 109 (58.6%) were normoglycaemic. Table-I is showing maternal and obstetrical characteristics between hypoglycemic and normoglycaemic IDMs. No statistical difference was seem among hypoglycemic or normoglycaemic IDMs in terms of maternal age, gravidity status, antenatal problems, obstetrical complications of ways of management of diabetes ($p>0.05$). Duration of disease was significantly more among mothers of hypoglycemic infants (27.62+28.8months vs. 19.69+24.41 months,

p=0.0444).

Table-II is showing comparison of characteristics of hypoglycemic and normoglycaemic IDMs. Mode of delivery, gender, gestational age, birth weight, gestational period did not seem to make any significant difference in between glycemic status of the IDMs studied (p>0.05). Significantly more large for gestational age (LGA) IDMs were found to be hypoglycemic in comparison to normoglycaemic ones (32.5% vs. 16.5%, p=0.0110).

Among a total of 77 IDMs noted to have hypoglycemia, 34 (44.1%) were born to mothers who had GDM while remaining 43 (55.9%) were born to pre-GDM mothers. Table number 3 showing the comparison of hypoglycemic IDMs among GDM and pre-GDM mothers. No statistically significant difference was observed in terms of maternal age, gravidity status, obstetrical complications or ways of management of diabetes (p>0.05). However, pregnancy-induced hypertension was significantly more prevalent among GDM when compared to IDMs of pre-GDM (17.6% vs. 2.3%, p=0.0202).

Table-IV highlights characteristics of hypoglycemic IDMs with respect to type of diabetes among mothers. Significantly more IDMs were preterm among pre-GDM mothers when compared to GDM mothers (53.5% vs. 23.5%, p=0.0077).

Maternal Characteristics		Hypoglycemic (n=77)	Normoglycaemic (n=109)	P-Value
Maternal Age (years)	<20	8 (10.4%)	7 (6.4%)	0.7778
	>20 to 30	34 (44.2%)	53 (48.6%)	
	>30 to 40	29 (37.7%)	40 (36.7%)	
	>40	6 (7.8%)	9 (8.3%)	
Gravidity Status	Multigravida	58 (75.3%)	79 (72.5%)	0.6641
	Primigravida	19 (24.7%)	30 (27.5%)	
Antenatal Problems	Hypertension	9 (11.7%)	12 (11.0%)	0.8854
	Pregnancy-induced hypertension	7 (9.1%)	8 (7.3%)	0.6657
	Pre-eclamptic toxemia	3 (3.9%)	4 (3.7%)	0.9363
Obstetrical Complications	Abortion	19 (24.7%)	22 (12.8%)	0.4667
	Intrauterine Death	7 (9.1%)	9 (8.3%)	0.8416
	Neonatal Death	6 (7.8%)	8 (7.3%)	0.9082
Management of Diabetes	Drug/Drugs	51 (66.2%)	67 (61.5%)	0.5062
	Diet	26 (33.8%)	42 (38.5%)	
Duration of Diabetes in months (mean+SD)		27.62+28.8	19.69+24.41	0.0444

Table-I. Maternal and obstetrical characteristics between hypoglycemic and normoglycaemic IDMs (n=186)

Characteristics of IDMs		Hypoglycemic (n=77)	Normoglycaemic (n=109)	P-Value
Mode of Deliver	Cesarean Section	68 (88.3%)	94 (86.2%)	0.6778
	Normal Delivery	9 (11.7%)	15 (13.8%)	
Gender	Male	40 (51.9%)	54 (49.5%)	0.7464
	Female	37 (48.1%)	55 (50.5%)	
Gestational Age in Weeks (Mean+SD)		36.84+1.12	36.73+1.25	0.5381
Birth Wight in grams (Mean+SD)		2764.43+513.5	2894.36+563.2	0.1098
Gestational Period	Term	46 (59.7%)	66 (60.6%)	0.9115
	Preterm	31 (40.3%)	43 (39.4%)	
Birth Weight	Normal	64 (83.1%)	78 (71.6%)	0.0677
	Low Birth Weight	13 (16.9%)	31 (28.4%)	
	Appropriate for Gestational Age	52 (67.5%)	91 (83.5%)	0.0110
	Large for Gestational Age	25 (32.5%)	18 (16.5%)	

Table-II. Comparison of characteristics of hypoglycemic and normoglycemic IDMs (n=186)

Maternal Characteristics		GDM (n=34)	Pre-GDM (n=43)	P-Value
Maternal Age (years)	<20	5 (14.7%)	3 (7.0%)	0.7515
	>20 to 30	15 (44.1%)	19 (44.2%)	
	>30 to 40	12 (35.3%)	17 (39.5%)	
	>40	3 (8.8%)	3 (7.0%)	
Gravidity Status	Multigravida	24 (70.6%)	34 (79.1%)	0.3913
	Primigravida	10 (29.4%)	9 (20.9%)	
Antenatal Problems	Hypertension	4 (11.8%)	5 (11.6%)	0.9852
	Pregnancy-induced hypertension	6 (17.6%)	1 (2.3%)	0.0202
	Pre-eclamptic toxemia	2 (5.9%)	1 (2.3%)	0.4232
Obstetrical Complications	Abortion	8 (23.5%)	11 (25.6%)	0.8357
	Intrauterine Death	3 (8.8%)	4 (9.3%)	0.9421
	Neonatal Death	2 (5.9%)	4 (9.3%)	
Management of Diabetes	Drug/Drugs	20 (58.8%)	31 (72.1%)	0.5782
	Diet	14 (41.2%)	12 (27.9%)	
Duration of Diabetes in months (mean+SD)		3.38+2.3	35.28+31.8	<0.0001

Table-III. Maternal characteristics with respect to type of diabetes among hypoglycemic IDMs (n=77)

Characteristics of IDMs		GDM (n=34)	Pre-GDM (n=43)	P-Value
Mode of Deliver	Cesarean Section	30 (88.2%)	38 (88.4%)	0.9852
	Normal Delivery	4 (11.8%)	5 (11.6%)	
Gender	Male	18 (52.9%)	22 (51.2%)	0.8767
	Female	16 (47.1%)	21 (48.8%)	
Gestational Age in Weeks (Mean+SD)		36.92+1.28	36.81+1.21	0.7005
Birth Wight in grams (Mean+SD)		2965.21+524.6	2923.41+521.4	0.7285
Gestational Period	Term	26 (76.5%)	20 (46.5%)	0.0077
	Preterm	8 (23.5%)	23 (53.5%)	
Birth Weight	Normal	27 (79.4%)	37 (86.0%)	0.4402
	Low Birth Weight	7 (20.6%)	6 (14.0%)	
	Appropriate for Gestational Age	20 (58.8%)	32 (74.4%)	0.1467
	Large for Gestational Age	14 (41.4%)	11 (25.6%)	

Table-IV. Characteristics of hypoglycemic IDMs with respect to type of diabetes (n=77)

DISCUSSION

Normal glucose homeostasis is vital for the overall well-being of newborns. Neonatal hypoglycemia has always been labeled as a frequent metabolic disorder among newborns. Hypoglycemia among neonates occurs especially in IDMs because of disturbed gluconeogenesis, mainly due to increased insulin production, declined substrate provision, low glucagon as well as catecholamine secretions.

"Pederson was among the 1st researchers who hypothesized that maternal hyperglycemia progressed into fetal hyperglycemia which further lead to hyper stimulation of the islet cells of the fetal pancreas and to secondary fetal hyperinsulinism.[16] IDMs are thought to have significantly increased risk of developing hypoglycemia. Systemic review done by Alemu BT et al[13] regarding neonatal hypoglycemia among IDMs found IDMs to have significantly increased rate of developing hypoglycemia as compared to neonates born to non-diabetic mothers (8 to 30% vs. 3%). In the present study, we found 41.4% of the IDMs to have hypoglycemia. Begum S et al from Bangladesh[15] witnessed 38.3% of

the newborns to report hypoglycemia. Other researchers have also reported hypoglycemia to be in the range of 25 to 48% among IDMs.[17-19] Kicklighter SD[20] noted about half of the IDMs to have hypoglycemia which is a little more than what we reported in the present study. Difference in diagnostic criteria used by different researchers and access to newborn healthcare facilities could be some of the important reasons for this difference in reported rates of hypoglycemia among IDMs. It was also seen that 80.5% of the IDMs were found to have hypoglycemia in the 1st 6 hours while 62.3% developed hypoglycemia in the 1st 2 hours. Many researchers have found decline in the plasma glucose of newborns following birth while recovery usually starts with 4 to 6 hours.[19,21,22]

In this study, maternal, obstetrical and demographical characteristics of mother and IDMs were not significantly different among hypoglycemic and normoglycaemic cases other than duration of diabetes mellitus (27.62+28.8months vs. 19.69+24.41 months, p=0.0444) and LGA (32.5% vs. 16.5%, p=0.0110) which were found significantly more among hypoglycemic IDMs. Begum S et al[15] have already reported duration of maternal diabetes to be a significant risk factor for the presence of hypoglycemia among newborns. Agarwal RK et al[19] recorded IDMs with hypoglycemia to have significantly increased birth weights and longer duration of maternal diabetes mellitus. Kicklighter SD[20] reported more commonly found among hypoglycemia among IDMs who were marcosomic when compared to appropriate for gestational age newborns. This could be due to hyperinsulinemia which might be secondary to pancreatic islet cells hyperplasia and cessation of the maternal glucose supply at the time of birth.

In the present work, among a total of 77 IDMs noted to have hypoglycemia, 34 (44.1%) were born to mothers who had GDM while remaining 43 (55.9%) were born to pre-GDM mothers. Literature reports 15 to 25% of the neonates to mothers with GDM and 20 to 25% with pre-GDM to have reported hypoglycemia which is less than we noted in the present work.[23] Other regional data have reported 43% of the newborn to GDM and 57% to pre-GDM mothers to have reported hypoglycaemia.[15] We also found improved control of diabetes among pre-GDM mothers when compared to those who had GDM. The reason could be because they were more accustomed and had better experience to control diabetes.

There were few limitations of this study as well. As this was a single center study with a relatively small sample size, further studies in the future are needed to further elaborate maternal, obstetrical and neonatal factors affecting glycemic status among newborns. As neonatal hypoglycemia is also lined with poor neurological outcomes, follow up studies should also be conducted among IDMs to estimate the burden and extent of neurological disorders among these individuals.

CONCLUSION

Hypoglycemia is frequent problem among IDMs. Many of the IDMs were noted have developed hypoglycemia in the 1st 6 hours of life while majority of the IDMs had hypoglycemia in the 1st 2 hours of life. Increased duration of diabetes among mothers, LGA as well as preterm IDMs are found to have significantly increased risk of developing hypoglycemia. Early identification and timely inventions are necessary to ensure favorable outcome in the IDMs.

REFERENCES

1. American Diabetes Association. **Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2020.** Diabetes Care. 2020; 43(Suppl 1):S183-S92.

2. Karcaaltincaba D, Kandemir O, Yalvac S, Guven S, Haberal A. **Prevalence of gestational diabetes mellitus and gestational impaired glucose tolerance in pregnant women evaluated by National Diabetes Data Group and Carpenter and Coustan criteria.** Int J Gynaecol Obstet 2009; 106:246-9.

3. Frise CJ, Williamson C. **Endocrine disease in pregnancy Clinical Medicine.** J. Clin. Med 2013; 13(2):176-81.

4. Ang C, Howe D, Lumsden M. Diabetes. In: James DK, Steer PJ, Weiner CP, Gonik B, editors. **High risk pregnancy management options.** 3rd ed. Philadelphia: Saunders; 2005: p. 986-1004.

5. Ferrara A. **Increasing prevalence of gestational diabetes mellitus: A public health perspective.** Diabetes Care 2007; 302:141-6.

6. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Arthi T, Thamizharasi M. **Prevalence of gestational diabetes mellitus in South India (Tamil Nadu) – A community based study.** J Assoc Physicians India 2008; 56:329-33.

7. Burakevych, N., McKinlay, C.J.D., Harris, D.L. et al. **Factors influencing glycaemic stability after neonatal hypoglycaemia and relationship to neurodevelopmental outcome.** Sci Rep 2019; 9:8132.

8. Hawdon, J. M. **Investigation, prevention and management of neonatal hypoglycaemia (impaired postnatal metabolic adaptation).** Paediatr Child Health (GBR). 2012; 22:131–5.

9. Cornblath M, Schwartz R. **Disorders of carbohydrate metabolism in infancy.** 3rd ed. Philadelphia: W B Saunders; 1991. p.1232-53.

10. Widness JA. **Fetal risks and neonatal complications of diabetes mellitus.** In: Brody SA, Ueland K, Kase N, editors. Endocrine Disorders in Pregnancy. Norwalk, CN: Appleton and Lange; 1989. p.273-97.

11. Straussman S, Levitsky L. **Neonatal hypoglycemia current opinion in endocrinology.** Diabetes Obes 2010; 17:20.

12. McGowan JE. **Neonatal hypoglycemia.** NeoReviews. 1999 Jul; 20(7):e6-15.

13. Alemu BT, Olayinka O, Baydoun HA, Hoch M, Elci MA. **Neonatal hypoglycemia in diabetic mothers: A systematic review.** Curr Pediatr Res 2017; 21(1):42-53.

14. Sperling MA. **Hypoglycemia.** In: Kleigman, Behrman, Jenson, Stanton, editors. Nelson Textbook of Pediatrics. 19th ed. Philadelphia: W B Saunders, Elsevier; 2008. p.517-31.

15. Begum S, Dey SK, Fatema K. **Neonatal glycemic status of infants of diabetic mothers in a tertiary care hospital.** Indian J Endocr Metab 2018; 22:621-6.

16. Catalano PM, Hauguel-De Mouzon S. **Is it time to revisit the Pedersen hypothesis in the face of the obesity epidemic?.** Am J Obstet Gynecol. 2011; 204(6):479-487.

17. Nold JL, Georgieff MK. **Infants of diabetic mothers.** Pediatr Clin N Am 2004; 51:619-37.

18. Alam M, Raza SJ, Sherali AR, Akhtar AS. **Neonatal complications in infants born to diabetic mothers.** J Coll Physicians Surg Pak 2006; 16:212-5.

19. Agrawal RK, Lui K, Gupta JM. **Neonatal hypoglycemia in infants of diabetic mothers.** J Paediatr Child Health 2000; 36:354-6.

20. Kicklighter SD. **Infant of diabetic mother.** E-medicine October 26, 2001. Available from www.emedicine.com/ped/topic485.htm. [Last accessed on 2004 Feb 25].

21. Roberton NRC, Rennie JM. **The infant of diabetic mother.** In: Hawdon JM, Aynsley-Green A, editors. Textbook of Neonatology. 3rd ed. Edinburgh: Churchill Livingstone; 1999. p.401-7.

22. Van Howe RS, Storms MR. **Hypoglycemia in infants of diabetic mothers: Experience in a rural hospital.** Am J Perinatol 2006; 23:105-10.

23. Robart MK, Stanton BF, St. Geme JW, Schor NF, Behrman RE. **Infant of diabetic mother.** In: Carlo WA, editor. Nelson Textbook of Pediatrics, 19th ed. Philadelphia: Elsevier (Saunders); 2012. p.627-9.

AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Abdur Rehman	Abstract, Introduction, Methodology, Discusstion, Resutls.	
2	Waqas Imran Khan		
3	Ahmad Iqbal Quddusi		
4	Aashee Nadeem		
5	Nazia Fatima		
6	Mubarak Ali Chaudary		
7	Imran Iqbal		