*Original Article* *นิพนธ์ต้นฉบับ*

# The Neonatal Hypoglycemia of Term Infants: A Prospective Comparative Study between Well Diet-controlled Gestational Diabetes (GDM A1) and Normal Pregnancy

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**Abstract** The objective of these prospective comparative study was to compare neonatal hypoglycemia and morbidities between term infants born to well diet-controlled gestational diabetes (GDM A1) women and those to normal pregnancy. A total of 41 infants born to GDM A1 women (diabetic group) and 40 infants born to nondiabetic women (control group) at ≥ 37 weeks of gestation at Department of Pediatrics, Somdejprasangkharaj 17th Hospital, Suphan Buri, were randomized into each group. Subjects were monitored for the development of hypoglycemia and other morbidities. Blood glucose screening was performed in diabetic group every 30-60 minutes three times, starting soon after birth and then at 3-hour intervals before each feeding for 24 hours. Breast feedings were started shortly after birth and provided every 3 hours for at least 24 hours. All women with GDM A1 and normal pregnancy had an HbA1c measured before delivery. It was found that there were no differences in demographic characteristics of maternal and infants between the two groups. Mean birth weight of both groups were 3104.6 gm vs 3207.8 gm, macrosomia were 3 infants (7.3%) vs 2 infants (5.0%), birth trauma were 3 infants (7.3%) vs 2 infants (5.0%), hyperbilirubinemia were 5 infants (12.2%) vs 6 infants (15.0%), hematocrit were 59.3 percent vs 52.1 percent. Blood glucose readings before feedings were low (<40 mg/dl) in 12 infants (29.3%) vs 9 infants (22.5%), but those confirmed for hypoglycemia were only 5 infants (12.2%) vs 4 infants (10.0%). However, no significant differences in the odds ratio (1.25; 95% CI 0.31, 5.03; p 0.753) of neonatal hypoglycemia according to diabetic in pregnancy were observed. No infants in either group had symptoms of hypoglycemia and required intravenous dextrose infusion for treatment. Hypoglycemic episodes in the infants from the diabetic group could be managed with oral feedings alone. Based on logistic regression analysis, birth weight, gestational age, sex, Apgar scores, and maternal HbA1c levels could not predict low glucose readings on initial screening in infants from the diabetic group. However, none of all infants had serious morbidities, hypoxic-ischemic encephalopathy, polycythemia, hypocalcemia, or hypomagnesemia. In conclusion, the infants born to the well diet-controlled GDM A1 at ≥ 37 weeks of gestation, the incidence of hypoglycemia and morbidities of infants in the diabetic group was similar to that of the infants born to the nondiabetic women. Low blood glucose levels during the first few hours of life can be prevented or treated with early and frequent oral feedings.

*Key words:* **neonatal hypoglycemia, neonatal morbidities, GDM-A1, gestational diabetes mellitus class A1, diet-controlled, term pregnancy**

## Introduction

The evidence that morbidity rates of type 1 and type 2 diabetes in pregnancy are rising, is largely based on global figures and individual clinicians' reports of younger pregnant women with the condition.[1-3] Until now, the association between gestational diabetes mellitus (GDM) and perinatal outcome is largely based on case series and many retrospective studies that found an increased risk of perinatal mortality and stillbirth as the diagnosis of diabetes approached. Infants born to women with GDM are at increasing risk of fetal macrosomia, neonatal hypoglycemia, hypocalcemia, hypomagnesemia, polycythemia, and hyperbilirubinemia, that remains a significant challenge.[1,3-7]

Because the risks associated with GDM are well recognized, screening and treatment to reduce maternal glucose levels reduce these risks. Most of professional groups, therefore, recommend routine screening, selective screening based on risk factors for gestational diabetes.[8-12] Many studies show that well control of GDM would reduce perinatal complications. Even when only dietary control is effective and maternal glucose levels remain normal, up to 25 percent of infants of women with GDM A1 may have hypoglycemia, hypocalcemia, polycythemia, or hyperbilirubinemia. Especially the high incidence and asymptomatic of hypoglycemia in neonatal period is very important because of the long-term effects of undiagnoses and delay treatment in newborn on brain growth and psychomotor development.[8,9,13,14]

Comprehensive care of infants of GDM women is based on studies that include all infants born to women with different classes of diabetes (classes A through D-R) as a group, and do not take into account the inherent differences between infants born to women with diabetes requiring insulin during pregnancy and infants born to women with diet-controlled GDM A[1,3,5-7,13,14] The infants born at term gestation to women with diet-controlled GDM A1 are less likely to experience the marked excursion in maternal glucose levels that may characterize insulin-requiring GDM A2 or insulin-dependent diabetes (IDDM),[2,3,7,8,14] but this group of infants is commonly managed like any other infants born to women with insulin-requiring GDM or IDDM.

However, no study has demonstrated the risk of neonatal outcome between GDM A1 and normal pregnancy. It was hypothesized that infants born at ≥ 37 weeks of gestation age to GDM A1 women may not have increased incidence of neonatal hypoglycemia and morbidity compared to infants born to nondiabetic pregnancy women and may not require extended routine monitoring of blood glucose or other metabolic problems, if early and frequent feeding practice is followed. Thus, the objective of this study was to compare neonatal hypoglycemia and morbidities between term infants born to well diet-controlled gestational diabetes (GDM A1) women and those to normal pregnancy.

## Methods

The present study randomly assigned population into two 40-pregnancy groups. The first group consisted of infants born at ≥ 37 weeks of gestation to diabetic women between 24 and 28 weeks of gestation who had GDM A1 at Somdejprasangkharaj 17th hospital, as a diabetic group; they were to receive diet-controlled routine care, and had normal blood glucose monitoring, over a period of 2 years. The second group, a control one, consisted of infants born at ≥ 37 weeks of gestation to nondiabetic pregnancy women who had no any other complications. These control group had a normal glucose challenge test (GCT), normal oral glucose tolerance test (OGTT), and normal HbA1c documented. Classification, diagnosis, treatment, and care of GDM were based on the American College of Obstetrics and Gynecology (ACOG) recommendation.[9] All women with diabetic and nor-

mal pregnancy group had an HbA1c measured after admission to the hospital for delivery to determine the adequacy of blood glucose control. Demographic and clinical characteristics of the maternal and the infants, born to women in the diabetic group and the control group, were obtained prospectively from the medical records.

Following the institutional guidelines, infants born to the diabetic women, but the nondiabetic pregnancy women, were admitted to the special care nursery for monitoring of blood sugar, other morbidities, and for earliest and frequent breast or formula feedings. Blood glucose screening was performed in all study infants according to the protocol for infants of GDM A1 women. Blood glucose screening was performed with chromogen reagent strips test (ACCU-CHEK Active) read by a reflectance meter; true serum glucose was measured to confirm hypoglycemic by the glucose oxidase method. The blood glucose screening for the infants in the diabetic group included blood glucose strip test determinations every 30 minutes three times, starting soon after birth and then at 3-hour intervals before each feeding for the next 24 hours. In the control infants, blood glucose strip test monitoring was done three times, the first starting soon after birth and before the start of feeding, the second before the next feeding, and the third before the next feeding at 24 hours. Feedings were started shortly after delivery and were preceeded by the measuremensts of blood glucose. Infant formula or breast feeding every 3 hours was to prevent hypoglycemia in both groups and all infants were observed for at least 24 hours.

If a blood glucose value was low before the first feeding, the test was repeated together with serum glucose level in order to confirm. If the blood glucose level remained abnormally low, or if the infant was symptomatic, it was given an intravenous dextrose infusion.[4,13]

The infants in this study were classified as large for gestational age (LGA), appropriate for gestational age (AGA), and small for gestational age (SGA). LGA infants with birth weight > 4,000 g were defined as macrosomic. Blood glucose strip test readings of ≤ 40 mg/dl were considered to be hypoglycemic and were confirmed by the true serum glucose concentration. Because it is not unusual to observe a single low blood glucose strip test value, the diagnosis of hypoglycemia was based on two consecutive low blood glucose strip test values taken no more than 30 minutes apart and confirmed with a laboratory serum glucose determination.[4,5,13] Hypocalcemia and hypomagnesemia were defined as total serum calcium concentration < 6 mg/dl and serum magnesium < 1.2 mg/dl, respectively.[13] Polycythemia was defined as a central hematocrit greater than 65 percent and hyperbilirubinemia as an indirect bilirubin level > 12 mg/dl and/or any jaundice requiring phototherapy.[15]

According to the protocol, hematocrit, serum calcium, magnesium, and phosphorus were measured in infants from the diabetic group once between 12 and 24 hours after birth, and the collection of specimens was timed according to blood glucose monitoring. Control infants were observed clinically for signs of polycythemia, hypocalcemia, and hypomagnesemia. Infants from both groups who required intravenous dextrose infusion soon after birth for indications other than hypoglycemia were excluded from present study.

The present study recruited 40 cases, who were admitted to the Somdejprasankharaj 17th hospital for delivery, in each group because of the least sample size was 39 cases which calculated from pilot study with 30 cases in each group, based on incidence of neonatal hypoglycemia, 5% (2-tailed) error type I and 20% (1-tailed) error type II of principal variable. The data was collected between October 2009 and September 2011. Of these, 40 with a gestational age ≥ 37 weeks had well strictly controlled diabetic group and

40 matched nondiabetic pregnancy women served as controls. Interested variables in this study included maternal factors; age, height, body weight, parity, abortion, HbA1c, residence, occupation, previous cesarean section, and infant factors; birth weight, gestational age, mode of delivery, sex, Apgar score, Ballard's score, macrosomia (birth weight > 4 kg), birth trauma, admitted to neonatal intensive care unit (NICU), respiratory distress syndrome, hyperbilirubinemia, hematocrit, serum calcium, serum magnesium, serum phosphorus and blood glucose protocol as above. Statistical analyses were performed to evaluate associations between independent and dependent variables of interest. Data were shown as frequency, percentage, and mean, SD where applicable. The unpaired t-test, Fisher's exact test, $X^2$ test, odds ratio with confidence interval at 95 percent, were used to analyze the variables as appropriate. Logistic regression analysis was used to test the contribution of birth weight, gestational age, sex, Apgar scores, Ballard's score, and maternal HbA1C levels for the prediction of low blood glucose strip test values on initial screening for blood glucose before the start of the first feedings in infants from the diabetic group. A p-value of less than 0.05 was considered to be statistically significant. Present study was approved by the human research ethics committee of Somdejprasangkharaj 17th hospital. The patients gave written informed consent and were adviced about evaluation through monitoring all about morbidities and the blood testing of their newborns.

## Results

The diabetic women had 41 infants; 39 singleton births and one set of twins, while all the nondiabetic pregnancy women had 40 infants; 40 singleton pregnancies. There were no differences in demographic characteristics variable of maternal and infant factors between the two groups (Table 1-2). The average ages were 27.08, 7.16 years (diabetic group) and 29.58, 6.55 years (control group). Most of the women were in Suphan Buri province (87.5%, 82.5%) and especially in Song Phi Nong district (50.0%, 45.0%). None of them had severe maternal morbidities, severe neonatal morbidity and neonatal death, but 3 and 4 infants had only thin meconeum stain, respectively, and one of each group was septic at birth.

A total of 41 infants born to diabetic group and 40 infants born to control group at ≥ 37 weeks of gestation were prospectively included. Infants of both the diabetic and control groups were similar in birth weight, gestational age, mode of delivery, sex ratio (Table 2), Apgar score, pattern of Ballard's score, fetal macrosomia, birth trauma, respiratory distress syndrome, hyperbilirubinemia, hematocrit, serum calcium, serum magnesium, and serum phosphorus (Table 3). All of infants from both groups had an Apgar score ≥ 7 at 5 minutes and none had any clinical evidence of hypoxic-ischemic encephalopathy. Hyperbilirubinemia infants requiring phototherapy were 5 (12.2%) and 6 (15.0%), respectively, two of each group also had ABO incompatability. The incidence of hyperbilirubinemia was similar in both groups.

None of the 41 infants from the diabetic group were polycythemic and none had hypocalcemia or hypomagnesemia. Hematocrit values in all infants from the diabetic group were 53.3, 3.5 percent; only 4 of the 41 infants had hematocrit values of ≥ 60 percent. Serum calcium and magnesium values in all infants from the diabetic group were 9.3, 0.7 mg/dl and 1.7, 0.2 mg/dl, respectively. None of the control infants had clinical signs of polycytehmia, hypocalcemia, or hypomagnesemia. In 3 of 10 of the infants in the diabetic group, who were LGA, had birth trauma: forceps mark, subconjunctival hemorrhage, and cephalhematoma. In 2 of 8 of the control group, who were LGA, had birth trauma: cephalhematoma, and Erb's palsy, complete recovery one month later. The incidence of birth injury were no significant difference in

**Table 1** Baseline maternal demographic data

| Variable | | GDM A1 group n=40 | Control group n=40 | p-value |
|---|---|---|---|---|
| Age (y) | | 27.08, 7.16 | 29.58, 6.55 | 0.107[#1] |
| Height (cm) | | 146.2, 48.1 | 157.8, 65.4 | 0.369[#1] |
| Body weight (kg) | | 65.8, 8.8 | 63.1, 7.5 | 0.144[#1] |
| Parity | | 2.4, 0.8 | 2.6, 1.1 | 0.364[#1] |
| Abortion | | 0.5, 0.6 | 0.8, 0.8 | 0.061[#1] |
| Previous history of Cesarean section | | 11 (27.5) | 17 (42.5) | 0.279[#2] |
| HbA1c (%) | | 6.3, 0.6 | 5.7, 1.2 | 0.092[#1] |
| Residences | Mueang Suphan Buri | 3 (7.5) | 5 (12.5) | 0.891[#2] |
| | Song Phi Nong district | 20 (50.0) | 18 (45.0) | |
| | U Tthong district | 12 (30.0) | 10 (25.0) | |
| | Others | 5 (12.5) | 7 (17.5) | |
| occupation | Government official | 9 (22.5) | 13 (32.5) | 0.670[#2] |
| | Merchant | 12 (30.0) | 8 (20.0) | |
| | Employee & Farmers | 7 (17.5) | 8 (20.0) | |
| | Housewife | 7 (17.5) | 6 (15.0) | |
| | Others | 5 (12.5) | 5 (12.5) | |

*p-value < 0.05(significant), [#1] unpaired t-test, [#2] chi-square test*
*Data were present as mean, SD or n (%) and p-value as appropriate*

**Table 2** Baseline infant demographic data

| Variable | | GDM A1 group n=41* | Control group n=40 | p-value |
|---|---|---|---|---|
| Birth weight (gm) | | 3104.6, 373.6 | 3207.8, 414.3 | 0.246[#1] |
| Gestational age (weeks) | | 38.2, 1.6 | 38.8, 1.2 | 0.061[#1] |
| Mode of delivery | Cesarean section | 12 (29.3) | 10 (25.0) | 0.666[#2] |
| | Vaginal delivery | 29 (70.7) | 30 (75.0) | |
| Sex | Male | 22 (53.7) | 19 (47.5) | 0.579[#2] |
| | Female | 19 (46.3) | 21 (52.5) | |

*p-value < 0.05 (significant), [#1] unpaired t-test, [#2] chi-square test*
*Data were present as mean, SD or n (%) and p-value as appropriate*
**GDM A1 group had 1 twin pregnancy from 40 women, so the number of infants totally was 41 cases*

both group. None of all infants had any congenital anomaly.

There was no significant difference in the value of blood glucose strip test, started 30-60 minutes of age before first feedings. Twelve (29.3%) of the infants from the diabetic group and nine (22.5%) of the infants from the control group showed low levels of blood glucose (<40 mg/dl) (Table 5). Then the serum

**Table 3** Clinical data on neonatal outcomes

| Variables | GDM A1 group n=41* | Control group n=40 | p-value |
|---|---|---|---|
| Apgar score > 7 at 5 min | 37 (90.2) | 39 (97.5) | 0.175[#3] |
| Ballard's score AGA | 26 (63.4) | 28 (70.0) | 0.785[#2] |
| LGA | 10 (24.4) | 8 (20.0) | |
| SGA | 5 (12.2) | 4 (10.0) | |
| Macrosomia (birth wt ≥ 4 kg) | 3 (7.3) | 2 (5.0) | 0.665[#3] |
| Birth trauma | 3 (7.3) | 2 (5.0) | 0.684[#3] |
| Admit to NICU | 3 (7.3) | 4 (10.0) | 0.692[#3] |
| Respiratory distress syndrome | 1 (2.4) | 1 (2.5) | NS |
| Hyperbilirubinemia (n, %) | 5 (12.2) | 6 (15.0) | 0.713[#2] |
| Hematocrit (%) | 53.3, 3.5 | 52.1, 2.5 | 0.082[#1] |
| Serum calcium (mg/dl) | 9.3, 0.7 | 9.1, 0.4 | 0.121[#1] |
| Serum magnesium (mg/dl) | 1.7, 0.2 | 1.8, 0.3 | 0.083[#1] |
| Serum phosphorus (mg/dl) | 4.8, 0.4 | 5.0, 0.7 | 0.121[#1] |

*p-value < 0.05(significant), [#1] unpaired t-test, [#2] chi-square test, [#3] chi-square with Yates' correction test*
*Data were present as mean, SD or n (%) and p-value as appropriate*
**GDM A1 group had 1 twin pregnancy from 40 women, so the number of infants totally was 41 cases*

**Table 4** All blood glucose value of strip test before start of first feeding and every 3-hour intervals after birth.

| Time after birth (monitor blood strip test) | GDM A1 group n=41 (mg/dl) | Control group n=40 (mg/dl) |
|---|---|---|
| 30 minutes (before start of first feeding) | 52.3, 16.7 | 51.6, 10.2 |
| 60 minutes | 54.8, 10.2 | |
| 90 minutes | 56.1, 13.3 | |
| 3 hours | 66.3, 11.4 | 59.8, 20.1 |
| 6 hours | 61.4, 13.9 | |
| 9 hours | 64.8, 10.5 | |
| 12 hours | 59.4, 11.3 | |
| 15 hours | 55.9, 20.9 | |
| 18 hours | 66.8, 19.2 | |
| 24 hours | 67.3, 13.9 | 63.4, 14.3 |

*Data were present as mean, SD*

glucose being done to confirm true hypoglycemia were shown only 5 (12.2%) and 4 (10.0%) infants, respectively. Also, there were no significant differences in the odds ratio by strip test (OR 1.43; 95% CI 0.52, 3.88; p 0.488) and confirm by serum glucose (OR 1.25; 95% CI 0.31, 5.03; p 0.753) of neonatal hypoglycemia according to diabetic in pregnancy were observed. After the start of oral feedings, in all but five infants in the diabetic group, subsequent blood glucose strip test obtained over a 24-hour period were ≥ 40 mg/dl.

**Table 5** Blood glucose data before start of first feeding, 3-hour, and 24-hour intervals after birth and low blood glucose condition.

| Parameters | GDM A1 group n=41 | Control group n=40 | p-value |
|---|---|---|---|
| **Blood glucose strip test (mg/dl)** | | | |
| before start of feedings | 52.3, 16.7 | 51.6, 10.2 | 0.822[#1] |
| 3 hours after birth | 66.3, 11.4 | 59.8, 20.1 | 0.079[#1] |
| 24 hours after birth | 67.3, 13.9 | 63.4, 14.3 | 0.219[#1] |
| **Low blood glucose condition** | | | |
| Low blood glucose strip test readings (< 40 mg/dl) before start of first feedings | 12 (0.29) | 9 (0.23) | 0.488[#2] |
| Odds ratio 1.43 95% CI 0.52, 3.88 | | | |
| True hypoglycemia (confirm by serum glucose < 40 gm/dl) | 5 (0.12) | 4 (0.10) | 0.753[#2] |
| Odds ratio 1.25 95% CI 0.31, 5.03 | | | |

*p-value < 0.05(significant), [#1] unpaired t-test, [#2] odd ratio (95% CI)*
*Data were present as mean, SD or n (%) and p-value as appropriate*
**GDM A1 group had 1 twin pregnancy from 40 women, so the number of infants totally was 41 cases*

None of the 41 infants from the diabetic group had symptoms of hypoglycemia. In the five (12.2%) infants in the diabetic with initial low blood glucose strip test values, the glucose readings obtained half an hour after the first feeding were higher than before and were > 40 mg/dl, and were normal for all subsequent feedings during a subsequent period of 24 hours. In the four (10.0%) infants of the control group who had low blood glucose strip test and been confirmed before the start of the first feedings, the blood glucose strip test values rose to ≥ 40 mg/dl when measurements were repeated one-half hour after the first feeding. None of the infants from the diabetic group and the control group became symptomatic for hypoglycemia and required intravenous dextrose infusion.

HbA1c values in diabetic women, whose infants were enrolled for present study, were 6.3, 0.6% and nondiabetic pregnancy were 5.7, 1.2%. The p-value of logistic regression, that test for the contribution of birth weight, gestational age, sex, Apgar scores, Ballard's score, and maternal HbA1C levels for the prediction of low blood glucose strip test values on initial screening for blood glucose before the start of the first feedings in infants in the diabetic group, was 0.831. These show that not any of those independent variables were correlated with neonatal hypoglycemia.

## Discussion

The GDM prevalence remained constant at 7.5 percent in 1999 to 7.4 percent in 2005.[16] However, the increase in preexisting diabetes, particularly among younger women early in their reproductive years, is of concern. Therefore, pregnant women with abnormal value of oral glucose tolerance test (OGTT) at 24 to 28 weeks of gestation had a significantly greater risk of developing GDM and should have planned for treatment, prognosis and neonatal outcome.[17,18] Infants of diabetic mothers (IDDM) have experienced a nearly 30-fold decrease in morbidity and mortality rates since the development of specialized maternal, fetal, and neonatal care for women with diabetes and their offspring. Before then, fetal and neonatal mor-

tality rates were as high as 65 percent. Today, 3-10 percent of pregnancies are affected by abnormal glucose regulation and control. Of these cases, 80-88 percent are related to abnormal glucose control of pregnancy or gestational diabetes mellitus.[13,19] Although there has been continuing improvement in outcome for infants born to diabetic mothers, these infants remain a high-risk population.

Despite evidence the poor diet-controlled and classes of GDM were related to the severity of morbidity of neonatal outcome, the present study showed that the neonatal morbidity in infants born to GDM A1 women, with well diet-controlled, and nondiabetic pregnancy women were similar. Unlike infants of insulin-dependent diabetic an insulin-requiring GDM women, infants born to GDM A1 women at ≥ 37 weeks of gestation, and who are otherwise healthy, are not at increased risk of developing hypoglycemia, hypocalcemia, hypomagnesemia, plycythemia, hyperbilirubinemia, birth trauma, or birth asphyxia.

The definition of clinically significant hypoglycemia remains one of the most contentious issues in contemporary neonatology.[20] It is not possible to define a blood glucose level that requires intervention in every newborn infant because there are uncertainties over the level and duration of hypoglycemia that can cause damage, and little is known of the vulnerability, or lack of it, in the brain of infants at different gestational age. The standard of care in most neonatology units involves close surveillance if the plasma glucose concentration is less than 40 mg/dl.[13] Intervention is recommended if plasma glucose remains below this level, if the level dose not increase after a feed, or if abnormal clinical signs develop.

The reduction of blood glucose levels during pregnancy in women with diet-controlled GDM A1 has led to a low incidence of transient hypoglycemia infants. This low incidence of hypoglycemia in infants from the diabetic group is not different from that of the control group in the present study, nor from the reported incidence of transient hypoglycemia that affects up to about 3 percent of apparently healthy term infants born to nondiabetic pregnancy women.[4] In addition, three measures are critical. The first was aggressive measures for self monitor blood glucose and self diet-controlled at home by diabetic pregnancies, the second was close fetal monitoring for hypoglycemic and the others morbidities of infants, and the third was early breastfeeding is established, milk becomes the main source of sugar for the baby. The lactose sugar in milk is converted to glucose and infant will also start to store glucose for between feeds.[21,22] Winning those three measures were our biggest challenge to achieving success in prevention of morbidities outcome.

Data from the medical literature have shown that at birth and umbilical cord plasma glucose levels correlate with maternal values.[23] In most cases, blood glucose levels decrease during the first 2 hours of life and then start to rise and stabilize.[4] In the present study, both the diabetic and control groups had a similar incidence of low blood glucose strip test (OR 1.43 95%CI 0.52, 3.88; p 0.488) and repeated low blood glucose strip test (OR 1.25 95%CI 0.3, 5.03; p 0.753). All these hypoglycemic episodes in the diabetic group could be successfully treated with oral feedings. None of the infants from both the diabetic and control groups were symptomatic or required intravenous dextrose infusion.

Approximately half of the infants of pre-existing diabetic and GDM women develop early transient hypocalcemia[5,16,17] and hyperphosphatemia[24]. It is speculated that relative maternal hyperparathyroidism leading to fetal hypoparathyroidism may be a factor in the pathogenesis of neonatal hypocalcemia and hyperphosphatemia. Often, hypocalcemic infants display low serum magnesium values.[4,6,7,24] Although the cause for the high incidence of this complication

is unclear, it is well recognized that it relates to the severity of maternal diabetes, and perinatal distress. Polycythemia, hyperbilirubinemia, and macrosomia have been reported in a greater proportion of infants of diabetic women than infants in the general population.[1-3,13,19] Birth trauma, resulting from mechanical forces (ie, compression, traction) during the birth process, accounts for < 2 percent of neonatal deaths and stillbirths, and had higher rates for infants who weighed more than 4,500 gm, which is in part related to efficacy of maternal glucose control.[13] Although totally 5 (6.2%) macrosomic infants were found in both groups 3 (7.3%) in diabetic group and 2 (5.0%) in control group-those showed no significant difference. These show that the risk of LGA or birth trauma in the diabetic women was not more than that of the nondiabetic pregnancy women. Risk factors of birth trauma included not only large infants, but also the pelvic cavity being compared to the infant size. However; no serious adverse fetal outcomes were reported in the present study. This might be the result of effective treatment, by diet-controlled protocol and blood glucose monitoring before delivery, in diabetic group of Somdejprasangkharaj 17th hospital. The infants of women with diet-controlled GDM A1 are less likely to experience the marked excursion in maternal glucose levels, thereby explaining the small number of macrosomic infants and the low frequency of other morbidities which approached that of infants of nondiabetic pregnancy women in the present study.

This study also revealed that the infants, born to GDM A1 at ≥ 37 weeks of gestation, do not have any maternal or infant factors that could predict the neonatal hypoglycemia, and no more increasing incidence of neonatal hypoglycemia and morbidities than nondiabetes women. Morever, routine monitoring of such infants for blood glucose for an extended period adds unjustified laboratory and personnel expense, is traumatic to the newborn infants, and prolongs their length of stay in the NICU. Unlike infants born to insulin-requiring GDM A2 or insulin-dependent diabetic women, infants born to GDM A1 women can be managed like any other normal term infant born to a nondiabetic pregnancies. They do not require routine glucose monitoring after the first 2-3 hours of life, and low blood glucose strip test readings or hypoglycemia in them during the first few hours after birth can be prevented and managed with early and frequent oral feeding.[13,21,22] However, results for these outcomes should be interpreted with caution, since the analysis included only a subgroup of the women.

## Conclusion

*Women with GDM A1 who are diagnosed and treated following treatment guidelines, overall pregnancy, demonstrate no incidence of neonatal hypoglycemia and severe neonatal complications and can be comparable to those with nondiabetic pregnancies.*

### Reference


1. Wood SL, Sauve R, Ross S, Brant R, Love EJ. Prediabetes and perinatal mortality. Diabetes Care 2000; 23(12):1752-4.
2. Cundy T, Gamble G, Townend K, Henley PG, MacPherson P, Roberts B. Perinatal mortality in type 2 diabetes mellitus. Diabetic Med 2000;17(1):33-9.
3. Macfarlane A, Tuffnell D. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. BMJ 2006;333(7560); 157-8.
4. Cordero L, Landon MB. Infant of diabetic mother. Clin Perinatol 1993;20:635-47.
5. DeMarini S, Mimouni F, Tsang RC. Impact of metabolic control of diabetes during pregnancy on neonatal hypocalcemia. Obstet Gynecol 1994;83:918-21.
6. Weintrob N, Karp M, Hod M. Short- and long-range complications in offspring of diabetic mothers. J Diabetes Complications 1996;10(5):294-301.
7. Nasrat HA, Salleh M, Ardawi M, Ghafouri H. Outcome of pregnancy in diabetic mothers. Int J Gynecol Obstet 1993;43(1):29-34.

8. Hoffman L, Nolan C, Wilson JD, Oats JJ, Simmons D. Gestational Diabetes Mellitus Management Guidelines: the Australian Diabetes in Pregnancy Society. Med J Aust 1998;169:93-7.
9. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, December 1994) gestational diabetes. Obstet Gynecol 2001:98(3):525-38.
10. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus: The Organizing Committee. Diabetes Care 1998;21(suppl 2):B161-7.
11. American Diabetes Association. Gestational diabetes mellitus. Diabetes Care 2002;25(suppl 1):S94-6.
12. Scott DA, Loveman E, McIntyre L, Waugh N. Screening for gestational diabetes: a systematic review and economic evaluation. Health Technol Assess 2002; 6(11):1-161.
13. Barnes-Powell LL. Infants of diabetic mothers: the effects of hyperglycemia on the fetus and neonate. Neonatal Netw 2007;26(5):283-90.
14. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Australian carbohydrate intolerance study in pregnant women (ACHOIS) trial group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352(24): 2477-86.
15. Cordero L, Treuer SH, Landon MB, Gabbe SG. Management of infants of diabetic mother. Arch Pediatr Adolesc Med 1998;152(3):249-54.
16. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care 2008;31(5):899-904.
17. Thanasuan S, Borriboonhirunsarn D. Incidence of gestational diabetes mellitus among pregnant women with one abnormal value of oral glucose tolerance test. J Med Assoc Thai 2006:89(8);1109-14.
18. Berkus MD, Langer O. Glucose tolerance test: degree of glucose abnormality correlates with neonatal outcome. Obstet Gynecol 1993;81(3):344-8.
19. Plagemann A. A matter of insulin: developmental programming of body weight regulation. J Matern Fetal Neonatal Med 2008;21(3):143-8.
20. Comblath M, Hawdon JM, Williams AF, Aynsley-Green A, Ward-Platt MP, Schwartz R, et al. Controversies regarding definition of neonatal hypoglycemia: suggested operational thresholds. Pediatrics 2000; 105(5):1141-5.
21. Fetus and Newborn Committee. Canadian Pediatric Society. Checking blood glucose in newborn babies. Pediatrics & Child Health 2004;9(10):731-2.
22. Canadian Paediatric Society, Fetus and Newborn Committee [Principal authors: K Aziz, P Dancey]. Screening guidelines for newborns at risk for low blood glucose. Paediatr Child Health 2004;9:723-40.
23. Srinivasan G, Pildes RS, Cattamanchi G, Voora S, Lilien LD. Plasma glucose values in normal neonates: a new look. J Pediatr 1986;109(1):114-7.
24. Tsang RC, Kleinman LI, Sutherland JM, Light IJ. Hypocalcemia in infants of diabetic mothers. Studies in calcium, phosphorus, and magnesium metabolism and parathormone responsiveness. J Pediatr 1972;80(3): 384-95.

**บทคัดย่อ** **ภาวะน้ำตาลในเลือดต่ำของทารกแรกเกิด: การศึกษาแบบไปข้างหน้าเปรียบเทียบ ระหว่างทารกอายุครรภ์ครบกำหนดที่คลอดจากสตรีตั้งครรภ์ที่มีเบาหวานในขณะตั้งครรภ์ (GDM A1) ที่รักษาด้วยการควบคุมอาหารกับจากสตรีตั้งครรภ์ปรกติ**

**สุภาพร สุทัศนทรวง**

กลุ่มงานกุมารเวชกรรม โรงพยาบาลสมเด็จพระสังฆราชองค์ที่ 17 อำเภอสองพี่น้อง สุพรรณบุรี

*วารสารวิชาการสาธารณสุข* **2555; 21:346-56.**

วัตถุประสงค์ของการศึกษาแบบ prospective comparative นี้ เพื่อเปรียบเทียบภาวะน้ำตาลในเลือดต่ำและภาวะแทรกซ้อนของทารกแรกเกิดอายุครรภ์ครบกำหนดที่คลอดจากสตรีตั้งครรภ์ที่มีเบาหวานในขณะตั้งครรภ์ (GDM A1) ที่รักษาด้วยการควบคุมอาหารได้ดี จากสตรีตั้งครรภ์ปรกติ โดยได้สุ่มเลือกทารกอายุครรภ์เท่ากับหรือมากกว่า 37 สัปดาห์ ในแผนกกุมารเวชกรรม โรงพยาบาลสมเด็จพระสังฆราชองค์ที่ 17 สุพรรณบุรี ที่คลอดจากสตรีตั้งครรภ์ที่มีเบาหวานในขณะตั้งครรภ์ชนิด A1 และรักษาด้วยการควบคุมอาหารได้ผลดี จำนวน 41 คน (กลุ่มทดลอง) และจากสตรีตั้งครรภ์ปรกติ (กลุ่มควบคุม) จำนวน 40 คน ด้วยการเฝ้าติดตามการเกิดภาวะน้ำตาลในเลือดต่ำและภาวะแทรกซ้อนอื่น ๆ ในทารกแรกเกิด ได้ตรวจคัดกรองระดับน้ำตาลในเลือดของทารกกลุ่มที่มารดาเป็นเบาหวานทุก 30-60 นาที 3 ครั้งทันทีหลังคลอด และรีบเริ่มให้นมมารดาให้เร็วที่สุดหลังคลอดและแบ่งให้ทุก 3 ชั่วโมงจนครบ 24 ชั่วโมง แล้วตรวจระดับน้ำตาลในเลือดซ้ำทุก 3 ชั่วโมงก่อนเริ่มให้นมจนครบรอบ 24 ชั่วโมง ตรวจหาระดับ HbA1c ในวันคลอดในสตรีทุกคนทั้งสองกลุ่ม ผลของการศึกษานี้แสดงว่า ไม่มีความแตกต่างกันในลักษณะของประชากรที่ศึกษาระหว่างทั้งสองกลุ่ม ทั้งลักษณะของมารดาและทารกแรกเกิด ผลของน้ำหนักทารกแรกคลอดจากทั้งสองกลุ่มคือ 3,104.6 กรัม เทียบกับ 3,207.8 กรัม ทารกตัวใหญ่มาก 3 ราย (7.3%) เทียบกับ 2 ราย (5.0%) ทารกบาดเจ็บจากการคลอด 3 ราย (7.3%) เทียบกับ 2 ราย (5.0%) ภาวะทารกตัวเหลือง 5 ราย (12.2%) เทียบกับ 6 ราย (15.0%) ความเข้มข้นเลือด ร้อยละ 59.3 เทียบกับ ร้อยละ 52.1 ผลการคัดกรองระดับน้ำตาลในเลือดทารกแรกคลอดที่ต่ำกว่า 40 มก/ดล พบมี 12 ราย (29.3%) เทียบกับ 9 ราย (ร้อยละ 22.5) แต่เมื่อตรวจเลือดเพื่อยืนยันระดับน้ำตาลต่ำจากห้องปฏิบัติการพบว่ามีเพียง 5 ราย (ร้อยละ 12.2) เทียบกับ 4 ราย (10.0%) อย่างไรก็ตาม ผลของ odds ratio (1.25; 95% CI 0.31, 5.03; p 0.753) ไม่พบความชุกของการเกิดภาวะน้ำตาลในเลือดต่ำของทารกแรกเกิดในสตรีตั้งครรภ์ที่เป็นเบาหวานชนิด GDM A1 แตกต่างจากสตรีตั้งครรภ์ปรกติ และไม่มีทารกรายใดที่มีอาการน้ำตาลในเลือดต่ำและต้องได้รับการรักษาด้วยการให้สารน้ำตาลทางกระแสเลือด ให้การรักษาเพียงให้สารอาหารทางปากเท่านั้น ตัวแปรต่าง ๆ คือ น้ำหนักทารกแรกคลอด อายุครรภ์ เพศ คะแนน Apgar ระดับ HbA1c ของมารดา ไม่สามารถใช้เป็นตัวทำนายการเกิดภาวะน้ำตาลในเลือดต่ำแรกคลอด (ในกลุ่มทดลอง) อย่างไรก็ตาม จากการศึกษานี้ไม่พบทารกรายใดมีภาวะแทรกซ้อนอย่างรุนแรง เช่น การบาดเจ็บทางสมองจากการขาดออกซิเจน ภาวะเลือดเข้มข้นมาก ภาวะแคลเซียมในเลือดต่ำ หรือ ภาวะแมกนีเซียมในเลือดต่ำ ผลสรุปจากการศึกษานี้ โดยยึดข้อมูลของทารกที่คลอดจากมารดาที่เป็นเบาหวานชนิด A1 ที่ควบคุมอาหารได้ดี และคลอดที่อายุครรภ์มากกว่า 37 สัปดาห์ พบว่า ความชุกของภาวะน้ำตาลทารกในเลือดต่ำแรกเกิด และภาวะแทรกซ้อนของทารกแรกคลอดในกลุ่มทดลอง ไม่ได้มีความแตกต่างจากกลุ่มตั้งครรภ์ปรกติ ดังนั้นจึงอาจจะไม่ต้องให้การดูแลอะไรเป็นพิเศษกว่าทารกทั่วไป และการเกิดภาวะน้ำตาลในเลือดต่ำในช่วง 2-3 ชั่วโมงแรกหลังคลอดของทารกจากมารดาที่เป็นเบาหวานชนิด A1 สามารถป้องกันได้ด้วยการให้ป้อนอาหารทางปากแรกคลอดให้เร็วที่สุด และบ่อย ๆ

***คำสำคัญ:*** **ภาวะน้ำตาลในเลือดต่ำของทารกแรกคลอด, ภาวะแทรกซ้อนทารกแรกเกิด, เบาหวานในสตรีตั้งครรภ์ ชนิด A1, โรคเบาหวานในขณะตั้งครรภ์, รักษาด้วยการควบคุมอาหาร, ตั้งครรภ์ครบกำหนด**