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Original Research

Comparison of the Efficacy of Intensive Insulin Therapy Regimens for Type A2 Gestational Diabetes Mellitus and Their Effects on Maternal and Infant Metabolic Indices

Xueqin Yin[1,†], Yongqiang Gao[2,†], Yan Liu[3,*]

[1]Department of Obstetrics, Puer People's Hospital, 665000 Puer, Yunnan, China
[2]Department of Imaging Medicine and Nuclear Medicine, Puer People's Hospital, 665000 Puer, Yunnan, China
[3]Department of Gynecology, Puer People's Hospital, 665000 Puer, Yunnan, China
*Correspondence: 18082996108@163.com (Yan Liu)
[†]These authors contributed equally.
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Abstract

Background: Type A2 gestational diabetes mellitus (A2GDM) is a challenging subtype of gestational diabetes, requiring insulin therapy in addition to exercise and dietary interventions. While multiple daily subcutaneous injections of regular insulin (RI) and insulin pumps are commonly used, their clinical efficacy and impact on maternal and infant metabolic indices remain unclear. **Methods**: This retrospective study included 98 patients with A2GDM admitted to Puer People's Hospital between March 2021 and September 2023. Patients were divided into a control group (n = 41) and an experimental group (n = 57) receiving insulin via an insulin pump. Both groups received treatment until delivery, and treatment efficacy, glucose metabolism, lipid metabolism, and maternal and infant complications were compared. **Results**: Pre-pregnancy, the experimental group had a lower body mass index (BMI) and fewer cases with a family history of diabetes. The experimental group achieved blood glucose targets faster, required a lower insulin dose, and had fewer hypoglycemic events ($p < 0.05$). Post-treatment, the experimental group showed greater improvements in fasting plasma glucose (FPG), 2-hour postprandial blood glucose (2hPBG), glycosylated hemoglobin (HbAlc), and homeostasis model assessment of insulin resistance (HOMA-IR), and lipid profile (total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]), with significantly better maternal and neonatal outcomes ($p < 0.05$). Complication rates were lower in the experimental group, including pregnancy-induced hypertension, cesarean section, polyhydramnios, and neonatal complications like macrosomia, hypoglycemia, and jaundice. **Conclusions**: Multiple subcutaneous injections via insulin pump, that simulates physiological insulin secretion, requires a lower insulin dose for managing A2GDM and demonstrates superior efficacy in blood glucose control, improvement of glucose and lipid metabolism, as well as enhancement of both maternal and neonatal outcomes.

Keywords: insulin; type A2 gestational diabetes mellitus; efficacy; glucose metabolism; lipid metabolism; maternal and infant outcomes; effect

1. Introduction

Gestational diabetes mellitus (GDM) is an abnormal glucose metabolism syndrome occurring during pregnancy. Based on the effect of blood glucose management and control, this special type of diabetes mellitus (DM) involved in pregnancy can be divided into two subtypes: A1 and A2 [1]. Type A1, more commonly encountered in clinical settings, refers to cases in which optimal blood glucose control can be achieved through exercise guidance and nutrition management. A2 denotes that routine management cannot maintain blood glucose at a normal level, necessitating the use of metformin (MET), glibenclamide (Gli), and other hypoglycemic agents or insulin for auxiliary control [2,3]. Auvinen *et al.* [4] conducted a 23-year cohort study and found that type A1 gestational diabetes mellitus (A1GDM) often develops within seven years prior to pregnancy, while type A2 gestational diabetes mellitus (A2GDM) shows a consistently higher incidence after delivery, with its risk linearly increasing to 50% by the end of the follow-up period, bringing about a life-long impact on the patients. A2GDM represents a prevalent complication in pregnant and lying-in women. Although the condition is diagnosed as DM associated with the gestation period, it is distinct from DM concurrently occurring during pregnancy. A2GDM carries a higher risk for both mothers and infants. If the blood glucose level cannot be stabilized, pregnant women are more prone to miscarriage, hypertensive disorder complicating pregnancy (HDCP) (including preeclampsia), infection, polyhydramnios, macrosomia, diabetic ketoacidosis (DKA), and type 2 diabetes mellitus (T2DM). Additionally, fetal growth restriction (FGR), neonatal hypoglycemia, and respiratory distress syndrome (RDS) may occur, impacting offspring health [5–7]. Literature suggests that A2GDM possibly leads to changes in the fetal heart structure. In contrast with fetuses under normal delivery conditions, fetuses of A2GDM patients display a thickened

interventricular septum, thickened left and right ventricular walls, as well as a bigger impact on cardiac morphology and structural integrity [8]. Based on this, early diagnosis and adoption of appropriate blood glucose management are critical for improving maternal and neonatal outcomes. In addition to routine diet control, exercise, and other lifestyle interventions, insulin administration remains the cornerstone of treatment for A2GDM [9,10]. A study has demonstrated that different administration methods of insulin may contribute to different therapeutic outcomes [11]. Therefore, it is particularly pivotal to select a more efficacious intensive insulin therapy regimen. Multiple subcutaneous injections and continuous subcutaneous insulin injection are two frequently employed methods at the current stage. In this study, we investigated the efficacy of different intensive insulin therapy regimens for the management of A2GDM, with the aim of identifying an effective strategy to support favorable delivery outcomes and improve fetal health, thereby enhancing overall maternal and neonatal well-being.

2. Materials and Methods

2.1 Patient Grouping

This retrospective study incorporated 98 patients diagnosed with A2GDM and treated at Puer People's Hospital between March 2021 and September 2023. The patients' ages ranged from 20 to 37 years, with a mean age of (27.02 $\pm$ 3.85) years; 24–39 weeks of gestation (WG), with an average WG of (30.15 $\pm$ 2.43) weeks. Based on the intensive insulin therapy chosen by the patients, they were allocated into the control group (subjected to multiple subcutaneous injections of regular insulin [RI], n = 41) and the experimental group (undergoing multiple subcutaneous injections via insulin pump simulating insulin secretion, n = 57). This study was carried out in keeping with the "Declaration of Helsinki". The study protocol was reviewed and approved by the Ethics Committee of Puer People's Hospital (2025-009-01). Written informed consent was obtained from all participants before their inclusion in the study.

2.2 Diagnostic Criteria

The selected subjects shall conform to the diagnostic criteria for GDM published in July 2022 by the National Medical Service Standards Committee of the Ministry of Health of the People's Republic of China. According to the internationally recognized International Association of Diabetes and Pregnancy Study Groups (IADPSG)/World Health Organization (WHO) diagnostic criteria [12] in terms of the 75 g oral glucose tolerance test (OGTT), GDM can be diagnosed if any of the following indicators is met: fasting plasma glucose (FPG) $\geq$5.1 mmol/L (92 md/dL), 1-hour post-load plasma glucose (1-h PG) $\geq$10.0 mmol/L (180 md/dL), or 2-hour post-load plasma glucose (2-h PG) $\geq$8.5 mmol/L (153 md/dL). If the blood glucose level still fails to meet the standard after 1–2 weeks of exercise and dietary intervention, along with FPG $\geq$5.3 mmol/L (95 md/dL), 1-h PG $\geq$7.8 mmol/L (140 md/dL), or 2-h PG $\geq$6.7 mmol/L (120 md/dL), A2GDM can be diagnosed.

2.3 Inclusion Criteria

All enrolled subjects met the diagnostic criteria for A2GDM and had singleton pregnancies, with complete clinical data available. Individuals receiving other drug therapies or other treatment regimens were excluded from our study. Moreover, patients with contraindications to the medications in this protocol, malignant tumors, immune system diseases, cognitive impairments, or hepatic/renal dysfunction were excluded. See **Supplementary Fig. 1**.

2.4 Different Intensive Insulin Therapy Regimens

All patients received routine health education and individualized interventions, including diet control and exercise guidance tailored to their condition. Based on this, the experimental and control groups were assigned different intensive insulin therapy regimens.

The control group received multiple daily subcutaneous injections of RI (MPA approval number: J20100116; Novo Nordisk [China] Pharmaceuticals Co., Ltd., Tianjin, China), administered 0.5 h before each meal with a daily dose distribution of 40% for breakfast, 20% for lunch, and 40% for dinner. Isophane protamine biosynthetic human insulin was injected subcutaneously every night before sleep. Blood glucose levels were monitored using an Accu-Chek Active glucometer (20182401730; Roche Diagnostics GmbH, Mannheim, Germany), with results recorded in detail, and the insulin dose was maintained between 0.5–1.0 U/(kg·d).

For the experimental group, continuous subcutaneous insulin infusion (CSII) was implemented using an insulin pump Fornia IP-101 (20182401730; Fornia Medical Equipment Co., Ltd., Shenzhen, Guangdong, China) with Novolin insulin (NMPA approval number: J20100116; Novo Nordisk [China] Pharmaceuticals Co., Ltd., Tianjin, China). A continuous catheter and needle were used to deliver insulin via the pump, programmed to provide a basal infusion rate and preprandial bolus doses. The total daily insulin dose was evenly divided between basal and bolus components (50% each), with the preprandial bolus doses distributed as 50% for breakfast, 25% for lunch, and 25% for dinner. The pump was programmed to control the infusion rate, maintaining the total insulin dose between 0.5–1.0 U/(kg·d). The Fornia IP-101 insulin pump, measuring approximately 8 cm $\times$ 5 cm $\times$ 2 cm and weighing 85 g, was typically worn on the abdomen or upper thigh, secured with an adhesive patch to ensure stability during daily activities and sleep. The infusion set, consisting of a soft cannula inserted under the skin, was changed every 2–3 days by trained nurses to minimize discomfort and infection risk. To enhance patient comfort, the pump was designed to be lightweight and waterproof, allowing patients to engage in

routine activities such as bathing and light exercise without restriction. Patients received comprehensive training on pump use, including proper attachment, catheter maintenance, and precautions to avoid dislodgement or damage during sleep (e.g., using a protective belt or positioning the pump away from pressure points). Safety measures included regular inspection of the infusion site for irritation or infection and instructions to contact the study team immediately if the pump malfunctioned or became dislodged. No pump damage was reported during the study, and patients reported minimal disruption to daily life, with most adapting to pump wear within 1–2 days.

To ensure uniformity and comparability between the experimental and control groups, this study implemented a standardized monitoring protocol. The experimental group, receiving insulin pump therapy simulating physiological insulin secretion, and the control group, receiving conventional multiple daily subcutaneous insulin injections, were randomized to ensure no significant differences in baseline characteristics, including age, gestational age, body mass index (BMI), and diabetes duration ($p > 0.05$, verified by *t*-tests or chi-square tests). Blood glucose levels were monitored seven times daily (fasting, preprandial, 1-hour postprandial for three meals, and bedtime) using the Accu-Chek Active glucometer (Roche Diagnostics GmbH, Mannheim, Germany), with measurements performed by trained nurses under standardized conditions and recorded in a unified electronic database. Hypoglycemia was defined as blood glucose $\leq$3.9 mmol/L. Hypoglycemic events were detected through routine seven-time daily blood glucose monitoring or additional measurements triggered by patient-reported symptoms, such as palpitations, trembling, or sweating. All patients received training from certified nurses at the start of the study to recognize hypoglycemia symptoms and perform self-monitoring using the provided glucometer. For mild hypoglycemia, patients were instructed to self-administer 15–20 g of oral glucose or juice, followed by a repeat blood glucose measurement after 15 min. Severe hypoglycemia, defined as requiring assistance from others, necessitated immediate contact with a healthcare facility, with 24-hour telephone support provided by the study team. Insulin doses were adjusted daily by trained nurses based on blood glucose levels, targeting preprandial levels $\leq$5.3 mmol/L, 1-hour postprandial levels $\leq$7.8 mmol/L, and 2-hour postprandial levels $\leq$6.7 mmol/L, with adjustments typically ranging from 0.1–0.2 U/kg·d. Treatment compliance was verified through insulin pump data downloads for the experimental group and daily injection logs for the control group. Pregnancy outcomes, such as pregnancy-induced hypertension and polyhydramnios, were monitored weekly using calibrated electronic sphygmomanometers and ultrasound examinations, while neonatal outcomes, including blood glucose, birth weight, and bilirubin levels, were assessed by neonatologists using standardized equipment at 6, 12, and 24 h post-delivery. All equipment was calibrated weekly, and data integrity was audited by an independent data manager to ensure consistency and reliability throughout the monitoring process.

2.5 Clinical Outcome Definition

To ensure the scientific rigor and reproducibility of maternal and neonatal outcomes related to A2GDM, this study clearly defines the diagnostic criteria and measurement methods for all clinical outcomes. Pregnancy-induced hypertension is defined as a systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg after 20 weeks of gestation, measured twice at least 4 h apart using a calibrated electronic sphygmomanometer with the patient at rest. Cesarean section is defined as the delivery of the fetus via surgical procedure, determined by obstetricians based on clinical indications. Polyhydramnios is diagnosed by an ultrasound-measured amniotic fluid index $\geq$24 cm or a maximum amniotic fluid pocket depth $\geq$8 cm. Ketoacidosis is defined as a blood ketone level $\geq$1.0 mmol/L with arterial blood pH $<$7.3, confirmed by clinical symptoms. Preeclampsia is defined as hypertension after 20 weeks of gestation accompanied by proteinuria or target organ damage. Preterm delivery is defined as birth before 37 weeks of gestation, and premature rupture of membranes is defined as membrane rupture causing amniotic fluid leakage before 37 weeks, both confirmed by obstetricians through clinical evaluation and ultrasound. Neonatal macrosomia is defined as a birth weight $\geq$4000 g or above the 90th percentile, measured using a calibrated electronic scale within 1 h of birth. Neonatal hypoglycemia is defined as a plasma glucose level $<$2.5 mmol/L within 24 h of birth, measured using a standard glucometer at 6, 12, and 24 h post-delivery. Low birth weight is defined as a birth weight $<$2500 g, measured similarly with a calibrated electronic scale. Neonatal respiratory distress syndrome is defined as rapid breathing, intercostal retractions, or oxygen saturation $<$90% post-birth, confirmed by chest X-ray or clinical evaluation by a neonatologist. Neonatal jaundice is defined as a total bilirubin level $>$12 mg/dL within 72 h of birth or clinically visible skin and scleral yellowing, measured using a transcutaneous bilirubinometer or serum bilirubin test. All measurements were performed by trained medical personnel under standardized conditions to ensure data accuracy and consistency.

2.6 Statistical Analysis

All data were analyzed using SPSS Statistics Version 24.0 (IBM, Chicago, IL, USA). Measurement data were expressed as mean $\pm$ standard deviation ($\bar{\chi} \pm$ SD). One-way analysis of variance (ANOVA) was used for comparisons among multiple groups, and independent-samples *t*-tests were used for inter-group comparisons. Enumeration data were expressed as frequencies and percentages. Pearson's chi-square test was used for categorical data when the expected frequencies were sufficient. When expected cell

counts were <5, the continuity correction chi-square test or Fisher's exact test was applied as appropriate. A p-value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline Data of Patients in the Two Groups Upon Enrollment

In the experimental group (n = 57): The mean age was (27.35 ± 3.65) years, the average WG was (30.09 ± 2.08) weeks, the average body mass was (68.41 ± 5.62) kg, and the pre-pregnancy body mass index (BMI) was (30.28 ± 4.26) kg/m^2; 33 primiparas and 24 multiparas; as for the educational level, there were 28 cases with junior high school education or below and 29 cases with high school education or above; 4 cases with a family history of DM and 53 cases without such history. In the control group (n = 41): average age of (26.56 ± 3.94) years, average WG of (30.23 ± 2.15) weeks, average body mass of (69.20 ± 6.43) kg, and pre-pregnancy BMI of (32.47 ± 3.91) kg/m^2; 25 primiparas and 16 multiparas; 19 cases with junior high school education or below and 22 cases with high school education or above; 9 cases with a family history of DM and 32 cases without a family history. Baseline characteristics including the age, WG, body mass, parity, and education level were compared between the two groups, with no statistically significant differences observed ($p > 0.05$). However, significant differences were found in pre-pregnancy BMI and family history of DM, with the experimental group exhibiting lower BMI values and fewer cases with a family history of DM compared with the control group ($p < 0.05$). See Table 1.

3.2 Multivariate Logistic Regression Analysis for A2GDM Patients Requiring Insulin Treatment

As shown in Section 3.1, the proportions of patients with different pre-pregnancy BMI and a family history of diabetes differed significantly between the two groups. Therefore, these two factors were included in a multivariate logistic regression equation to analyze their impact on insulin application. The results confirmed that high BMI pre-pregnancy and a family history of DM were both independent influencing factors for A2GDM patients requiring insulin treatment ($p < 0.05$). Refer to Table 2.

3.3 Time of Blood Glucose Levels Reaching the Standard, Insulin Dose, and Incidence of Hypoglycemia in the Two Groups

The experimental group displayed a time of (4.15 ± 0.59) d for blood glucose levels reaching the standard, which was shorter than that in the control group, which attained (7.62 ± 0.83) d; the insulin dose was (32.78 ± 5.63) U/kg·d in the experimental group, lower than that needed in the control group, which attained (51.49 ± 8.77) U/kg·d; the incidence of hypoglycemia was 3.51%, lower than that in the control group (17.07%); the variances showed statistical significance ($p < 0.05$). Detailed data are shown in Table 3. Our findings demonstrated that the application of multiple subcutaneous injections via an insulin pump that simulates insulin secretion can achieve better blood glucose control versus multiple subcutaneous injections of RI.

3.4 Differences in Glucose Metabolism Between the Two Groups Before and After Treatment

Prior to treatment, FPG, 2 hours postprandial blood glucose (2hPBG), fasting insulin, glycosylated hemoglobin (HbAlc), and homeostasis model assessment of insulin resistance (HOMA-IR) displayed no statistically significant variances between the two groups ($p > 0.05$). Following treatment with different methods, the two groups experienced improvement in these indicators compared with pre-treatment levels ($p < 0.05$). The experimental group showed (4.01 ± 0.49) mmol/L for FPG, (7.12 ± 0.82) mmol/L for 2hPBG, (5.13 ± 0.50) % for HbAlc, and (2.08 ± 0.27) for HOMA-IR, and these values were all lower than those monitored from the control group during the same period, with the differences suggesting statistical significance ($p < 0.05$). See Table 4. These observations reflected that both methods can improve glucose metabolism for A2GDM patients; however, multiple subcutaneous injections via an insulin pump simulating insulin secretion demonstrated superior efficacy in enhancing this parameter.

3.5 Variances in Lipid Metabolism Between the Two Groups Preceding and Following Treatment

Prior to treatment, no statistically significant variances were found in total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), or low-density lipoprotein cholesterol (LDL-C) between the two groups ($p > 0.05$). Subsequent to treatment, these indicators all improved versus the levels preceding treatment in both groups ($p < 0.05$). Following treatment, the experimental group exhibited (4.18 ± 0.37) nmol/L for TC, (4.51 ± 0.43) nmol/L for HDL-C, and (4.21 ± 0.49) nmol/L for LDL-C, all superior to those in the control group during the same period, and the variances had statistical significance ($p < 0.05$). See Table 5 for details. Our findings suggested that multiple subcutaneous injections via an insulin pump simulating insulin secretion can play a better role in improving lipid metabolism for A2GDM patients compared with multiple subcutaneous injections of RI.

3.6 Differences in Pregnancy Outcomes Between the Two Groups

Pregnancy-induced hypertension (PIH), cesarean section, polyhydramnios, ketoacidosis, preeclampsia, premature delivery, and premature rupture of fetal membranes are prevalent adverse pregnancy outcomes in A2GDM women. In our research, the experimental group encompassed 3 cases of PIH, 4 cases with cesarean section, 3 cases of polyhydramnios, 1 case of ketoacidosis, 3 cases of preeclampsia, 2 cases of premature delivery, and no premature rupture

Table 1. Comparison of baseline data between the two groups.

Group	n	Age (years)	WG (weeks)	Body mass (kg)	Pre-pregnancy BMI (kg/m^2)	Parity		Education level		Family history of DM	
						Primipara	Multipara	Junior high school education or below	High school education or above	Presence	Absence
Experimental group	57	27.35 ± 3.65	30.09 ± 2.08	68.41 ± 5.62	30.28 ± 4.26*	33 (57.89%)	24 (42.11%)	28 (49.12%)	29 (50.88%)	4 (7.02%)	53 (92.98%)*
Control group	41	26.56 ± 3.94	30.23 ± 2.15	69.20 ± 6.43	32.47 ± 3.91	25 (60.98%)	16 (39.02%)	19 (46.34%)	22 (53.66%)	9 (21.95%)	32 (78.05%)
χ^2/t		1.022	0.324	0.646	2.597	0.094		0.074		4.622	
p		0.309	0.747	0.520	0.010	0.760		0.786		0.032	

Note: * suggests compared with the control group, $p < 0.05$.

n, number of patients; WG, weeks of gestation; BMI, body mass index; DM, diabetes mellitus; SD, standard deviation.

Table 2. Multivariate logistic regression analysis for A2GDM patients requiring insulin treatment.

Factor	β	S.E.	Wald	OR	95% CI	p
Pre-pregnancy BMI	1.326	0.577	5.281	3.766	1.215–11.669	0.022*
Family history of DM	1.156	0.563	4.216	3.177	1.054–9.578	0.041*

Note: * suggests the factor is an independent influencing factor for A2GDM patients requiring insulin therapy, $p < 0.05$.

S.E., standard error; OR, odds ratio; A2GDM, type A2 gestational diabetes mellitus.

Table 3. Time of blood glucose levels reaching the standard, insulin dose, and incidence of hypoglycemia in the two groups.

Group	n	Time of blood glucose reaching the standard (d)	Insulin dose (U/kg·d)	Incidence of hypoglycemia (times)
Experimental group	57	4.15 ± 0.59*	32.78 ± 5.63*	2 (3.51%)*
Control group	41	7.62 ± 0.83	51.49 ± 8.77	7 (17.07%)
χ^2/t		24.205	12.852	-
p		<0.001	<0.001	0.039[a]

Note: [a] Fisher's exact test was used due to expected frequency <5. * suggests compared with the Control group, $p < 0.05$.

Table 4. Differences in glucose metabolism between the two groups before and after treatment.

Group	n	FPG (mmol/L)		2hPBG (mmol/L)		HbAlc (%)		HOMA-IR		Fasting insulin (μIU/mL)
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment
Experimental group	57	7.45 ± 0.57	4.01 ± 0.49*	12.36 ± 1.16	7.12 ± 0.82*	7.91 ± 0.75	5.13 ± 0.50*	4.25 ± 0.31	2.08 ± 0.27*	12.85 ± 2.50
Control group	41	7.48 ± 0.63	5.19 ± 0.55*	12.31 ± 1.48	8.25 ± 0.91*	7.89 ± 0.81	6.60 ± 0.42*	4.23 ± 0.36	3.11 ± 0.36*	12.72 ± 2.60
t		0.246	11.171	0.187	6.427	0.126	15.328	0.294	16.190	0.305
p		0.806	<0.001	0.852	<0.001	0.9	<0.001	0.769	<0.001	0.761

Note: * means compared with pre-treatment levels in the same group, $p < 0.05$.

FPG, fasting plasma glucose; 2hPBG, 2 hours postprandial blood glucose; HbAlc, glycosylated hemoglobin; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 5. Differences in lipid metabolism between the two groups before and after treatment.

Group	n	TC (mmol/L)		HDL-C (mmol/L)		LDL-C (mmol/L)	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Experimental group	57	8.35 ± 0.79	4.18 ± 0.37*	2.45 ± 0.23	4.51 ± 0.43*	8.32 ± 0.78	4.21 ± 0.49*
Control group	41	8.39 ± 0.86	6.35 ± 0.59*	2.47 ± 0.21	3.96 ± 0.40*	8.33 ± 0.95	5.68 ± 0.53*
t		0.238	22.345	0.440	6.429	0.057	14.157
p		0.812	<0.001	0.661	<0.001	0.955	<0.001

Note: * suggests compared with pre-treatment levels in the same group, $p < 0.05$.

TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 6. Differences in pregnancy outcomes between the two groups.

Group	n	PIH	Cesarean section	Polyhydramnios	Ketoacidosis	Preeclampsia	Premature delivery	Premature rupture of fetal membranes
Experimental group	57	3 (5.26%)*	4 (7.02%) *	3 (5.26%)*	1 (1.75%) *	3 (5.26%)*	2 (3.51%)*	0 (0.00%)*
Control group	41	11 (26.83%)	9 (21.95%)	9 (21.95%)	5 (12.20%)	8 (19.51%)	7 (17.07%)	3 (7.32%)
χ^2		9.058	4.622	6.180	-	4.859	-	-
p		0.003	0.032	0.013	0.042[a]	0.028	0.034	0.049

Note: [a] Fisher's exact test was used due to expected frequency <5. * suggests compared with the control group, $p < 0.05$.

PIH, pregnancy-induced hypertension.

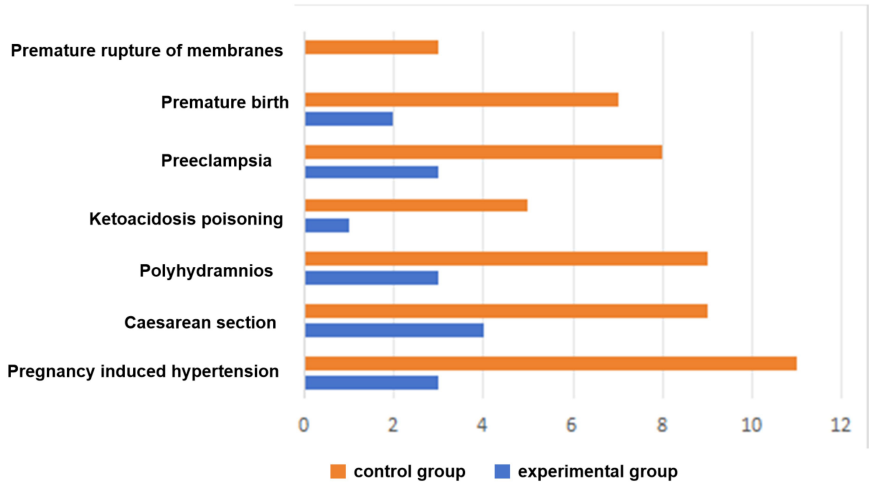

Fig. 1. Differences in pregnancy outcomes between the two groups.

Table 7. Differences in neonatal outcomes between the two groups.

Group	n	Macrosomia	Neonatal hypoglycemia	Low birth weight	Respiratory distress	Neonatal jaundice
Experimental group	57	5 (8.77%)*	1 (1.75%)*	3 (5.26%)*	2 (3.51%)*	6 (10.53%)*
Control group	41	10 (24.39%)	5 (12.20%)	8 (19.51%)	7 (17.07%)	11 (26.83%)
χ^2		4.487	-	-	-	4.421
p		0.034	0.042[a]	0.040	0.039[a]	0.036

Note: [a] Fisher's exact test was used due to expected frequency <5; * suggests compared with the control group, $p < 0.05$.

of fetal membranes. The incidence of the above outcomes was substantially lower than that observed in the control group, and the variances showed statistical significance ($p < 0.05$). See Table 6 and Fig. 1 for details. Our results revealed that the application of multiple subcutaneous injections via insulin pump simulating insulin secretion in A2GDM treatment can reduce the incidence of adverse pregnancy outcomes.

3.7 Differences in Neonatal Outcomes Between the Two Groups

Newborns delivered by A2GDM patients are at increased risk for complications such as macrosomia, neonatal hypoglycemia, low birth weight, neonatal respiratory distress, and neonatal jaundice. In this study, neonatal outcomes were statistically analyzed between the two groups. As displayed in Table 7 and Fig. 2, there were 8.77% newborns with macrosomia, 1.75% with hypoglycemia, 5.26% with low birth weight, 3.51% with respiratory distress, and 10.53% with jaundice. These proportions were all noticeably lower than those observed in the control group, and the differences were statistically significant ($p < 0.05$). These findings demonstrated that compared with multiple subcutaneous injections of RI, multiple subcutaneous injections via insulin pump simulating insulin secretion contribute to substantial improvement in neonatal outcomes.

4. Discussion

Pregnancy represents a unique physiological state characterized by significant increases in growth hormones, glucocorticoids, and sex hormones, which elevate insulin requirements [6,13]. These hormones antagonize insulin action, exacerbating IR during gestation [7]. Consequently, some pregnant women experience marked blood glucose fluctuations, particularly with excessive nutritional supplementation, leading to GDM [14,15]. With its incidence rising annually, A2GDM, which accounts for over 50% of GDM cases, cannot be adequately managed through diet and exercise alone. Uncontrolled A2GDM disrupts glucose, lipid, and protein metabolism, causing vascular pathology under chronic inflammatory conditions. This restricts tissue and organ blood supply, increasing risks of premature delivery, preeclampsia, premature rupture of membranes, and cesarean section, while also complicating delivery. For fetuses, uncontrolled A2GDM heightens the likelihood of hypoglycemia, macrosomia, respiratory distress, and other adverse outcomes [5,16,17], posing significant threats to maternal and neonatal health. Therefore, A2GDM requires heightened clinical attention, and effective blood glucose control strategies are essential to improve outcomes. Our study identified baseline differences in pre-pregnancy BMI (30.28 vs. 32.47 kg/m^2, $p = 0.010$) and family history of diabetes (7.02% vs. 21.95%, $p = 0.032$) between the CSII and multiple daily injections

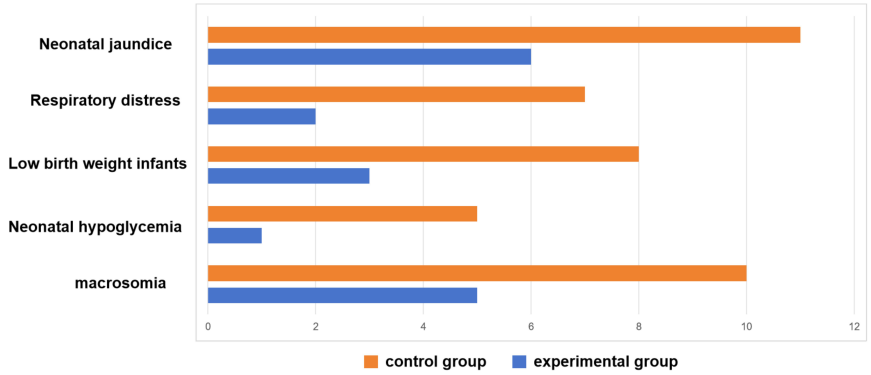

Fig. 2. Differences in neonatal outcomes between the two groups.

(MDI) groups (Table 1). To address their potential confounding effects, we conducted multivariate logistic regression analysis, confirming these factors as independent predictors of insulin treatment requirements (Table 2, OR = 3.766 and 3.177, $p < 0.05$). However, the clinical significance of these differences is limited, as the BMI difference (~2 kg/m^2) is below thresholds associated with a substantial metabolic impact, and the family history difference is unlikely to dominate A2GDM's pathophysiology, which is primarily driven by gestational hormonal changes. Moreover, other baseline characteristics, including age, gestational weeks, and body mass, showed no significant differences ($p > 0.05$, Table 1), ensuring overall group comparability.

Insulin remains the cornerstone of clinical blood glucose management. Extensive research confirms its dual role in promoting glycogenolysis and suppressing gluconeogenesis, achieving sustained glycemic control through multiple pathways [18–20]. MDI of RI effectively manage A2GDM but have practical limitations, including operational inconvenience, susceptibility to subjective factors, and suboptimal glycemic control precision, which may hinder efficacy in some patients. In contrast, CSII offers an advanced insulin delivery method that mimics physiological insulin secretion [21]. Our study compared the efficacy of CSII and MDI in A2GDM, focusing on their impact on glucose and lipid metabolism and maternal and neonatal outcomes. The CSII group achieved target blood glucose levels faster, required lower insulin doses, and experienced fewer hypoglycemic events compared with the MDI group. Post-treatment, the CSII group exhibited significantly lower FPG, 2hPBG, HbA1c, and HOMA-IR levels, alongside improved lipid profiles (TC, HDL-C, and LDL-C). These findings indicate that while both insulin regimens improve glycemic and lipid metabolism in A2GDM, CSII provides superior glycemic control, reduced insulin requirements, and enhanced maintenance of glucose and lipid homeostasis. Additionally, CSII reduces hypoglycemia risk, offering a safer profile. Combined with adequate nutrition, exercise, and dietary interventions, CSII modulates insulin polypeptide levels and glucose tolerance, further improving metabolic outcomes [22,23]. Notably, CSII alleviates the burden of multiple daily injections, reducing patient discomfort and enhancing convenience, efficiency, and safety for A2GDM management.

This study also evaluated maternal and neonatal outcomes for both insulin regimens. The CSII group demonstrated significantly lower rates of maternal complications, including pregnancy-induced hypertension (PIH), cesarean section, polyhydramnios, ketoacidosis, preeclampsia, premature delivery, and premature rupture of membranes, compared to the MDI group. Similarly, neonates born to mothers in the CSII group had reduced incidences of hypoglycemia, low birth weight, respiratory distress, and jaundice. These results underscore the superior efficacy of CSII in improving maternal and neonatal outcomes. This advantage likely stems from two key mechanisms: First, CSII mimics physiological insulin secretion through continuous basal infusion and adjustable preprandial bolus doses, allowing precise glycemic control tailored to meal timing and fasting periods. This precision reduces postprandial glucose spikes and prevents morning or nocturnal hypoglycemia and ketoacidosis [23,24]. Second, intensive short-term glycemic control with CSII rapidly achieves target glucose levels, minimizing the adverse effects of sustained hyperglycemia, preserving residual pancreatic β-cell function, and mitigating excessive glucose fluctuations that harm both mother and fetus [25]. These benefits enhance maternal quality of life and safeguard neonatal health. Prior studies, including those by Li *et al.* [26] and Wang *et al.* [27], have reported similar findings, confirming that CSII significantly lowers blood glucose, modulates serum protein factors, improves lipid and inflammatory profiles, and reduces adverse pregnancy outcomes in A2GDM. Our results further support the clinical value and safety of CSII for A2GDM management, highlighting its potential for broader clinical application.

Despite these findings, prior studies, including those by Gong *et al*. [23] and Kjölhede *et al*. [25], highlight limitations in A2GDM research. For instance, Gong *et al*. (2024) [23] compared CSII and MDI in pregnant women with type 1 diabetes but was constrained by a small sample size and single-center design, limiting generalizability. Similarly, Kjölhede *et al*. (2021) [25], a secondary analysis of an observational cohort, lacked randomization and long-term follow-up, restricting causal inferences and insights into sustained outcomes. These limitations underscore the need for larger, multicenter randomized controlled trials to validate CSII's benefits in A2GDM.

Advancements in insulin delivery technology offer promising prospects for A2GDM management. Modern insulin pumps integrated with continuous glucose monitoring (CGM) systems provide real-time glucose feedback and automated insulin delivery, enhancing glycemic control precision and reducing hypoglycemic events. Emerging closed-loop systems, often termed artificial pancreas systems, dynamically adjust insulin doses based on real-time glucose levels, potentially offering superior outcomes for A2GDM patients. However, these technologies require further evaluation in pregnant populations to confirm their safety and efficacy.

Implementing CSII in low-resource settings presents significant challenges. High costs of insulin pumps and consumables, limited access to trained healthcare professionals, and inadequate infrastructure for device maintenance restrict adoption in rural or developing regions. Low health literacy and socioeconomic constraints further hinder patient adherence. To address these barriers, cost-effective pump designs, simplified training programs for healthcare providers, and telemedicine support could improve accessibility. Future research should explore scalable strategies to integrate advanced insulin delivery systems into diverse healthcare settings, ensuring equitable access for A2GDM patients.

5. Limitation

Our study has limitations. As a retrospective analysis with a small sample size and limited case diversity, its generalizability is constrained. Prospective, multicenter, large-scale studies are needed to further validate our findings.

6. Conclusions

To sum up, multiple subcutaneous injections of RI and multiple subcutaneous injections via an insulin pump that simulates insulin secretion are both effective in managing A2GDM. However, in comparison, the insulin pump approach, which requires a lower dose of insulin, is more efficacious in controlling blood glucose levels, improving glucose and lipid metabolism, and enhancing both maternal and neonatal outcomes, making it suitable for clinical implementation and wider adoption.

Availability of Data and Materials

The datasets used during the current study are available from the corresponding author upon reasonable request.

Author Contributions

XY, YL designed the research study; XY, YL and YG performed the research; XY, YL and YG collected and analyzed the data. XY, YL and YG have been involved in drafting the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Puer People's Hospital (2025-009-01), complies with the Declaration of Helsinki. Written informed consent was obtained from all participants before their inclusion in the study.

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Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, authors used ChatGPT to assist in checking spelling and grammar. The authors reviewed and edited the content as necessary and take full responsibility for the final version of the manuscript.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG41004.

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