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RESEARCH ARTICLE

Comparison of Efficacy Between Short Acting Insulin & Rapid Acting Insulin in Controlling Blood Glucose Level Among Newly Detected Diabetic Disorder in Pregnancy

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Abstract

Background: Hyperglycemic disorders during pregnancy, including gestational diabetes mellitus (GDM) and diabetes in pregnancy (DIP) are increasing worldwide with the adoption of updated diagnostic criteria. These disorders are associated with adverse maternal, fetal and neonatal outcomes; however, optimal glycemic control can significantly reduce complications. Postprandial glucose regulation is a critical component of management. Rapid-acting insulin analogues, such as insulin aspart may provide improved postprandial glucose control with a lower risk of hypoglycemia compared with regular insulin. This study aimed to compare the short-term efficacy and safety of insulin aspart versus regular insulin in pregnant women with hyperglycemic disorders.

Methods: A randomized controlled trial was conducted among 79 pregnant women with GDM or DIP at the Feto-maternal Medicine OPD and IPD, Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, from January to December 2023. Participants were randomly assigned to receive either regular insulin (n=39) or insulin aspart (n=40) after failure of medical nutrition therapy. Blood glucose levels and hypoglycemic episodes were monitored for two weeks.

Result: Total 79 respondents were included in this study. The study showed mean postprandial blood glucose levels were significantly controlled (81.6%) with Rapid acting insulin, Insulin Aspart in comparison to regular insulin (58.3%) with p-value: 0.029 when assessed after two weeks of treatment. In control group 38.9% experienced level 1 and 5.5% experienced level 2 hypoglycemia. On the contrary 15.8% and 2.6% of rapid acting insulin developed level 1 and level 2 hypoglycemia respectively. So, the proportion of hypoglycemia was significantly higher in control group with Regular insulin. But none of the two group showed any level 3 hypoglycemia. Time required for controlling blood sugar also less (mean for control group 212.57±59.89 versus mean for experimental group 173.41±72.85 in hours). Regarding insulin dose control group required significantly higher dose (25.63±15.5 versus 15.67±8.44) of insulin(p-value:0.003).

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Conclusion: The result of this study demonstrated that effective postprandial glycemic control in women with hyperglycemic disorder in pregnancy can be brought about by Rapid insulin, Insulin Aspart with shorter duration and less chance of hypoglycemia.

Keywords: GDM, DIP, Regular Insulin, Rapid Acting Insulin, Insulin Aspart, Efficacy.

1. Introduction

Diabetes is one of the most common metabolic complications of pregnancy.[1] Incidence of type1, type 2 diabetes are increasing in reproductive age. Globally incidence of diabetes is 10.5% and prediabetes is 34.5%. Among them 4.5% are of childbearing age. [2] The prevalence of GDM is increasing globally due to obesity.[1] The global prevalence of GDM varies from 1% to 28%.[3] According to incidence and impact GDM is a global health problem. There is variation in prevalence of GDM in Asia due to different population and screening criteria. In 2019 a meta-analysis showed the prevalence of GDM in South-Asia is 11.4% by using new screening criteria. A demographic health survey of 2017-2018 in Bangladesh showed prevalence of GDM is 35% and one third pregnant women have GDM, which is 3-4 times higher than previous studies.[4] According to the World Health Organization (WHO) criteria, hyperglycemia first detected during pregnancy should be classified as either gestational diabetes mellitus or diabetes mellitus in pregnancy. [5] GDM is diagnosed when one or more of the following conditions are present during a 75-g oral glucose tolerance test: fasting plasma glucose 5.1–6.9 mmol/L (92–125 mg/dL), 1-hour plasma glucose ≥10.0 mmol/L (180 mg/dL), or 2-hour plasma glucose 8.5–11.0 mmol/L (153–199 mg/dL). Diabetes mellitus in pregnancy is diagnosed when fasting plasma glucose is ≥7.0 mmol/L (126 mg/dL), 2-hour plasma glucose is ≥11.1 mmol/L (200 mg/dL) or random plasma glucose is ≥11.1 mmol/L with classical symptoms of diabetes. [5] Pregnancy is associated with complex metabolic and hormonal adaptations that influence glucose homeostasis. During early pregnancy, increased estrogen levels improve insulin sensitivity; however, insulin resistance progressively increases during the late second and third trimesters due to the anti-insulin effects of placental hormones, particularly human placental lactogen. [6] Increased production of cortisol, progesterone, estriol, placental insulinase activity and accelerated insulin metabolism further contribute to maternal insulin resistance. [6] Normally, pancreatic β-cells compensate by increasing insulin secretion to maintain normal glucose levels. However, women who cannot adequately increase insulin production develop GDM. [7] Although glucose tolerance usually returns to normal after delivery women with GDM have a substantially increased risk of developing type 2 diabetes mellitus and cardiovascular disease later in life. [8] The pathophysiology of GDM is similar to that of type 2 diabetes mellitus, characterized by insulin resistance combined with impaired pancreatic β-cell compensation. A small proportion of women diagnosed with GDM may have underlying autoimmune β-cell dysfunction associated with future type 1 diabetes mellitus. [7] Hyperglycemia during pregnancy has significant adverse effects on both mothers and offspring. Maternal complications include gestational hypertension, preeclampsia, increased cesarean delivery rates and future metabolic disorders. [9,10] Neonates born to mothers with GDM have increased risks of macrosomia, birth trauma, neonatal hypoglycemia, congenital abnormalities, childhood obesity, metabolic syndrome and future type 2 diabetes mellitus. [11] The degree and timing of maternal hyperglycemia significantly influence pregnancy outcomes. Hyperglycemia during the first trimester is associated with an increased risk of congenital malformations and pregnancy loss, whereas persistent uncontrolled hyperglycemia later in pregnancy increases the risk of fetal overgrowth and intrauterine complications. [12–14] Therefore, achieving strict glycemic control is considered the cornerstone of management of diabetes during pregnancy. The recommended glycemic targets include maintaining fasting blood glucose below 5.3 mmol/L and 2-hour postprandial glucose below 6.7 mmol/L, according to current recommendations. [15] Lifestyle modification, including medical nutrition therapy and regular physical activity, remains the initial management approach for GDM. However, approximately 15–30% of women with GDM require pharmacological treatment, mainly insulin therapy, when adequate glycemic control cannot be achieved through lifestyle intervention alone. [16] Insulin remains the preferred pharmacological treatment because it does not cross the placenta and has an established safety profile in pregnancy. [17] Regular human insulin has traditionally been used as mealtime insulin therapy. However, its delayed onset of action, prolonged duration and mismatch with physiological

insulin secretion may increase the risk of postprandial hyperglycemia and late hypoglycemia.[18] Rapid-acting insulin analogues were developed through molecular modification of human insulin to better replicate normal physiological insulin response. Insulin Aspart is a rapid-acting insulin analogue characterized by faster absorption, earlier onset of action and shorter duration compared with Regular Insulin. [19] Insulin Aspart can be administered approximately 5–10 minutes before meals, reaches peak activity within 40–50 minutes, and has a duration of action of approximately 3–5 hours. [20] These pharmacokinetic properties allow improved control of postprandial glucose levels and may reduce the risk of hypoglycemia compared with conventional Regular Insulin therapy. Previous studies have suggested that rapid-acting insulin analogues may provide better postprandial glycemic control without increasing maternal or fetal risks. [21] Although Insulin Aspart is considered safe during pregnancy and is increasingly used worldwide, evidence regarding its comparative efficacy with Regular Insulin among pregnant women, particularly in developing countries such as Bangladesh, remains limited. Therefore, this study was undertaken to evaluate the efficacy and safety of Rapid-Acting Insulin Analogue (Insulin Aspart) compared with Regular Human Insulin for achieving glycemic control in women with diabetes during pregnancy. The findings may contribute to optimizing insulin selection and improving maternal and fetal outcomes.

2. Materials and Methods

2.1 Study Design and Study Setting

This study was designed as a randomized controlled trial (RCT) conducted to compare the efficacy and safety of rapid-acting insulin (Insulin Aspart) versus short-acting regular insulin (Actrapid) for achieving glycemic control among pregnant women with gestational diabetes mellitus (GDM) and diabetes in pregnancy (DIP). The study was conducted in the Feto-Maternal Medicine Outpatient Department (OPD) and Inpatient Department (IPD), Department of Obstetrics and Gynecology, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh. The study period was from 1st January 2023 to 31st December 2023.

2.2 Study Population

The study population included pregnant women attending the Feto-Maternal Medicine OPD and IPD of DMCH in any trimester of pregnancy who were diagnosed with gestational diabetes mellitus or diabetes in pregnancy based on oral glucose tolerance test (OGTT) criteria. Participants were selected after fulfilling the inclusion and exclusion criteria and providing written informed consent. Pregnant women receiving any medication affecting blood glucose metabolism were excluded.

2.3 Sample Size Calculation

The sample size was calculated using the statistical formula for hypothesis testing of the difference between two means:

$$N = \frac{(\sigma_1^2 + \sigma_2^2)(Z_\alpha + Z_\beta)^2}{(\mu_1 - \mu_2)^2}$$

Where,

N = Required sample size in insulin aspart and regular insulin groups

μ1 = Mean blood glucose level after treatment with insulin aspart

μ2 = Mean blood glucose level after treatment with regular insulin

σ1 and σ2 = Standard deviation of blood glucose levels in respective groups

Zα = Standard normal value at 1% significance level

Zβ = Standard normal value at 80% power

The values were obtained from the study by Pettitt et al. (2007). Considering μ1 = 4.2, μ2 = 4.8, σ1 = 0.57, σ2 = 0.86, Zα = 2.58, and Zβ = 0.85, the calculated sample size was approximately 35 patients per group. Considering a 10% loss to follow-up, the final sample size was increased, and a total of 79 pregnant women were enrolled in the study.

2.4 Sampling Technique and Randomization

Patients were selected by purposive and convenient sampling methods from pregnant women attending the Obstetrics and Gynecology Department of DMCH. After enrollment, eligible participants were allocated into two groups using block randomization.

- **Group A (Control group):** Received short-acting regular insulin (Actrapid).
- **Group B (Experimental group):** Received rapid-acting insulin analogue (Insulin Aspart).

2.5 Inclusion Criteria

Participants included:

- Pregnant women with abnormal OGTT detected at booking, 24–28 weeks, or any trimester of pregnancy.

- Patients attending Feto-Maternal Medicine OPD/ IPD, DMCH.
- Age between 18 and 40 years.
- Patients willing to participate and provide informed consent.

2.6 Exclusion Criteria

Patients were excluded if they had:

- Previously diagnosed diabetes mellitus requiring treatment.
- Current use of steroid medications.
- Fetal congenital abnormalities where pregnancy termination was possible and follow-up data might become incomplete.
- Incomplete clinical or laboratory information.

2.7 Operational Definitions

2.7.1 Gestational Diabetes Mellitus (GDM)

Diagnosed according to WHO 2013 criteria when any one of the following was present:

- Fasting plasma glucose: 5.1–6.9 mmol/L (92–125 mg/dL)
- Two-hour plasma glucose after 75 g oral glucose load: 8.5–11.0 mmol/L (153–199 mg/dL)

2.7.2 Diabetes in Pregnancy (DIP)

Diagnosed when:

- Fasting plasma glucose ≥7.0 mmol/L (126 mg/ dL), or
- Two-hour plasma glucose ≥11.1 mmol/L (200 mg/ dL) after 75 g OGTT, or
- Random plasma glucose ≥11.1 mmol/L (200 mg/ dL) with classical symptoms of diabetes.

2.7.3 Rapid-Acting Insulin

Insulin that begins action within approximately 15 minutes and is administered immediately before or after meals. In this study, Insulin Aspart was considered rapid-acting insulin.

2.7.4 Short-Acting Insulin

Insulin with onset of action within 30 minutes to 1 hour and administered approximately 30 minutes before meals. Regular insulin (Actrapid) was used as short-acting insulin.

2.8 Study Procedure and Follow-up

Pregnant women fulfilling the selection criteria were enrolled after detailed explanation of the study objectives and procedures. Sociodemographic information, obstetric history, medical history and family history were recorded using a structured questionnaire. Complete physical examination including blood pressure measurement, height, weight and BMI calculation was performed. Gestational age was confirmed by early ultrasonography whenever available. OGTT was performed at first contact. Patients diagnosed with abnormal glucose tolerance initially received medical nutritional therapy for 1–2 weeks. Those who failed to achieve glycemic targets were randomized into intervention and control groups. Patients were monitored with fasting and postprandial blood glucose measurements on alternate days. The target glucose levels were fasting 3.9–5.3 mmol/L and two-hour postprandial 5.6–6.7 mmol/L. Treatment efficacy was assessed by time required to achieve glycemic control, total insulin dose requirement, patient compliance and occurrence and severity of hypoglycemia.

2.9 Outcome Variables

2.9.1 Primary Outcome Variables

- Time required to achieve postprandial blood glucose control.
- Achievement of target glycemic level.

2.9.2 Secondary Outcome Variables

- Total insulin dose required.
- Frequency and severity of hypoglycemia.

2.10 Ethical Consideration

The study protocol was approved by the Ethical Review Committee of Dhaka Medical College Hospital. Written informed consent was obtained from all participants after explaining the study objectives, procedures, risks and benefits in an understandable language. Confidentiality and privacy of all patient information were strictly maintained.

2.11 Data Analysis

Data were analyzed using SPSS version 23.0. Continuous variables were expressed as mean ± standard deviation or median with range depending on data distribution. Normality was assessed using the Shapiro–Wilk test. Categorical variables were presented as frequency and percentage. Chi-square test or Fisher's exact test was used to compare categorical outcomes. Mann–Whitney U test was applied for non-normally distributed continuous variables, including insulin dose requirement and

time needed for glycemic control. Risk ratio with 95% confidence interval was calculated to determine the effect of rapid-acting insulin on glycemic control and hypoglycemia risk. A p-value <0.05 was considered statistically significant.

3. Results

Total 79 pregnant women (39 in the control group and 40 in the experimental group), were enrolled for the study after doing OGTT at booking or at 24-28 weeks or in any time of their visit when found abnormal and could not be controlled by diet and exercise. But 3 patients in control group and 2 patients in experimental group were noncompliant in maintaining adequate diet, dose, record keeping of glucose profile and visit. Finally, 38 patients in experimental group and 36 patients in control group had completed the study with us. Here Group A got Insulin Actrapid and Group B got Insulin Aspart. The statistical analysis was done among these 74 patients.

Table 1. *Distribution of the participants according to demographic characteristics*

		Group A (n1=39)	Group B (n2=40)	Total	P value
Age (years)	>18-<25	6 (15.4)	9 (22.5)	15 (19.0)	[a]0.690[ns]
	25-30	19 (48.7)	19 (47.5)	38 (48.1)	
	>30	14 (35.9)	12 (30.0)	26 (32.9)	
	Mean ± SD	29.74±5.06	28.20±4.87	28.96±4.99	[c]0.171[ns]
	Median (Range)	30 (19-40)	28 (18-37)	29 (18-40)	
Socio economic condition	Upper class	7 (17.9)	5 (12.5)	12 (15.2)	
	Middle class	25 (64.1)	27 (67.5)	52 (65.8)	[a]0.793[ns]
	Lower class	7 (17.9)	8 (20.0)	15 (19.0)	
Education	Illiterate	4 (10.3)	3 (7.5)	7 (8.9)	[b]0.889[ns]
	Primary education	24 (61.5)	24 (60.0)	48 (60.8)	
	Secondary education and above	11 (28.2)	13 (32.5)	24 (30.4)	
Occupation	Housewife	34 (87.2)	33 (82.5)	67 (84.8)	[a]0.562[ns]
	Working	5 (12.8)	7 (17.5)	12 (15.2)	

[a] Chi-square test, [b] Fisher's exact test, [c] Student t test was done, ns=non-significant

Table 1 shows the demographic characteristics of the participants. The majority (48.1%) of the participants were from 25-30 years of age followed by >30 years (32.9%) and the mean age of the participants was 28.96±4.99 years. Almost 66% of the participants belong to the middle class and more than 60% of participants had completed their primary education. More than 84% of the participants was housewife. The participants in Group A and Group B were demographically and statistically indifferent (p-value:>0.05).

Table 2. *Distribution of the participants according to physical characteristics*

		Group A (n1=39)	Group B (n2=40)	Total	P value
Systolic blood pressure	Mean ± SD	117.42±18.25	113.79±12.38	115.67±15.67	*[b]0.420 ns*
	Median (Range)	110 (100-160)	110 (100-150)	110 (100-160)	
Diastolic blood pressure	Mean ± SD	75.80±10.57	76.21±9.03	76.0±9.78	*[b]0.919 ns*
	Median (Range)	80 (60-100)	80 (60-100)	80 (60-100)	
Body mass index (kg/m^2)	Underweight	0 (0.0)	1 (2.5)	1 (1.3)	*[a]0.722 ns*
	Healthy weight	9 (23.1)	12 (30.0)	21 (26.6)	
	Overweight	21 (53.8)	20 (50.0)	41 (51.9)	
	Obese	9 (23.1)	7 (17.5)	16 (20.3)	

a Fisher's exact test, b Mann Whitney U test was done, ns=non-significant

Table 2 shows no significant difference between groups was observed in terms of physical characteristics (p-value: >0.05)

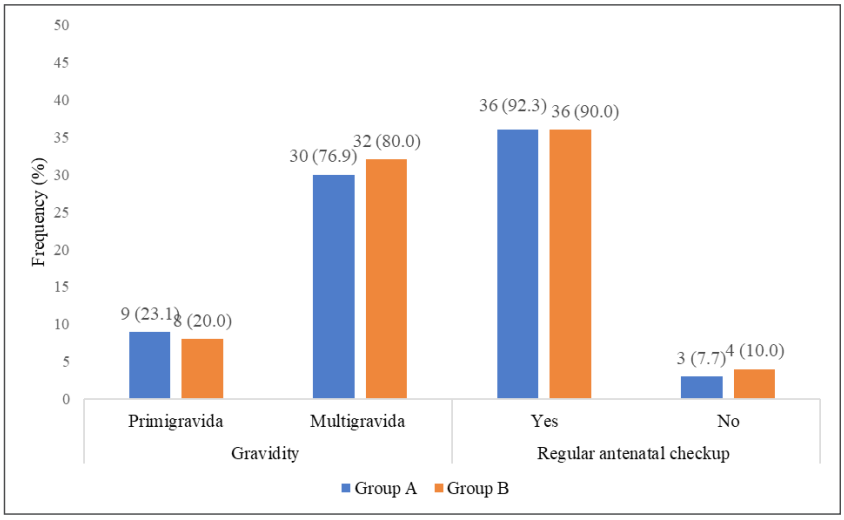

Figure 1. *Bar diagram showing obstetrical history of the participants*

Figure 1 shows no significant difference between groups was observed in terms of obstetrical history of the study participants (p-value: >0.05).

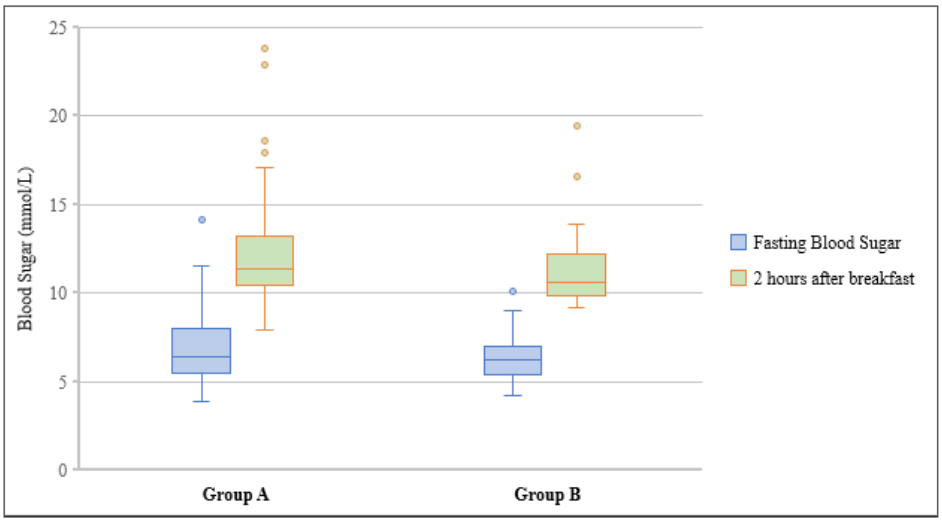

Figure 2. *Baseline Fasting and 2 hours after breakfast blood sugar of the participants*

Figure shows no significant difference in Fasting and 2 hours after breakfast blood glucose among study groups were observed.

Table 3. *Baseline Fasting and 2-Hours After Breakfast Blood Glucose of the Participants*

Blood Glucose Parameter	Group A (n=39) Median (Range)	Group B (n=40) Median (Range)	Total (N=79) Median (Range)	P value
Fasting Blood Sugar (mmol/L)	6.4 (3.90–14.10)	6.2 (4.20–10.10)	6.3 (3.90–14.10)	0.284[a]
2-Hours After Breakfast Blood Sugar (mmol/L)	11.4 (7.90–23.80)	10.6 (9.20–19.40)	11.07 (7.90–23.80)	0.176[a]

[a]Mann–Whitney U test was performed, ns = Not statistically significant (p > 0.05)

Table 3 shows no significant difference in Fasting and 2 hours after breakfast blood glucose among study groups were observed (p-value: >0.05).

Table 4. *Association of Controlled blood sugar between treatment groups at the end of the second week*

Treatment	Blood sugar		Total	P value
	Controlled (n)=%	Uncontrolled (n)=%		
Group A (Insulin Actrapid)	21 (58.3%)	15 (41.7%)	36 (100.0%)	0.029[s]
Group B (Insulin Aspart)	31 (81.6%)	7 (18.4%)	38 (100.0%)	
Total	52 (70.3%)	22 (29.7%)	74 (100.0%)	

Chi-square test was done, s= significant

Table 4 shows following treatment for two weeks, it was observed that the blood sugar level was controlled in 58.3% of participants of Group A and 81.6% in Group B. Blood sugar was significantly controlled in higher proportion in Group B (p-value: 0.029).

Table 5. *Risk ratio analysis for determining the impact of giving intervention (rapid-acting) on study participants at the end of the second week*

Treatment	Blood sugar		Risk ratio (95% Confidence interval)	P value
	Controlled	Uncontrolled		
Group A (Insulin Actrapid)	21 (58.3%)	15 (41.7%)	0.44 (0.20-0.96)	0.038[s]
Group B (Insulin Aspart)	31 (81.6%)	7 (18.4%)		

Risk ratio analysis was done, S=significant

Table 5 shows that, giving rapid-acting insulin as an intervention than short-acting insulin (reference) decreases the risk of uncontrolled diabetes mellitus. The risk ratio (RR) is 0.44 and the 95% CI of the risk ratio is 0.20-0.96 (p-value: 0.038). Pregnant women who received rapid insulin for diabetes mellitus were 56% less likely to experience uncontrolled diabetes mellitus than those who received short-acting insulin within 2 weeks.

Table 6. *Distribution of hypoglycemia in Treatment groups at the end of second week*

Nature of hypoglycemia	Group A(Insulin Actrapid) N=36		Group B (Insulin Aspart) N=38	
	Number of participants	Number of events	Number of participants	Number of events
Level 1: <3.9 mmol/L	12 (33.3%)	16 (88.9%)	5 (13.16%)	6 (100.0%)
Level 2: <3.0 mmol/L	2 (5.5%)	2 (11.1%)	0 (0.0%)	0 (0.0)
Level 3: A severe event characterized by altered mental or physical status, requiring assistance for the treatment of hypoglycemia	-	-	-	-

Table 6 shows among the participants who were in group A (short-acting insulin), 33.3% experienced level 1 (<3.9 mmol/L) hypoglycemia, and 5.5% experienced Level 2 (<3.1 mmol/L) hypoglycemia. A total of 38.8% of participants in Group A experienced hypoglycemia. On the other hand, only 13.16% of group B (rapid-acting insulin) experienced hypoglycemia. Proportionately, evidence of hypoglycemia was more in group A than in group B.

Table 7. *Risk ratio analysis for determining the risk of hypoglycemia from giving intervention (rapid-acting) to study participants at the end of the second week*

Treatment	Hypoglycemia		Risk ratio (95% Confidence interval)	P value
	Yes	No		
Group A (Insulin Actrapid)	14 (38.9%)	22 (61.1%)	0.34 (0.14-0.84)	0.02
Group B (Insulin Aspart)	5 (13.2%)	33 (86.8%)		

Risk ratio analysis was done, S=significant

Table 7 shows that, giving rapid-acting insulin as an intervention than short-acting insulin (reference) decreases the risk of hypoglycemia. The risk ratio (RR) is 0.34 and the 95% CI of the risk ratio is 0.14-0.84 (p-value: 0.02). Pregnant women who received rapid insulin for diabetes mellitus were 66% less likely to experience hypoglycemia than those who received short-acting insulin within 2 weeks.

Table 8. *Time required (in hours) for controlling blood sugar within 2 weeks of initiating treatment*

Time required for controlling blood sugar (hours)	Group A(Insulin Actrapid) (n1=36)	Group B(Insulin Aspart) (n2=38)	P value
Mean ± SD	212.57±59.89	173.41±72.85	0.037[s]
Median (range)	240 (96-288)	144 (96-288)	

Mann Whitney U test was done, s= significant

Table 8 shows patients treated with rapid-acting insulin (173.41±72.85 hours) needed much less time than patients treated with short-acting insulin (212.57±59.89 hours) (p-value: 0.037).

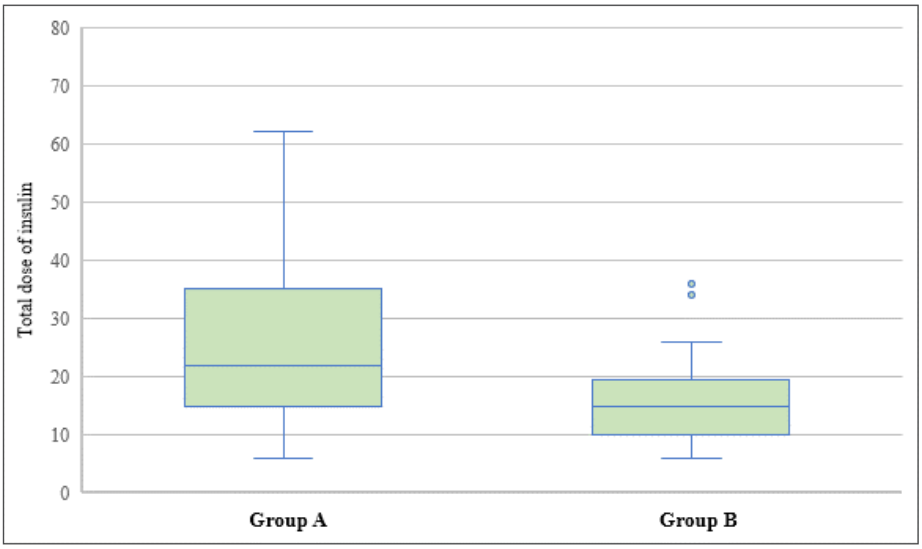

Figure 3. *Total dose of insulin required for blood sugar controlling*

Figure shows significantly higher doses of insulin were needed for controlling blood sugar of Group A participants than Group B.

Table 9. *Total dose of insulin required for blood sugar controlling*

Insulin		Group A(Insulin Actrapid) (n1=36)	Group B(Insulin Aspart) (n2=38)	P value
The total dose of insulin	Mean ± SD	25.63±15.15	15.67±8.44	0.003[s]
	Median (range)	22 (6.0-62.0)	15 (6.0-36.0)	

Mann Whitney U test was done, s= significant

Table 9 shows significantly higher doses of insulin were needed for controlling blood sugar of Group A participants than Group B (p-value: 0.003).

4. Discussion

This RCT was done to find out whether Rapid Acting Insulin (Insulin Aspart) can effectively control hyperglycemic disorder in pregnancy than Regular Insulin or not. A total number of 79 (39 in the control group and 40 in the experimental group) patients were allocated in this study by block randomization, from obstetrics and Feto-maternal Medicine outpatient department of Dhaka Medical College Hospital, Dhaka during the period of January 2023 to December, 2023. The sociodemographic characteristics of the study subjects in relation to Intervention and Control group is shown in table 1. The table showed that the demographic characteristics in the term of age, socioeconomic status, education, occupation are statistically indifferent. The majority (48.1%) participants were from 25-30 years. Kai Wei Lee et al. in the study of Prevalence and risk factors of GDM in Asia: a systematic review and meta-analysis, also reported age group >-25 years are a significant risk factor of GDM (OR 2.17,95%CI 1.96-2.41).[22] In the study of Prevalence and Risk factors of GDM in Bangladesh Tapash et al. found 40% of women aged 25 years or more had GDM. (OR 2.03,95% CI 1.13-3.65).[4] In this study considering BMI, 51.9% were in overweight ,26.8% were in normal weight and 20.3% were obese but there was no significant difference between the two groups in respect of BMI (p=0.722). Parichehr Pooransari et al.in their study also found mean BMI value of the participants (GDM) was in overweight group without any significant difference in between two like our study.[23] Maryam Saeedi et al. also demonstrated increased incidence of GDM when BMI is ≥25 or <25.[3] Other demographic parameters were statistically indifferent in this study. No significant difference had been found in obstetrical history of the study participants (p-value:>0.05). The physical parameters and obstetrical parameters were not significant between two groups. In this single blinded study, the baseline fasting and 2 hours after breakfast blood sugar of all participants between experimental and control group was insignificant. After MNT when they failed to achieve target level, Insulin Aspart was given to intervention group and Regular Insulin in control group and monitored for 2 weeks. Following treatment for 2 weeks blood sugar was controlled in 58.3% participants of control group and 81.6% in intervention group 41.7% of control

group and 18.4 % of intervention group failed to control within 2 weeks. Thus, blood sugar was significantly controlled in intervention group with p-value 0.029. As the Risk Ratio (RR) is 0.44 and the 95% CI of the risk ratio is 0.20-0.96 (p-value:0.038). So pregnant women who were treated with Rapid Insulin (Insulin Aspart) were 56% less likely to experience uncontrolled blood sugar status than those who received Regular Insulin within 2 weeks.Pettitt et al. in 2003 also conducted a comparative study of Insulin Analogue, Insulin Aspart and Regular Insulin with no insulin in GDM and concluded that Insulin Aspart was very effective(p-value:<0.001) in reducing peak post-prandial glucose concentration whereas Regular Insulin did not show any significant difference(p-value=0.034)[24] which supports our study. In this study we found the Risk Ratio (RR) is 0.44 and the 95% CI of the risk ratio is 0.20-0.96 (p-value:0.038). So pregnant women who were treated with Rapid Insulin (IAsp) were 56% less likely to experience uncontrolled blood sugar status than those who received Regular Insulin within 2 weeks. Mathiesen ER et al. conducted a RCT with 322 women to control hyperglycemia in type 1 diabetic pregnacy with Insulin Aspart and Regular Insulin & found mean postprandial glucose increment was lower after each main meal with Insulin Aspart ,the treatment differences -0.75 mmol/L[95% CI -1.25 to -0.25];p=0.003 at 12 weeks of gestation and -0.40mmol/L[95%CI-0.80 to -0.01];p=0.044 at 36 weeks gestation.[25] which also supports our study though their study period was more and included type 1 DM pregnant lady. Another randomized parallel group trial in 2007 by Pettitt et al. compared efficacy of Insulin Aspart with Regular Insulin with GDM. Here women were followed from diagnosis to 6weeks post- partum. Change from baseline values for average glucose (IAsp -1.09 +/- 0.54 mmol/l, RI -0.54 +/- 0.74 mmol/l; P = 0.003) was significantly lower after Insuiln Aspart treatment than RI treatment.[26] In our study we also found similar presentation in the form of less likely chance of uncontrolled postprandial blood sugar (p=0.038) with Rapid insulin (IAsp) though study period was different. A clinical trial was carried out in 2007 by Cianni et al. on 96 patients with GDM and reported that Rapid acting glucose analogue showed better post prandial glucose control than Regular Insulin when not controlled by diet alone. Though they compared both IAsp and Lispro with Regular Insulin.[27] Even in non-pregnant women meta-analysis of Rapid insulin, Insulin Aspart versus Regular Insulin was done by Simon Heller et al. and RCT by Home PD et al. for the treatment of diabetes mellitus. Simon Heller et al. did randomized with duration of 12 weeks and consisted at least two arms of with Rapid insulin, Insulin Aspart & Regular Insulin. They found that postprandial blood was significantly lower after treatment with Rapid insulin, Insulin Aspart in comparison with Regular Insulin. (p<0.001). [28] Home PD et al. in a RCT of Insulin Aspart versus Regular Insulin in type 1 DM also found benefit of Rapid Acting Insulin.It was prospective, multi-centre, randomized, open-labelled, parallel-group trial lasting 6 months in 88 centres in eight European countries and including 1,070 adult subjects with Type 1 diabetes. After 6 months, Insulin Aspart was superior to human insulin as eight-point blood glucose profiles showed lower post-prandial glucose levels (mean baseline-adjusted -0.6 to -1.2 mmol/l, P < 0.01) after all main meals with Insulin Aspart.[29] Trials were randomized and found benefit of IAsp over Regular Insulin.[28,29] Kirsten Norgaard et al. also found IAsp to be safe in effective for GDM and Type 1 DM in a systematic review and meta-analysis. [30] All these studies support our study that Rapid Acting Insulin is more effective in controlling hyperglycemic disorder in pregnancy. In our study among the participants of group A (control group), 33.3% developed level 1 hypoglycemia (<3.9 mmol/L) and 5.5% developed level 2 (<3.1 mmol/L) hypoglycemia. So total occurence of hypoglycemia among participants were 38.8%. In group B (experimental group) 13.16% experienced level 1 hypoglycemia and none experienced level 2 hypoglycemia. Total 13.16% of group B experienced hypoglycemia. Significant hypoglycemia was found in group A (control group) than in group B in two weeks insulin treatment. The risk ratio (RR) is 0.34 and the 95% CI of the risk ratio is 0.14-0.84 (p value:0.02). Pregnant women who received rapid insulin for diabetes mellitus were 66% less likely to experience hypoglycemia than those who received short-acting insulin within 2 weeks. So Rapid Acting Insulin seems to be safer in treating hyperglycemia in pregnancy. Parichehr Pooransari et al. in a retrospective study to see efficacy of Rapid Acting Insulin, Insulin Aspart and Regular Insulin over 150 pregnant women also found frequency of hypoglycemia (p-value:0.001) was significantly lower in Insulin Aspart group.[23] In multicentered RCT of 6 months study of type 1 DM patients, Philip Raskin et al. found episodes of hypoglycemia were also similar in between two groups. But Insulin Aspart was associated with less major nocturnal hypoglycemia [31] though it was

conducted in non-pregnant women. In systematic review and meta-analysis by Kirsten Norgaard et al. the risk of major hypoglycemic events was numerically lower, but not significantly different, for Insulin Aspart (rate ratio 0.72 [95% CI 0.36; 1.46]).[30] M. C. Deepaklal et al.also found Insulin Aspart safe as there was no episode of minor or major hypoglycemia reported in the study of Insulin Aspart in patients with GDM and pregestational DM.[32] In our study no participants experienced level 2 and level 3 hypoglycemia in experimental group. Metheisen et al. also found less chance of major hypoglycemia in the RCT of 322 pregnant women of type 1 DM. The study showed Major hypoglycemia occurred at a rate of 1.4 vs. 2.1 episodes/year exposure with IAsp and HI, respectively (relative risk 0.720 [95% CI 0.36–1.46]). Risk of major/major nocturnal hypoglycemia was 52% (RR 0.48 [0.20–1.143]; *P* = NS) lower with IAsp compared with HI.[25] In our study time required to control blood sugar in experimental group was 173.41±72.85 hours. On the contrary in control group, it was 212.57 ± 59.89 hours. (p-value:0.037). Also, total dose of insulin was significantly higher (p-value:0.003) in control group than in experimental group.Though fewer study demonstrated comparison of dose of insulin in two groups, Parichehr Pooransari et al. found insulin dose (p-value:0.005) was significantly lower in Insulin Aspart group. Also, length of hospital stay and insulin therapy were significantly shorter in Insulin Aspart group. All these are similar to our study result.[23] The current study showed blood sugar was significantly controlled with Rapid Acting Insulin as RR is 0.44 and the CI of the risk ratio is 0.20-0.96 with less chance of hypoglycemia. As our new approach is to turn the pyramid of obstetric care, timely diagnosis of hyperglycemic disorder in pregnancy and effective treatment to reduce its related maternal and fetal complications are desirable. Effective and safe use of insulin in pregnancy can help us in this regard. Use of Rapid Acting Insulin can help us in proper treatment of hyperglycemic disorders in pregnancy with less side effects and more benefits.

5. Conclusion

The result of this study demonstrated that Rapid Acting Insulin (Insulin Aspart) had better control than Regular Insulin in treating hyperglycemic disorder in pregnancy without adversely affecting maternal characteristics. So, Rapid Acting Insulin can be used to control hyperglycemic disorder in pregnancy.

Limitations

The present study had some limitations despite careful methodology. The sample size was relatively small, which may limit the generalizability of the findings. The study was conducted at a single tertiary care hospital (DMCH), so the results may not represent the entire population of Bangladesh. The study duration was also short and long-term maternal and neonatal outcomes could not be assessed. Differences in insulin requirements among GDM, type 1 diabetes, and type 2 diabetes mothers were not evaluated. Financial constraints and difficulties with regular follow-up also affected complete data collection.

Recommendations

Large-scale multicenter studies with longer follow-up are recommended to validate these findings and assess maternal fetal and neonatal outcomes. Improved awareness among obstetricians and pregnant women, early diagnosis, regular monitoring and proper management of hyperglycemic disorders in pregnancy may reduce complications and improve maternal and perinatal outcomes.

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