Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

A Comparative Study of Maternal, Fetal and Neonatal Outcomes in Pregnancy with Diabetes Treated with Human Regular Insulin and Rapid Acting Insulin Analogs

[1]Dr. Goutam Chatterjee, [2]Dr. Debobroto Roy, [3]Dr. Banhi Shikha Modak, [4]Dr. Krishna Pada Das,

[1]RMO Cum Clinical Tutor, MS (GLO), Department of Obstetrics and Gynecology, Burdwan Medical College, Burdwan University, Burdwan , West Bengal 713104.

[2]Assistant Professor, MS (GRO), Department of Obstetrics and Gynecology, Burdwan Medical College, Bardhaman University, Burdwan , West Bengal 713104.

[3]Specialist Medical Officer, MS (GRO); DNB (GRO), Department of Obstetrics and Gynecology, Chandannagar Sub Divisional Hospital, Chandannagar, Chinsurah, West Bengal 712136.

[4]Assistant Professor, MS (G10), Department of Obstetrics and Gynecology, Burdwan Medical College, Burdwan University, Burdwan , West Bengal 713104.

Corresponding Author: Dr. Debobroto Roy

Assistant Professor, MS (GRO), Department of Obstetrics and Gynecology, Burdwan Medical College, Bardhaman University, Burdwan , West Bengal 713104.

(Received: 14 April 2024 Revised: 1 May 2024 Accepted: 18 June 2024)

KEYWORDS

Pregnancy, Diabetes, Human Regular Insulin, Rapid-Acting Insulin Analogs, Maternal Outcomes, Neonatal Outcomes, Fetal Health.

ABSTRACT:

Introduction: Diabetes in pregnancy poses significant risks to both maternal and fetal health, necessitating careful management to optimize outcomes. Traditional management often involves the use of Human Regular Insulin (HRI), while Rapid-Acting Insulin Analogs (RAIA) have emerged as an alternative. This study aims to compare maternal, fetal, and neonatal outcomes in pregnancies managed with HRI versus RAIA.

Aims: The primary aim is to evaluate the efficacy and safety of HRI and RAIA in managing diabetes during pregnancy. Secondary aims include assessing the incidence of adverse maternal and neonatal outcomes, such as preterm birth, macrosomia, and neonatal hypoglycemia.

Materials and Methods: Our study was a single center randomized control trial conducted in the department of Obstetrics & Gynecology of Ramakrishna Mission Seva Pratishthan (RKMSP), Vivekananda Institute of Medical sciences (VIMS). After obtaining necessary approval from the 'Institutional Ethical Committee' and written informed consent from the participants.134 patients were included in this study

Results: We showed that During the 1st trimester, FBS values were 116.86 ± 9.81, 111.83 ± 5.95, and 122 ± 8.64 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.201, not significant). FBS during the 2nd trimester were 99.50 ± 4.28, 95.67 ± 1.51, and 102.20 ± 5.59 mg/dl in the I.Asp, I.Lisp, and RHI group respectively (p = 0.050, not significant). 3rd trimester FBS values were 91.86 ± 4.41,89.67 ± 2.34 and 94.00 ± 2.83 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.185, not significant).

Conclusion: The findings suggest that RAIA may offer comparable, if not superior, control of maternal blood glucose with potentially fewer complications compared to HRI. However, further research, including randomized controlled trials, is necessary to confirm these findings and establish definitive clinical guidelines.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

Introduction

Diabetes mellitus is a chronic metabolic disorder due to either insulin deficiency or peripheral tissue resistance (decreased sensitivity) to the action of insulin. It has been recognized as a clinical syndrome since ancient times and remains a crippling global health problem today. The ancient literature of Egypt, India, China contain reference to diabetes. The Indian physician 'Charaka' in his famous classic "CHARAKA SAMHITA" based on the teaching of "Atreva Punarbash" described 'Madhumeha' (honey urine).[1] Pregnancy is a state of persistent insulin resistance. The problem exists both in insulin secretion and action. The ultimate outcome is the hyperglycemia. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) defined hyperglycemia first discovered during pregnancy as either 'overt diabetes' or 'gestational diabetes mellitus (GDM)'. [2] Gestational diabetes mellitus (GDM) is defined as any glucose intolerance with onset or first recognition during pregnancy. It includes previously undetected type 1 or type 2 diabetes mellitus or first presentation of diabetes during pregnancy that generally occurs in the second half of pregnancy.[3] Overt diabetes or Pregestational diabetes (PGDM) is called when diabetes is present before the onset of pregnancy. The condition may be pre-existing or detected for the first time during present pregnancy. Of all the pregnancies complicated by diabetes, GDM accounts for about 90%.[3] Depending on the population sample and diagnostic criteria, the prevalence of GDM varies from 1-20% and is rising worldwide, parallel to the increment in the prevalence of obesity and type 2 diabetes mellitus (T2DM).[4] The burden of the disease varies in direct proportion to the prevalence of T2DM in a given population, or ethnic group. In our country, due to high prevalence of diabetes among general population, Indian women have 11 fold increased risk of developing glucose intolerance during pregnancy compared to Caucasian women.[5] The Diabetes In Pregnancy Study group India (DIPSI) reported guidelines for diagnosing GDM and recommends universal screening of all pregnant women for diabetes in our country.[6] The recent data on the prevalence of GDM in India is 16.55%.[7] Pregnancy complicated by diabetes increases the risk of maternal, fetal and neonatal complications. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) Study [8] found significant associations between adverse pregnancy outcomes and higher levels of maternal Glucose can lead to several complications, such as the development of polyhydramnios, preeclampsia, premature labour, increased perinatal loss, foetal macrosomia, congenital deformity, growth limitation, shoulder dystocia, and an increased rate of caesarean delivery due to macrosomia. Neonatal problems encompass hypoglycemia, respiratory distress syndrome, hyperbilirubinemia, hypocalcaemia, and other related conditions.The user's text is "[8]".Optimal regulation of blood sugar levels before and after meals is crucial for achieving better outcomes for the mother, foetus, and newborn. The treatment should focus on reaching a fasting plasma glucose level of approximately 90 mg/dl and a 2-hour postprandial level of around 120 mg/dl, as recommended by the current Indian recommendations for diagnosing and managing gestational diabetes mellitus.[9]

Materials and Methods

Study Design:

Our study was a single centre randomized control trial.

Study Setting:

This study was carried out in the Department of Obstetrics & Gynecology of Ramakrishna Mission Seva Pratishthan (RKMSP), Vivekananda Institute of Medical sciences (VIMS), 99 Sarat Bose Road, Kolkata–700026. This is a tertiary care multi-disciplinary medical institution which serves as a training centre for postgraduate medical students under The West Bengal University of Health Sciences. This 550-bedded hospital has a full-fledged obstetric and gynecological service and about 8000 patients attend the obstetrics & gynecological out-patient department (OPD) every year.

Place of Study:

Antenatal and postnatal mothers are taken care of in the OPD and indoor of the Department of Obstetrics & Gynecology of RKMSP (VIMS). Deliveries are conducted in the well equipped Labor Room and Operation Theatre with close monitoring. Normal and healthy neonates are cared under pediatricians and well trained nursing staff in the postnatal ward. Newborn

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

care unit and the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics and Neonatology take care of the sick newborns. The present study involved monitoring and follow up of the patients in all these places (departments).

Period of Study:

One year (December 2016 to November 2017).

Study Population:

Antenatal mothers attending the antenatal OPD in the Department of Obstetrics and Gynecology of RKMSP (VIMS) who met the eligibility criteria (diagnosed of having GDM or PGDM requiring insulin therapy after detailed history taking, clinical examination and investigations) during the study period in this centre were consented and formed the study population.

Sample Size:

Sample size (n) =

$2 (Z\alpha + Z1\text{-}\beta)2 \sigma 2$

$\delta 2$

Assuming p value <0.05 to be significant and considering effect to be two sided, we get – $Z\alpha = 1.96$,

Assuming power of study to be 90%, we get – $Z1\text{-}\beta = 1.28$,

From previous studies, we get –

An effect size (expected difference in mean peak glucose concentration between the treatment groups), $\delta = 0.8$ (to be statistically significant), and standard deviation (σ) = 1.1,

$2 (1.96 + 1.28)2 \text{ x } (1.1)2$

So, Sample size in each group will be == 40

$(0.8)2$

Hence minimum 40 patients should be taken in each group. As there is three treatment groups in our study, i.e, RHI, I.Asp and I.Lisp, so, total sample size will be = 40 x 3 = 120.

Considering 10% drop out, total sample size would be, n = 132.

A total of 134 women with GDM and PGDM were recruited initially in our study.

Inclusion Criteria:

1. Singleton pregnancy
2. Booking visit at first trimester
3. Patients willing to give informed consent
4. GDM patients not responding to MNT and requiring insulin
5. PGDM patients requiring insulin therapy.

Exclusion Criteria:

1. Multiple pregnancy
2. Booking visit after first trimester
3. Patients not giving informed consent
4. GDM patients controlled by MNT or oral hypoglycemic agents (OHA)
5. PGDM patients controlled by MNT and OHA
6. Patients treated by insulin other than RHI or RAIA
7. Women with chronic hypertension
8. Women with autoimmune disease except Type-1 diabetes
9. Women receiving steroid therapy (except antenatal corticosteroid for fetal lung maturity)

Result

Table 1 Association between groups with all parameters

	PGDM							
	Insulin Type							
	I.Asp		I.Lisp		RHI			
	Mean	SD	Mean	SD	Mean	SD	p Value	Significance
FBS 1st trimester (mg/dl)	116.86	9.81	111.83	5.95	122.00	8.64	0.201	Not Significant
FBS 2nd trimester (mg/dl)	99.50	4.28	95.67	1.51	102.20	5.59	0.050	Not Significant
FBS 3rd trimester (mg/dl)	91.86	4.41	89.67	2.34	94.00	2.83	0.185	Not Significant
2 h ABF 1st trimester	213.71	21.27	210.83	11.60	216.50	12.69	0.869	Not Significant

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

(mg/dl)								
2 h ABF 2nd trimester (mg/dl)	167.13	15.38	153.83	6.46	166.00	6.48	0.099	Not Significant
2 h ABF 3rd trimester (mg/dl)	134.86	7.10	130.50	4.72	137.00	7.62	0.289	Not Significant
2 h ALN 1st trimester	204.43	19.71	208.33	11.55	212.00	4.32	0.713	Not Significant
2 h ALN 2nd trimester	154.88	11.87	145.50	7.37	166.00	13.56	0.026	Significant
2 h ALN 3rd trimester	129.71	7.23	123.83	6.21	135.75	10.84	0.094	Not Significant
Mean 2 h PPBS 1st trimester (mg/dl)	201.76	14.42	204.56	7.01	208.67	8.64	0.619	Not Significant
mean 2 h PPBS 2nd trimester (mg/dl)	156.54	11.59	146.06	4.45	160.53	9.67	0.049	Significant
mean 2 h PPBS 3rd trimester (mg/dl)	129.76	4.90	124.44	4.03	132.83	8.26	0.082	Not Significant

Table 2 Association between groups with all parameters

Fetal outcomes			Insulin Type			Total	p Value	Significance
			I.Asp	I.Lisp	RHI			
PGDM	Fetal complications	CHD	1(12.5)	0(0)	0(0)	1(5.26)	0.429	Not Significant
		IUFD	1(12.5)	0(0)	0(0)	1(5.26)		
		FGR	1(12.5)	1(16.67)	1(20)	3(15.79)		
		Macrosomia	0(0)	3(50)	3(60)	6(31.58)		
		MSL	2(25)	0(0)	0(0)	2(10.53)		
		NTD	1(12.5)	0(0)	1(20)	2(10.53)		
		None	2(25)	2(33.33)	0(0)	4(21.05)		
	Total		8(100)	6(100)	5(100)	19(100)		
GDM	Fetal complications	IUFD	1(3.13)	1(2.78)	1(2.56)	3(2.8)	0.912	Not Significant
		FGR	2(6.26)	4(11.11)	3(7.69)	9(8.41)		
		Macrosomia	3(9.38)	3(8.33)	5(12.82)	11(10.28)		
		MSL	4(12.5)	5(13.89)	3(7.69)	12(11.21)		
		None	22(68.75)	23(63.89)	27(69.23)	72(67.29)		
	Total		32(100)	36(100)	39(100)	107(100)		

Table 1 shows During the 1st trimester, FBS values were 116.86 ± 9.81, 111.83 ± 5.95, and 122 ± 8.64 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.201, not significant). FBS during the 2nd trimester were 99.50 ± 4.28, 95.67 ± 1.51, and 102.20 ± 5.59 mg/dl in the I.Asp, I.Lisp, and RHI group respectively (p = 0.050, not significant). 3rd trimester FBS values were 91.86 ± 4.41,89.67 ± 2.34 and 94.00 ± 2.83 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.185, not significant).

Mean values for PPBS 2 hour ABF during the 1st trimester were 213.71 ± 21.27, 210.83 ± 11.60,216.50 ± 12.69 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.869, not significant). During the 2nd trimester, those values were 167.13 ± 15.38, 153.83 ± 6.46 and

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

166.00 ± 6.48 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.099, not significant). 2 h ABF values during the 3rd trimester were 134.86 ± 7.10, 130.50 ± 4.72 and 137.00 ± 7.62 mg/dl in the I.Asp, I.Lisp and RHI group respectively(p = 0.289, not significant).

During 1st trimester, 2 h ALN glucose values were 204.43 ± 19.71, 208.33 ± 11.55 and 212.00 ±

4.32 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.713, not significant). Those values during 2nd trimester were 154.88 ±11.87, 145.50 ± 7.37 and 166.00 ± 13.56 mg/dl in the I.Asp, I.Lisp and RHI group respectively which shows significant difference with p value = 0.026. During 3rd trim., 2 h ALN values were 129.71 ± 7.23, 123.83 ± 6.21 and 135.75 ± 10.84 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.094, not significant).

Mean 2 h PPBS values during the 1st trimester were 201.76 ± 14.42, 204.56 ± 7.01 and 208.67 ±8.64 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.619, not significant). During the 2nd trimester, those values were 156.54 ± 11.59, 146.06 ± 4.45 and 160.53 ± 9.67 mg/dl in the I.Asp, I.Lisp and RHI group respectively which shows significant difference (p = 0.049). Mean 2 h PPBS values during the 3rd trimester were 129.76 ± 4.90, 124.44 ± 4.03 and 132.83 ± 8.26 mg/dl in the I.Asp, I.Lisp and RHI group respectively (p = 0.082, not significant).

The table 2 shows that fetal outcomes were comparable in the three insulin groups of women with PGDM without any significant difference (p = 0.429). Macrosomia was the majority of fetal complications in the I.Lisp (50% of women) and RHI (60% of women) group. Fetal congenital anomalies in the form of congenital heart disease (CHD) was reported in one (12.5%) subject of I.Asp group and neural tube defects (encephalocele) were reported in one woman of each of I.Asp (12.5%) and RHI (20%) group. Intrauterine fetal death (IUFD) occurred in one (12.5%) woman of I.Asp group. Fetal growth restriction (FGR) occurred in one subject of each of the three insulin groups. Meconium stained liquor (MSL) due to fetal distress during labor was reported in two (25%) woman of I.Asp group. No significant differences in the fetal outcomes were observed among the groups (p = 0.912) in GDM. Macrosomia was observed in 3 (9.38%), 3 (8.33%) and 5 (12.82%) women of I.Asp, I.Lisp and RHI groups respectively. No fetal congenital malformation was reported in GDM patients.

Discussion

Our study was a single center randomized control trial conducted in the department of Obstetrics & Gynecology of Ramakrishna Mission Seva Pratishthan (RKMSP), Vivekananda Institute of Medical sciences (VIMS). After obtaining necessary approval from the 'Institutional Ethical Committee' and written informed consent from the participants, a total of 134 women were recruited based on the inclusion and exclusion criteria

Throughout the investigation, a total of eight women discontinued their participation in the experiment for various reasons. Ultimately, a total of 126 women (107 with GDM and 19 with PGDM) consistently participated in the interventions during their pregnancy. The distribution of these women was as follows: 40 in the I.Asp group, 42 in the I.Lisp group, and 44 in the RHI group.

The baseline variables, including age, weight, height, and BMI, were nearly same and comparable across all groups, with no significant variations seen. The age range of the women in the PGDM program was between 20 and 38 years. The average age was 26.50 ± 6.93 years in the I.Asp group, 26.00 ± 4.15 years in the I.Lisp group, and 29.40 ± 2.70 years in the RHI group. The age of the women with gestational diabetes mellitus (GDM) ranged from 18 to 36 years. The mean age was 25.81 ± 4.29 years in the I.Asp group, 25.42 ± 4.07 years in the I.Lisp group, and 26.33 ± 4.51 years in the RHI group. The average BMI of women with overt diabetes was 28.39 ± 1.78, 29.08 ± 1.50, and 27.78 ± 1.21 kg/m2 in the I.Asp, I.Lisp, and RHI groups, respectively. This difference was not statistically significant (p = 0.407). Similarly, the average BMI of women with GDM was 24.82 ± 2.25, 24.50 ± 2.09, and 24.69 ± 2.27 kg/m2 in the I.Asp, I.Lisp, and RHI groups, respectively. This difference was also not statistically significant (p = 0.834). The body mass index (BMI) of the women with pregestational diabetes mellitus (PGDM) was greater compared to the women with gestational diabetes mellitus (GDM).

All the women (100%) with PGDM had positive family

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

history of diabetes among their first degree relatives and more than half of GDM women (56.07%) had the same positive family history. One study conducted by Bhat et al.[10] in South India reports that 37.3% patients with GDM and 12% patients in control group had family history of diabetes in first-degree relatives which is much less than reported in our study. This finding of our study gives a signal that in India, routine screening for GDM of all the pregnant women is essential at the first antenatal visit.

Mean fasting blood sugar (FBS) values of all the treatment groups in both GDM and PGDM were comparable throughout pregnancy. There were no statistically significant differences among the treatment groups, i.e, all the three insulins (I.Asp, I.Lisp and RHI) were equally effective in reducing fasting hyperglycemia throughout pregnancy.

I.Asp and I.Lisp had significantly better control of postprandial hyperglycemia after breakfast than RHI in GDM ($p = 0.003$, 2^{nd} trim. $p = 0.001$, 3^{rd} trim.), although no significant differences were observed in overt diabetes. All three insulins were also effective in reducing postprandial hyperglycemia after lunch throughout pregnancy in both GDM and PGDM, although, I.Lisp and I.Asp had much better control than RHI and the differences were significant among the treatment groups at 2^{nd} trimester ($p = 0.026$) in PGDM and at 3^{rd} trimester ($p = 0.011$) in GDM. Postprandial blood glucose levels after dinner were lower with I.Asp and I.Lisp throughout pregnancy in both PGDM and GDM, but the differences were insignificant.

The estimated mean values of 24 hour blood glucose were significantly lower with I.Asp and I.Lisp at 2^{nd} and 3^{rd} trim. ($p = 0.035$ and 0.009 respectively) in GDM and only at the 2^{nd} trimester($p = 0.042$) in PGDM. Similarly, mean prandial blood glucose excursions during pregnancy were significantly lower with I.Asp and I.Lisp than RHI at 2^{nd} and 3^{rd} trim. ($p = 0.025$ and 0.001 respectively) in GDM, but differences were insignificant in PGDM.

Overall glycemic control, assessed by HbA1c values at 6 weeks of starting therapy and at 36-38^{th} week of gestation, was good in all the treatment groups without any significant differences. Target HbA1c value of 6.5 or less was achieved by most of the patients in all the treatment groups at 36-38^{th} week of gestation in both GDM and overt diabetes.

All these findings of our study were almost similar with that observed in a study conducted by Mathiesen ER et al[11] which showed that postprandial hyperglycemic excursions were lower with IAsp than with HI, especially after breakfast, with no difference in preprandial glucose control, although glycemic control, assessed by A1C, was similar with IAsp and HI.

Regarding hypoglycemic episodes, 11 (almost 58%) women with PGDM had total 23 episodes during day time throughout pregnancy. Maximum number of the hypoglycemic episodes (12 epi.) occurred in subjects of I.Asp group, but women of RHI group (80%) were maximally affected. Most of the episodes were of minor type. Most of the women (60%) having major episodes belonged to the RHI group. I.Lisp group had no major episodes. Whereas, a total of 48 hypoglycemic episodes occurred during day time in 28 (26.17%) women with GDM. Most of the women having hypoglycemia including major episodes were in the I.Lisp group (39%), although intergroup differences were insignificant.

Observed rates of nocturnal hypoglycemia were lower with I.Asp and I.Lisp than RHI in PGDM women, although this did not reach statistical significance. A total of seven (37%) women had 11 episodes out of which 60% of subjects having almost half of total episodes were in the RHI group. No major episode was reported during night in PGDM. GDM women had almost similar hypoglycemic profiles with no significant differences among the treatment groups. A total of 33 nocturnal episodes occurred in 23(21.5%) women. Only one major nocturnal episode was reported in the I.Lisp group.

Most of the hypoglycemic episodes occurred during daytime hours, which allowed subjects to treat these episodes easily.Maternal adverse effect profiles were almost similar in all the treatment groups. Majority of women of GDM and PGDM had no significant adverse effects. Only few had injection site reactions (erythema, swelling and rash) possibly related to the insulin injection. 4 (12.5%) patients of I.Asp group, 5 (14%) of I.Lisp group and 2 (5%) of RHI group in GDM had injection site reactions. The differences were statistically insignificant. Only one (12.5%) woman with PGDM experienced injection site

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

rash in the I.Asp group.

Similar findings were observed by Mathiesen ER et al[11] in their study which showed that the observed rate of major episodes including nocturnal episodes was lower for I.Asp-treated than RHI-treated subjects. Maternal safety profiles of I.Asp and RHI were comparable. Also Garg et al [12]reported relatively few major hypoglycemic episodes in 62 insulin lispro-treated pregnant women with type 1 diabetes. In a clinical study done by Pettitt DJ, Ospina P, Jovanovic L, et al [13]it was found that the overall safety and effectiveness of I.Asp was comparable to RHI in pregnant women with GDM, indeed, I.Asp was more effective than RHI in providing postprandial glycemic control in women with GDM.

In another study, Jovanovic L et al[14] found insulin lispro to be more efficacious than RHI in rapidly lowering postprandial glucose levels and decreasing HbA1C levels with lesser incidence of hypoglycemia.

In our study, maternal outcomes in overt diabetes were comparable among the treatment groups without any significant differences. Polyhydramnios was the majority of maternal complications in the I.Asp (25% of women) and RHI (40% of women) group and PROM in the I.Lisp group(33.33%). Preeclampsia occurred in 12.5%, 16.6% and 20% women of I,Asp, I.Lisp and RHI groups respectively. Among the women with GDM, preeclampsia (9.38% of I.Asp, 11.11% of I.Lisp and 5.13% of RHI group) and preterm labor (6.25% of I.Asp, 5.56% of I.Lisp and 5.13% of RHI group) were the majority of complications. No significant differences in the outcomes were observed among the treatment groups as majority of women with GDM remained uncomplicated throughout the pregnancy.

Fetal outcomes were almost similar in all the treatment groups in PGDM without any significant differences. Rates of macrosomia were higher in overt diabetes (31.58%) than gestational diabetes (10.28%). Fetal congenital anomalies in the form of congenital heart disease (CHD) was reported in one (12.5%) subject of I.Asp group and neural tube defects (encephalocele) were reported in one woman of each of I.Asp (12.5%) and RHI (20%) group. Intrauterine fetal demice (IUFD) occurred in one (12.5%) woman of I.Asp group. In the GDM variety, majority of women of all the three insulin groups had no fetal complications and no significant differences in thefetal outcomes among the groups were observed. No fetal congenital malformation was reported in GDM patients. Macrosomia was observed in 3 (9.38%), 3 (8.33%) and 5 (12.82%) women of I.Asp, I.Lisp and RHI groups respectively. Three subjects (one in each group) had IUFD.

In a study conducted by Deepaklal MC, Joseph K, Rekha K, et al,[15] it was found that insulin aspart was safe and effective in achieving targeted glycemic control in GDM and PGDM resulting in improved perinatal outcomes in terms of reduced incidence of macrosomia, preterm and postterm deliveries and complicated mode of deliveries and the study also showed that the incidence of maternal and fetal complications in GDM was similar to PGDM patients.

In another study done by Di Cianni et al,[16]macrosomia was seen in 15.6% of human insulin group, 12.1% in insulin lispro group and 9.6% in insulin aspart group and data did not reach statistical significance.

Majority of women with overt diabetes were delivered by cesarean section – either elective or emergency (62.5%, 66.67% and 80% in the I.Asp, I.Lisp and RHI groups respectively). On the other hand, among GDM women, majority of RHI group (54%) had vaginal deliveries (VD) including instrumental deliveries by applying forceps and most of them of I.Asp and I.Lisp group(62.51% and 58.33% respectively) were delivered by C.S. Intergroup differences were insignificant.

Majority (79.44%) of women with gestational diabetes were delivered at term (≥ 37wks). Observed rates of preterm deliveries (before 37 completed weeks) among the subjects with GDM were 28.13%, 16.67% and 17.95% in the I.Asp, I.Lisp and RHI groups respectively and the differences were not significant. Whereas, Most (63.16%) of the women with overt diabetes had preterm deliveries. But most of the PGDM women (66.67%) of I.Lisp group were delivered at term.

In a study conducted by Deepaklal MC, Joseph K, Rekha K, et al,[15]cesarean section rate was found to be 53.3% in GDM group and 49.4% in pre-GDM group when they were treated with I.Asp and there was no significant difference between the groups. They also

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

demonstrated that 47.1% patients in GDM group and 50.6% patients in pre-GDM group had preterm deliveries.

The mean birth weights of babies born to moms with PGDM were greater than those born to mothers with GDM. The inter-group disparities in birth weights were not statistically significant in both cases of GDM and PGDM. The incidence of neonatal macrosomia (birth weight > 3.5 kg) was higher in the RHI group compared to the other two groups, with rates of 60% in mothers with pregestational diabetes mellitus (PGDM) and 12.82% in mothers with gestational diabetes mellitus (GDM). The highest recorded birth weight was 4.35 kg in the RHI group, whereas in the I.Asp and I.Lisp groups, the birth weights were 3.86 kg and 4.18 kg, respectively.

The majority of newborn babies born to moms with PGDM (56.25%) and GDM (77.88%) had a favourable Apgar score (≥7) at five minutes after birth. There were no significant differences between the groups.

The incidence of newborn hypoglycemia was greater in women with pregestational diabetes mellitus (PGDM) at a rate of 37.5%, compared to women with gestational diabetes mellitus (GDM) at a rate of 10.54%. The incidence of neonatal hypoglycemia was higher in the RHI group (75%) in cases of pregestational diabetes mellitus (PGDM) and in the I.Asp group (16.13%) in cases of gestational diabetes mellitus (GDM). A single newborn (2.63%) in the RHI group presented with congenital talipes equinovarus (CTEV). There were no notable variations in the newborn outcomes observed among the three insulin groups in both gestational diabetes mellitus (GDM) and pregestational diabetes mellitus (PGDM).

While the majority (60%) of the newborn babies in the study did not need to be admitted to the Neonatal Intensive Care Unit (NICU), 40% of them were admitted for additional medical care due to problems. The incidence of NICU admission in newborns was higher in mothers with PGDM (81.25%) compared to moms with GDM (33.65%). However, there were no statistically significant differences seen across the treatment groups.

In a study conducted by Durnwald CP and Landon MB,[16]it was found that Women treated with lispro demonstrated improved glycemic control during pregnancy compared to those receiving regular insulin, but perinatal outcomes were similar between the two groups. Mean infant birth weight was greater in the lispro group, whereas the rates of large for gestational age infants, congenital malformation, gestational age at delivery, NICU admission, and neonatal hypoglycemia were similar between the two groups.

There were significant differences among the treatment groups in the mean total daily insulin doses throughout pregnancy in both GDM and PGDM and these were significantly higher in the RHI group than I.Asp and I.Lisp group. Mean total daily insulin doses of PGDM women were higher than that of GDM. Insulin doses gradually increased throughout pregnancy from the starting of therapy to the end of pregnancy in all the treatment groups.

Conclusion

We conclude that, the safety and effectiveness of insulin aspart and insulin lispro were shown to be identical to conventional human insulin in women with gestational and pre-gestational diabetes mellitus. The pregnancy outcomes were also comparable. Treatment with I.Asp and I.Lisp demonstrated superior postprandial glycaemic control with a slightly lower occurrence of major hypoglycemia, although this difference was not statistically significant. The levels of HbA1c, mostly ≤6.5%, were comparable between the two treatment groups. However, the cost of therapy was significantly higher in the I. Lisp group compared to the I.Asp and RHI group in gestational diabetes mellitus (GDM).

References

1. Sharma R, Dash V (trans). Agnivesa's Charaka Samhita: Text with English translation and critical exposition. Varanasi:Chowkhamba; 1994.
2. Metzger BE, Gabbe SG, Persson B, et al. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33:676–682.
3. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(4), 1318-1326 | ISSN:2251-6727

expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26:S5–S20.

4. Bevier WC, Jovanovic-Peterson L, Peterson CM. Pancreatic disorders of pregnancy. Diagnosis, management, and outcome of gestational diabetes. EndocrinolMetabClin North Am. 1995;24:103–138.
5. Dornhost A, Paterson CM, Nicholls JS, Wadsworth J, Chiu DC, Elkeles RS, Johnston DG, Beard RW. High prevalence of GDM in women from ethnic minority groups. Diabetic Med 1992;9:820-2.
6. V Seshiah. DIPSI Guidelines - Kolkata Declaration, Fifth National Conference of Diabetes in Pregnancy Study Group, India. 5th-7th Feb, 2010, Kolkata.
7. Seshiah V, Balaji V, Madhuri S Balaji, Sanjeevi CB, Green A. Gestational Diabetes Mellitus in India. JAssoc Physic of India 2004;52:707–11.
8. Metzger BE, Lowe LP, Dyer AR, et al. HAPO Study Cooperative Research Group: Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358:1991–2002.
9. Diagnosis and Management of GDM: Indian Guidelines. Association of Physicians of India. Medicine Update 2013; Vol 13: Chapter 55
10. Bhat M, KN Ramesha, Sarma SP, et al. Determinants of gestational diabetes mellitus: A case control study in a district tertiary care hospital in south India. Int J Diabetes Dev Ctries. 2010;30:91-6
11. Mathiesen ER, Kinsley B, Amiel SA, Heller S, et al. Maternal glycemic control and hypoglycemia in type 1 diabetic pregnancy: a randomized trial of insulin aspart versus human insulin in 322 pregnant women. Diabetes Care. 2007;30:771-6
12. Garg SK, Frias JP, Anil S, et al. Insulin lispro therapy in pregnancies complicated by type 1 diabetes: glycemic control and maternal and fetal outcomes. Endocr Pract. 2003;9:187–193
13. Jovanovic L, Pettitt DJ, Ospina P, et al. Efficacy, safety and lack of immunogenicity of insulin aspart compared with regular human insulin for women with gestational diabetes mellitus. Diabet Med. 2007; 24(10): 1129–1135
14. Jovanovic L, Ilic S, Pettitt DJ, et al. The metabolic and immunologic effects of insulin lispro in gestational diabetes. Diabetes Care. 1999;22:1422-6
15. Deepaklal MC, Joseph K, Rekha K, et al. Insulin aspart in patients with gestational diabetes mellitus and pregestational diabetes mellitus. Indian J Endocrinol Metab. 2015;19(5):658-62
16. Durnwald CP, Landon MB. A comparison of lispro and regular insulin for the management of type 1 and type 2 diabetes in pregnancy. J Matern Fetal Neonatal Med. 2008 May;21(5):309-13