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THESE POUR LE DIPLÔME D'ETAT DE DOCTEUR EN MÉDECINE

Pompe sous cutanée d'insuline ou multi-injections au cours de la grossesse diabétique de type 1 : résultats maternels et fœtaux.

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par Ameline BIROTA

JURY

Président :

Monsieur le Professeur Damien SUBTIL

Assesseurs :

Monsieur le Docteur RAZKA Thameur

Madame le Docteur LEMAITRE Madleen

Directrice de thèse :

Madame le Professeur Anne VAMBERGUE

Travail du Service d'Endocrinologie-Diabétologie du CHU de Lille

TABLE DES MATIÈRES

ABRÉVIATIONS

BMI : Body Mass Index

BW : Birth Weight

CGMS : Continuous Glucose Monitoring System

CI : Confidence Interval

CNIL : Commission Nationale de l'Informatique et des Libertés

DM : diabetes mellitus

SCIII : Continuous Subcutaneous Insulin Infusion

FIT : Functional Insulin Therapy

GA : Gestational Age

HbA1c : glycated hemoglobin

ICU : Intensive Care Unit

IUFD : Intra-uterine Fetal Death

LADA : Latent Autoimmune Diabetes in Adults

LGA : Large for Gestational Age

MODY : Maturity-Onset Diabetes of the Young

NICU : neonatal intensive care unit

NNH : neonatal hypoglycemia

OR : Odds Ratio

SGA : Small for Gestational Age

T1D/T2D : Type 1/Type 2 Diabetes mellitus

WHO : World Health Organization

I. RÉSUMÉ DE L'ARTICLE

CONTEXTE ET OBJECTIFS : De nos jours, la prévalence des complications materno-foetales reste supérieure à celle des patientes non diabétiques (1). Les recommandations de l'ADA 2014 sur la gestion des grossesses des femmes diabétiques de type 1 préconisent au même plan les schémas de multi-injections et les pompes à insuline sous cutanées (2). Dans la littérature, la pompe n'a pas encore fait la preuve univoque de sa supériorité dans la prévention des complications materno-foetale chez la patiente diabétique de type 1 et des études récentes retrouvent une prévalence plus élevée de certaines complications (Large for Gestational Age, prématurité, …) (3,4) chez les patientes traitées par pompe. Le but de cette étude est donc de comparer l'efficacité des deux méthodes de traitement, pompe à insuline et multi-injection, en termes de réduction des complications chez les femmes enceintes diabétiques de type 1.

MÉTHODE : étude rétrospective, observationnelle, monocentrique conduite au CHU de Lille, France incluant 834 femmes enceintes avec un diabète de type 1 suivies par l'Unité Diabète et Grossesse dont l'accouchement a eu lieu au CHU de Lille, France, entre 1997 et 2023. A partir des dossiers médicaux, nous avons extrait et comparer leurs caractéristiques pré gestationnelles, les différentes complications maternelles et foetales liées à leur grossesses en fonction de leur mode d'administration d'insuline, par pompe à insuline (SCII) ou par multi-injection (MDI).

RESULTATS :

Caractéristiques maternelles : Les utilisatrices de SCIII étaient généralement plus âgées (30.0 years ± 4.8 vs 28.6 years ± 5.1 p <0.001), avaient un diabète de plus longue durée d'évolution (16.6 years ± 7.5 vs 12.2 years ± 7.9 p <0.001), un IMC plus élevé (24. 4 kg/m2 (21.9; 28.1) vs 23.2 kg/m2 (21.1; 26.0) p<0. 00) et davantage de complications préexistantes liées au diabète (173 (34.0%) vs 71(22.1%) p<0.001. L'HbA1c prégestationnel était similaire dans les deux groupes (7.4 ± 1.1% vs 7.8 ± 1.9% (p=0.21)) mais avec une proportion significativement plus importante de patiente traitée par MDI atteignant l'objectif d'HbA1C prégestationnel inférieur ou égal à 6.5% (97 (20.0%) vs. 80 (29.6%) p=0.003)).

Contrôle glycémique : L'HbA1c était significativement plus bas dans le groupe traité par SCII au 1er trimestre (6.8 ± 0.9 % vs. 7.0 ± 1.2 % p=0.049), puis les HbA1c étaient similaires dans les deux groupes au 2e et 3e trimestre. La proportion de femmes atteignant les cibles glycémiques de la grossesse préconisées par l'ADA était similaire dans les deux groupes tout au long de la grossesse.

Résultats maternels : Il n'y a pas eu de différences significatives dans les taux de césarienne (262 (51.5%) vs (146 (45.3%), de césariennes d'urgence (172 (66.2%) vs. 100 (69.9%) p=0.44), de pré-éclampsie (60(11.9%)vs. 30 (9.4%)p= 0.25), d'hémorragie du post partum, de dystocie des épaules (45 (16.2%) vs 23(12.2%) (p=0.23).d'aggravation d'hypertension chronique (87(17.2%) vs. 43(13.4%) p=0.15), de néphropathie (114(22.5%) vs 75 (23.4%). p=0.75) ou de rétinopathie (118(23.3%) vs. 74(23.1%) p=0.93). La prise de poids gestationnelle n'était pas significativement

différente entre les deux groupes (13.8 kg +/- 5.4 kg vs 14.5 kg +/- 5.3 kg p= 0.082).

Résultats néonataux : La SCII a été associée à un poids de naissance plus élevé 3610 (3250-3980) g vs 3500(3103-3900) g p=0.011) et d'une plus grande prévalence d'hypocalcémie (70(65.4%)vs. 36 (45,6%) p= 0.007) mais il n'y avait pas de différences significatives entre le taux de LGA(269(54.7%) vs (124(54.5%) p=0.25), de nouveau-né macrosome (124 (24.5%) vs 61(19.1%) p=0.070), de prématurité (61(12%) vs. 45(14%)p=0.41), de détresse respiratoire (45 (9.1%)vs. 27 (8.6%) p=0.82) et d'hypoglycémie néonatale (230 (46.4%) vs. 153 (48.4%) p=0.57).

Analyse multivariée : Les analyses de régression logistique n'ont confirmé aucune association significative entre le mode de traitement et les taux de complications fœto-maternelles (LGA, macrosomie, de prééclampsie, de détresse respiratoire, de prématurité, de césarienne d'urgence et d'hypoglycémie néonatales, ni en analyse brute ni en analyse ajustée sur les facteurs de confusion suivant : la durée du diabète, l'IMC, l'historique d'hypertension, de rétinopathie, de néphropathie, la parité et le tabagisme avant la grossesse.

CONCLUSION : Les traitements par SCIII et MDI ont montré des résultats de complications maternelles et néonatales similaires malgré des caractéristiques maternelles différentes en période pré gestationnelle.

II. ABSTRACT

BACKGROUNDS AND OBJECTIVES : Today, the prevalence of maternal-fetal complications remains higher than in non-diabetic patients (1). The 2024 ADA recommendations for the management of pregnancy in women with type 1 diabetes advocate both regimens: multiple injections and subcutaneous insulin pumps (2). In the literature, the pump has not yet unequivocally demonstrated its superiority in preventing maternal-fetal complications in type 1 diabetic patients, and recent studies show a higher prevalence of certain complications (Large for Gestational Age, prematurity, etc.) in pump-treated patients (3,4). The aim of this study is therefore to compare the efficacy of the two treatment methods, insulin pump and multi-injections, in terms of reducing complications in pregnant women with type 1 diabetes.

MATERIALS AND METHOD: A retrospective, observational, monocentric study conducted at the University Hospital of Lille, France, including 834 pregnant women with type 1 diabetes followed by the Diabetes and Pregnancy Unit whose delivery took place at the University Hospital of Lille, France, between 1997 and 2023. Using medical records, we extracted and compared their pre-gestational characteristics and the various maternal and fetal complications associated with their pregnancies, depending on whether they were receiving insulin by pump (SCII) or by multi-injection (MDI).

RESULTS :

Maternal characteristics: SCIII users were generally older (30.0 years ± 4.8 vs 28.6

years ± 5.1 p <0.001), had a longer duration of diabetes (16.6 years ± 7. 5 vs 12.2 years ± 7.9 p <0.001), higher BMI (24. 4 kg/m2 (21.9; 28.1) vs 23.2 kg/m2 (21.1; 26.0) p<0. 00) and more pre-existing diabetes-related complications (173 (34.0%) vs 71(22.1%) p<0.001. Pregestational HbA1c was similar in both groups (7.4 ± 1.1% vs. 7.8 ± 1.9% p=0.21) but with a significantly higher proportion of MDI-treated patients achieving pregestational HbA1c target inferior to 6.5% (97 (20.0%) vs. 80 (29.6%) p=0.003).

Glycemic control: HbA1c was significantly lower in the SCII group in the 1st trimester (6.8 ± 0.9% vs. 7.0 ± 1.2% p=0.049), then HbA1c was similar in both groups in the 2nd and 3rd trimesters. The proportion of women achieving the ADA pregnancy glycemic targets was similar in both groups throughout pregnancy.

Maternal outcomes: There were no significant differences in the rates of caesarean section (262 (51.5%) vs. 146 (45.3%), emergency caesarean section (172 (66.2%) vs. 100 (69.9%) p=0.44), pre-eclampsia, post-partum haemorrhage, shoulder dystocia (45 (16. 2%) vs. 23(12.2%) p=0.23).worsening of chronic hypertension (87(17.2%) vs. 43(13.4%) p=0.15), nephropathy (114(22.5%) vs. 75 (23.4%). p=0.75) or retinopathy (118(23.3%) vs. 74(23.1%) p=0.93). Gestational weight gain was not significantly different between the two groups (13.8 kg +/- 5.4 kg vs. 14.5 kg +/- 5.3 kg p= 0.082).

Neonatal outcomes: SCII was associated with higher birth weight (3610 (3250-3980) g vs. 3500(3103-3900) g p=0.011). and a higher prevalence of hypocalcemia (70(65.4%)vs. 36 (45.6%) p= 0.007) but there were no significant

differences in the rate of LGA (269(54. 7%) vs (124(54.5%) p=0.25), macrosomic neonates (124 (24.5%) vs 61(19.1%) p=0.070), prematurity (61(12%) vs. 45(14%) p=0.41), respiratory distress (45 (9.1%) vs 27 (8.6%) p=0.82) and neonatal hypoglycemia (230 (46.4%) vs. 153 (48.4%) p=0.57).

Multivariate analysis: Logistic regression analyses confirmed no significant association between mode of treatment and rates of maternal-fetal complications (LGA, macrosomia, preeclampsia, respiratory distress, prematurity, emergency cesarean section and neonatal hypoglycemia, neither in crude analysis nor in analysis adjusted for the following confounding factors: duration of diabetes, BMI, history of hypertension, retinopathy, nephropathy, parity and smoking before pregnancy.

CONCLUSION: SCIII and MDI treatments showed similar maternal and neonatal complication outcomes despite different maternal characteristics in the pregestational period.

III. INTRODUCTION

La grossesse chez la femme diabétique de type 1 demeure un défi pluridisciplinaire complexe en raison des risques accrus de complications materno-fœtales (1). Parmis ces complications, on retrouve les hypoglycémies, les décompensations cétosiques, la pré-éclampsie, l'hémorragie de la délivrance, des césariennes, l'aggravation des complications microangiopathiques préexistantes à la grossesse, des malformations congénitales, l'excès de croissance fœtale, la prématurité induite ou spontanée, les hypoglycémies néonatales, la dystocie des épaules ou la détresse respiratoire (2).

De nos jours, la prévalence de ces complications est toujours supérieure à celle observée chez les femmes non diabétiques. Chaque complication possède ses propres facteurs de risque, et l'accompagnement spécifique au suivi des grossesses diabétiques vise à réduire leur survenue.(5)

L'EXCÈS DE CROISSANCE FOETALE

Sur le plan clinique, l'excès de croissance fœtale, principalement caractérisé par la macrosomie (poids de naissance supérieur à 4 kg) ou un nouveau-né large pour l'âge gestationnel (LGA), reste fréquemment rapporté chez les enfants de femmes diabétiques de type 1, malgré l'intensification des objectifs glycémiques (6). Dans notre étude, nous utiliserons les courbes de référence françaises (AUDIPOG), qui

tiennent compte de l’âge gestationnel, du sexe biologique, du rang de naissance, ainsi que des caractéristiques prégestationnelles de la mère (âge, taille et poids)(7).

Les grossesses compliquées par une naissance LGA sont associées à des risques accrus de complications obstétricales, telles que l’hémorragie du post-partum, les traumatismes périnéaux, la dystocie des épaules, la détresse respiratoire fœtale, ainsi que les césariennes d'urgence dues à l’arrêt de progression du travail. À moyen terme, l'excès de croissance fœtale est également corrélé à une prévalence accrue d’obésité infantile, (8,9) et à un risque plus élevé de développer un syndrome métabolique à l’âge adulte (10,11).

Chez les femmes non diabétiques, les principaux facteurs de risque d'excès de croissance fœtale incluent le diabète gestationnel, l’obésité prégestationnelle, la multiparité, un antécédent d’enfant LGA, un fœtus de sexe masculin et une gestation prolongée au-delà de 42 semaines d’aménorrhée. (50).

En revanche, chez les femmes diabétiques de type 1, cette observation repose sur l’effet anabolisant de l’insuline par le biais de l'hyperinsulinisme fœtal secondaire à l’hyperglycémie maternelle, ce qui favorise la prise de poids fœtale. Les taux de LGA chez ces femmes continuent d’augmenter dans les pays développés, comme le montrent des études nationales suédoises et écossaises (12,13).

D’autres hypothèses telles que le rôle des lipides (14) ou l'amélioration de la placentation au début de la grossesse (13) tentent d’expliquer cette tendance grandissante de LGA alors que les méthodes pour atteindre des cibles glycémiques toujours plus strictes évoluent rapidement.

LA PRÉMATURITÉ

La prématurité, qu'elle soit spontanée ou induite, complique environ 20 à 40 % des grossesses des patientes diabétiques de type 1, soit une fréquence 5 à 10 fois supérieure à celle observée dans la population générale (1,15).

L'HYPOGLYCÉMIE NÉONATALE

En ce qui concerne l'hypoglycémie néonatale, il n'existe pas de définition universelle dans la littérature, ce qui complique la comparabilité des études. Dans cette étude, nous avons choisi d'utiliser la définition de l'ADA, à savoir une glycémie inférieure à 0,35 g/dL dans les 48 premières heures de vie, ou inférieure à 0,40 g/dL après 48 heures ou la nécessité d'une injection intraveineuse de glucose (16). Cette définition permet une standardisation qui ne repose pas sur des évaluations cliniques souvent imprécises chez le nouveau-né, où les signes d'hypoglycémie sont souvent absents ou non spécifiques (16).

Sur le plan physiopathologique, l'hypoglycémie néonatale est principalement liée à l'hypertrophie pancréatique secondaire à l'hyperinsulinisme induit par l'hyperglycémie maternelle.

Chez la femme diabétique de type 1, un mauvais équilibre glycémique tout au long de la grossesse et une glycémie élevée au moment de l'accouchement semblent etre des facteurs prédictifs de l'hypoglycémie néonatale (17)

SURPOIDS, OBÉSITÉ ET GROSSESSE CHEZ LES PATIENTES DIABÉTIQUES DE TYPE 1

Dans ce contexte de surabondance alimentaire et la propagation du mode de vie sédentaire, les diabétiques de type 1 n'échappent pas à la épidémie de surpoids et d'obésité mondiale (18).

Le surpoids et l’obésité sont des facteurs de risque bien établis pour de nombreuses complications obstétricales, incluant l’hypertension gravidique, la prééclampsie, les césariennes, la prématurité et l'excès de croissance fœtale, fausses couches ainsi que les difficultés d’adaptation à la vie extra-utérine. Ces complications deviennent particulièrement préoccupantes chez les femmes diabétiques de type 1, où la combinaison de surpoids et de diabète crée un effet synergique qui amplifie encore davantage le risque de complications (19,20).

Ce lien entre surpoids et diabète aggrave considérablement les issues périnatales, rendant une gestion optimisée du poids prégestationnel et per gestationnel essentielle.

L'EXCÈS DE GAIN DE POIDS GESTATIONNEL

L'excès de gain de poids gestationnel complique environ 60 % des grossesses des femmes diabétiques de type 1 (21) et est associé principalement à un risque accru d'excès de croissance fœtale, en grande partie lié à l'augmentation de l'insulinorésistance au cours de la grossesse (22).

Il est également bien documenté qu'une prise de poids gestationnel supérieure aux recommandations augmente le risque de naissance LGA dans la population générale. Toutefois, son rôle spécifique dans les grossesses diabétiques de type 1 reste à mieux cerner, surtout compte tenu du fait que la prévalence du surpoids et de l'obésité chez les diabétiques de type 1 est aujourd'hui comparable à celle de la population générale (18). Par ailleurs, le surpoids et l'obésité pré gestationnelle ont été identifiés comme un facteur prédictif d’un gain de poids gestationnel excessif, exacerbant encore davantage les risques liés à la macrosomie et aux complications néonatales.

OBJECTIFS GLYCEMIQUES CHEZ LA FEMME DIABETIQUE DE TYPE 1 ENCEINTE

Chez la femme einceinte, les objectifs glycémiques sont stricte : il s'agit de maintenir la glycémie à jeun en dessous de 0,95 g/L puis une glycémie 1 heure après le début du repas en dessous de 1,40 g/L et une glycémie 2 heures après le début du repas en dessous de 1,20 g/L.

En raison des changements dans la physiologie des hématies pendant la grossesse, les taux physiologiques de HBAC diminuent au cours d'une grossesse chez la patiente non diabétique.

Les seuils préconisés d'HbA1c de 6,5% en prégestationnel puis à 6 % ont été proposé afin de limiter les complications foetales à travers des études observationnelles bien que l'HbA1c ne reflète pas l'hyperglycémie post-prandiale plus directement liée à la macrosomie foetale. L'objectif peut être relâché à <7% en cas de risque d'hypoglycémie.

Les objectifs du système de surveillance continue de la glycémie (CGMS) visent à maintenir le patient dans un intervalle glycémique optimal, avec un temps passé dans la cible supérieure à 70%, un temps en hyperglycémie inférieur à 25% et un temps en hypoglycémie sévère inférieur à 1%. Chez les patientes diabétiques de type 1, le CGMS a prouvé, dans l'essaie contrôlé randomisé CONCEPTT, un contrôle légèrement meilleur de l'HbA1c, moins de temps passé en hyperglycémie, et a aussi retrouvé moins de nouveau-nés LGA et moins de risques d'hypoglycémie

chez les nouveau-nés (23)Selon les recommandations de l’ADA 2024, ces objectifs de temps dans la cible doivent d’ajouter aux objectifs glycémiques pré et post prandiaux, et non pas s’y substituer.

L'INSULINOTHÉRAPIE PAR POMPE SOUS-CUTANÉE OU PAR SCHÉMA MULTI-INJECTIONS

Enfin, l'insulinothérapie, associée à l'éducation nutritionnelle et à l'activité physique, permet de limiter l'hyperglycémie, élément central du risque de complications materno-foetales (1). Les deux techniques de délivrance d'insuline les plus couramment utilisées en pratique sont la pompe à insuline et le schéma basal-bolus (2). L’utilisation quotidienne de la pompe à insuline, bien qu’elle ait démontré son efficacité et sa sécurité chez les patients diabétiques de type 1, nécessite une formation approfondie, tant pour les patientes que pour les équipes soignantes (2). L'un des défis majeurs est la mise en place d'une prise en charge pluridisciplinaire cohérente et coordonnée, particulièrement importante dans le contexte où une génération de patients diabétiques de type 1 traités par pompe dès le plus jeune âge, conformément aux recommandations de l’ISPAD, atteint désormais l'âge de procréer (24).

En 2024, bien que la littérature ne parvienne pas à un consensus sur la supériorité de la pompe à insuline (SCII) par rapport au schéma multi-injections (MDI) dans la prévention des complications maternelles et fœtales chez la patiente diabétique de type 1, les deux méthodes sont recommandées de manière équivalente par l'American Diabetes Association (2).

La gestion thérapeutique des patientes diabétiques de type 1 pendant la grossesse repose sur une approche pluridisciplinaire qui combine un ajustement fréquent des

doses d'insuline, des conseils diététiques adaptés et un suivi obstétrical rapproché. Cette coordination est cruciale pour atteindre une gestion glycémique optimale et minimiser les risques de complications néonatales et obstétricales. Malgré des objectifs glycémiques de plus en plus stricts, les taux de complications chez les femmes diabétiques de type 1 restent toujours supérieurs à ceux de la population générale (2).

Cependant, deux études récentes (3,4) ont contredit l'idée répandue, mais encore non consensuelle, que le SCII prévient mieux les complications materno-foetales chez les femmes atteintes de DT1 que le MDI. Thorius et al. 2024 (4) ont constaté que les utilisateurs de SCII avaient un risque plus élevé de LGA et d'accouchement prématuré, tandis que CONCEPTT (4). a trouvé une augmentation des troubles hypertensifs et de l'hypoglycémie néonatale chez les utilisateurs de SCII.

Bien que les caractéristiques maternelles différent dans l'étude de Thorius et al. 2024, les utilisateurs de SCII dans les deux cas présentaient des facteurs de risque de complications de grossesses plus élevés. En termes de contrôle glycémique, les résultats étaient mitigés, avec de meilleurs résultats pré-gestationnels pour SCII dans Thorius et al. mais un meilleur contrôle glycémique pour MDI dans CONCEPTT.

Aussi l'objectif de notre étude est de comparer l'efficacité des deux méthodes de traitement, pompe à insuline et multi-injection, en termes de réduction des complications chez les femmes enceintes diabétiques de type 1.

TABLEAU RÉCAPITULATIF DE BIBLIOGRAPHIE

SCII vs MDI	studied population country date	design	main result	Glycemic outcome	strengths and limitation
Hauffe 2019	339 pregnancies in Germany SCII = 199 MDI = 140 switch to SCII during pregnancy =34	observational retrospective cohorte	-Despite equal glycemic control, the rate of LGA infants was higher in SCII. -Primiparity and PE had attenuating effects on LGA, while T3 HbA1c and excess maternal weight gain were predictive of LGA -Pre-pregnancy BMI and SCII determined the risk of excess weight gain. -Diabetes duration and smoking did not independently influence LGA.	**-no differences in HbA1c levels in any trimester between both groups** **-** Subgroup of SCII initiated in T1 had the same GC than SCII. **-**In both groups, HbA1c levels improved during pregnancy. -In SCII, more women achieved T1 HAB1c <6,5% and T3 HbA1c<6%	***-retrospective*** ***- no randomization*** ***-tertiary center*** ***-lack of data*** ***-insulin dose not available***
Kallas-Koeman 2014	387 Canadian women SCII= 122 MDI = 252 2006–2010	retrospective 2 tertiary centers	-Rates of severe hypoglycemia, diabetic ketoacidosis, gestational HTA, and weight gain were similar between groups. -In SCII, the rate of LGA was higher and a trend toward more neonatal hypoglycemia in infants was shown	**-SCII had lower mean HbA1c in all trimesters even after adjustment for** maternal age, duration of diabetes, the presence of retinopathy and/or nephropathy, and preconception care **- More SCII achieved HbA1c ≤6.1% in T2** **- More SCII achieved HAB1C ≤7.0% in each trimester** -HbA1c improved over time in both groups	***-SCII initiated months to years before conception instead of short before or during pregnancy.*** ***-retrospective*** ***-underreported diabetes complication, severe maternal hypoglycmia, non visible birth defects, spontaneous abortions and jaundice after hospital discharge.*** ***-SCII were not publicly funded during study period***
Gong 2024	121 Chinese pregnant women MDI =65 SCII = 56	observational prospective multicentered	SCII has more risk of **neonatal jaundice and NICU transfert**. adjusted for maternal age, duration of diabetes, BMI and daily dose in insulin :	-HbA1c improved over time in both groups -In T1 and T2, SCII had nonsignificant lower HbA1c levels than MDI	***-large proportion of planified pregnancy*** ***-young cohort*** ***-no CGMS*** ***-no randomisation***

SCII vs MDI	studied population country date	design	main result	Glycemic outcome	strengths and limitation
	2015-2017			-In T3, HbA1c was significantly lower for SCII -in T3, more CSII users achieved HbA1c <6.5% -HbA1c decreased more in SCII between PG and T3	
Thorius 2024	17 countries 2,003 pregnant women MDI =1280 SCII = 723 2013–2018	observational multicentered international prospective	-In SCII : more risk of delivering LGA and pre term birth were higher adjusted for : diabetes duration, history of hypertension/ retinopathy/nephropathy, nulliparity, maternal BMI at enrollment, educational level, smoking, HbA1c at baseline, HbA1c at delivery and gestational weight gain.	-In T1, SCII had significantly lower mean HbA1c levels compared with MDI users -In T2 and T3, no differences in mean HbA1c values between SCII and MDI	-international **large Sample Size** -**Adjustment for relevant** confounding factors via a directed acyclic graph (DAG) model -one year after birth follow-up data up -no randomisation **-No CGMS Data**
Feig 2018 CONCEPTT	randomization was stratified by SCII or MDI and by baseline HbA1c MDI =123 SCII =125	a prespecified observational analysis of a randomized controlled trial	Main CONCEPTT key findings (2017) : in CGMS users : Improvements in reduction of LGA, neonatal hypoglycemia and NICU admissions in CGM users -SCII had more hypertensive disorders of pregnancy, more neonatal hypoglycemia and more NICU admissions but LGA, macrosomia, SGA did not differ between SCII and MDI.	**-SCII were less likely to achieve T2 and T3 HbA1c targets** **-**Both groups had similar mean T1 HbA1c, at baseline, 24 weeks and 34 weeks **-MDI had a larger decrease in HbA1c between randomisation to 34 week in MDI**	

SCII vs MDI	studied population country date	design	main result	Glycemic outcome	strengths and limitation
Kjölhede 2021	185 Swedish women MDI = 131 SCII = 54 2014 and 2017	secondary analysis of an observational retrospective cohort multicentered (2 tertiary clinics)	No significant differences in glycemic indices, maternal and neonatal outcomes between women administering insulin by MDI and by pump adjusted for parity, maternal age, smoking, body mass index, CGMS and duration of type 1 diabetes.	-In both groups, HbA1c improved between T1 and T2 and T1 and T3 but not between T2 and T3 -Mean HbA1c levels were similar during all pregnancy in both groups (no statistical differences)	-GCSM data available -limited sample size -no randomisation -no pre conceptional HbA1c -suboptimal glycemic control through pregnancy
Wang 2022	646 pregnancies of 478 American women MDI = 242 pregnancies SCII = 404 pregnancies 2004–2017	observational monocenter retrospective	Despite the association with better glycemic control during pregnancy, SCII had higher mean birth weight, macrosomia and LGA even adjusted for age, race, pre-pregnancy BMI, parity, chronic hypertension, nephropathy, retinopathy, infant sex, education level and calendar year of delivery	-SCII had lower mean HbA1c levels in T1 ant T2	-retrospective and one center data -highly educated and predominantly non hispanic white -one of the largest US base pregnant type 1 diabetes cohort -use of multiple imputation techniques to handle missing data and incorporating statistical methods to account for the within-individual correlation of repeated pregnancies -sensitivity analysis
Żurawska-Kliś 2021	209 Polish women MDI = 95 SCII = 114 2003 and 2019	observational, retrospective, single center study	-The rate of pregnancy loss, such as abortions, fetal and neonatal death did not differ between the groups. -There were no differences in term, the mode of delivery, neonatal birth weight, the rate of macrosomy, LGA or SGA. -SCII had a higher Apgar score but the proportion of neonates with an Apgar score <7 was similar.	-a significantly higher proportion of SCII reached the target value of HbA1c -T1 and T2 HbA1c was lower in SCII -T3 HbA1c and total change in HbA1c were comparable	-one center : same education -caucasian population with normal BMI -retrospectif abd observational -SCII was initiated in preconception or T1.

SCII vs MDI	studied population country date	design	main result	Glycemic outcome	strengths and limitation
			-In planned pregnancy compared to unplanned ones, HbA1c was significantly lower in T1 and a significantly higher rate achieved the target HbA1c during planning and T1 -Unplanned pregnancy and a high T1 HbA1c were independent predictors of both LGA and macrosomia	between groups.	
Ogassavara 2023	174 Brazilian women SCII= 37 MDI = 137 2008- 2021	observational prospective one tertiary center	-more Cesarean section in the SCII and more congenital malformation in MDI but lost of statistical significance after adjusting for T3 HbA1c, age, diabetes duration, pre-pregnancy BMI, preeclampsia and gestational hypertension	-HbA1c levels improved throughout gestation but stayed suboptimal in both groups	-few SCII because of socio-economic condition of Brazil (not even from private health insurance) and when funded by the government only for more severe DM with glycemic variability and difficult to control hypoglycemia -Brazil has the second higher rate of Cesarean section of the world -suboptimal glycemic control through pregnancy -observational -no information of preconceptional HbA1c -no CGMS data

SCII vs MDI	studied population country date	design	main result	Glycemic outcome	strengths and limitation
Cyganek 2017	375 polish women macrosomia = 84 no macrosomia = 291 1998 -2012	retrospective, observational one center cross-sectional cohort study	-mother of macrosomic newborn were treated more frequently with SCII -macrosomia predictors : duration of diabetes, maternal age and weight, HbA1c and fasting blood sugar in T3 -T3 HbA1c was the strongest predictor of BW: 1 % of HbA1c was associated with a 1.68-fold increase in odds of macrosomia (p = 0.001). -The risk of macrosomia predicted for a T3 HbA1c of 6.0 % was approximately 25 %. -no risk of macrosomia threshold in HbA1c distribution identified but there is a linear relationship between T3 HbA1c and the risk of macrosomia	-HbA1c decreased systematically during the gestational period: -The proportion HbA1c < 6.1 % increased significantly in T1,T2 and T3 similar glycaemic control within treatment groups	-use of macrosomia instead of LGA -maternal weight and MBi used as independent variables -observational not randomized -different glucose meter use through the years -iron and folic acid deficiency anemia that could affect HbA1c were not assessed
GC : glycemic control , PC : preconceptional					

SCII vs MDI	Maternal characteristics	LGA	Preterm birth	PE	Cesarean section	Neonatal hypoglycemia
Hauffe 2019	SCII had a longer duration of diabetes, were more likely to be primiparous, have preconception care and a lower preconception HbA1c SCII were less likely to smoke during pregnancy,	LGA MDI = 33.6% vs **44.7% p =0.04** SCII had a higher birth weight and LGA	<37 weeks MDI = 26.4% vs SCII = 20.1% p= 0.17 <34 weeks MDI =9.3% vs SCII = 6% p=0.26	MDI = 8.6% vs SCII = 10.1% p=0.65	MDI = 60% vs 59.8% p=0.97	MDI = 37.2% vs SCII = 38.6% p=0.80

SCII vs MDI	Maternal characteristics	LGA	Preterm birth	PE	Cesarean section	Neonatal hypoglycemia
Kallas-Koeman 2014	SCII were older, had a longer duration of diabetes, more retinopathy, a higher rates of preconception care, smoked less often in pregnancy and lived in more educated neighbourhoods	MDI= 39.2% vs **SCII=55% p = 0.007** aOR = 1.29 (0.65-2.57) adjusted for insulin therapy, maternal age, retinopathy, nephropathy,parity, smoking, BMI and mean pregnancy HbA1c.	<37 weeks MDI = 31.8% vs SCII = 32.4% p = 0.91 <34 weeks MDI = 8.8% vs SCII = 3.6% p =0.08	MDI = 6.1%vs SCII = 5.8% p = 0.93	MDI = 64.2% vs SCII = 69% p= 0.38 aOR = 1.87 (0.86-4.00) SCII was not significantly associated	MDI = 34.8% vs SCII=45.7% p=0.06 a trend towards more neonatal hypoglycaemia among SCII
Gong 2024	-SCII had a longer duration of diabetes and received preconceptional care -SCII and MDI had same rate preconception microvascular complication, history of HTA, nulliparity, education level -Preconception HbA1c and on-target HbA1c were similar between SCII and MDI.	LGA MDI =13.85% vs SCII=12.50% p = 0.761 aOR = 0.80 (0.19 -3.36) adjusted for maternal age, duration of diabetes, BMI and daily dose in insulin **similar rate of LGA in both groups**	MDI = 15.38% vs SCII=14.29% p=0.800 aOR 0.88 (0.32-2.43) adjusted for maternal age, duration of diabetes, BMI and daily dose in insulin similar rate of preterm birth in both groups	MDI = 6.15vs SCII=5.36 p=0.852 aOR = 0.86 (0.19-4.03) adjusted for maternal age, duration of diabetes, BMI and daily dose in insulin similar rate of PE in both groups	MDI = 58.46% vs SCII = 69.64% p 0.188 aOR = 1.78 (0.83-3.82) similar rate of cesarean section in both groups	MDI = 10.77% vs SCII =14.29 p= 0.249 aOR = 1.42 -0.48-4.20)
Thorius 2024	-SCII had longer duration of diabetes, a higher baseline BMI, a higher prevalence of retinopathy, were better educated and less likely to smoke cigarettes around conception -At enrollment, SCII had a lower HbA1c level and a greater proportion of HbA1c level <9% -At enrollment, SCII and MDI had	MDI= 52.2% vs **SCII = 59% P = 0.026** aOR = 1.36 (1.09: 1.70) HbA1c at baseline aOR = 1.38 (1.09: 1.74) HbA1c at delivery aOR = 1.32 (1.05: 1.66)	MDI = 32.1% vs SCII = 39.6% aOR = 1.46 (1.17: 1.82) HbA1c at baseline aOR = 1.64 (1.23: 2.07)	MDI= 8.3% vs SCII = 10.8% aOR = 1.21(0.85: 1.74) HbA1c at baseline aOR = 1.32(0.90: 1.93)	MDI= 60.1% vs SCII = 53.6% aOR = 0.65 (0.52: 0.81) HbA1c at baseline aOR = 0.67(0.54: 0.84) HbA1c at delivery aOR	MDI = 18.3% vs SCII = 20.3% aOR 1.16 (0.88-1.54)

SCII vs MDI	Maternal characteristics	LGA	Preterm birth	PE	Cesarean section	Neonatal hypoglycemia
	a similar proportion of HbA1c level <6.5%	LGA rate and risk were higher in SCII compared with MDI	HbA1c at delivery aOR = 1.46 (1.16: 1.84) Gestational weight gain aOR = 1.66 (1.25: 2.19) The proportion and the risk of preterm delivery were higher in SCII	HbA1c at delivery aOR = 1.19(0.83: 1.72) Gestational weight gain aOR = 1.05 (0,68: 1.62) The risk of PE were not significantly different in both groups	= 0.61 (0.49: 0.77) Gestational weight gain aOR = 0.63 (0.48: 0.81) C-section rate and risk were higher in MDI compared with SCII	
Feig 2018	SCII were more likely to take preconception vitamins, less likely to smoke (P = 0.02), more often married or in stable relationships SCII and MDI were of similar age. Both had similar glycemic control,	MDI= 60% vs SCII = 63.6% p =0.55	<37 weeks : MDI 36.2% vs SCII = 43.2% p =0.10 <34 weeks : MDI = 6% vs SCII = 8.1%	MDI = 10.3% vs SCII=14.4% p= 0.31	MDI = 63.8% vs SCII = 73% p= 0.34	MDI = 31.8% vs SCII = 19.1% p=0.05
Kjolhede 2021	-Pump users more often used CGSM -SCII had a longer duration of diabetes, a higher prevalence of retinopathy and albuminuria -Other characteristics didn't differer	LGA MDI =49% vs SCII=63% aOR = 1.91 (0.93-3.91) p= 0.08 **No statistical differences between groups in LGA rate**	MDI =26% vs SCII=32% aOR = 1.44 (0.66-3.16) p= 0.36 No statistical differences between groups in preterm birth rate	MDI =21% vs SCII=13% aOR = 0.86 (0.32-2.41) p= 0.80 No statistical differences between groups in PE rate	MDI =45% vs SCII=50% aOR = 1.44 (0.56-2.26) p= 0.74 No statistical differences between groups in Cesarian section rate	MDI = 25% vs SCII = 20% p =0.76 aOR 0.80 (0.34-1.89) p =0.62
Wang 2022	-SCII were significantly older, with a higher percentage being non-Hispanic white and were better educated	LGA MDI = 46.7% vs **SCII = 58.4%** **aOR = 1,65 (1.06-2.58)**	MDI= 27.3% vs SCII = 23.9% aOR = 0.91	not assessed	MDI = 73.6 % vs SCII = 75.3% aOR= 1.48 (0.35-	MDI = 20% vs SCII = 21.7% a OR 0.95 (0.43-2.11)

SCII vs MDI	Maternal characteristics	LGA	Preterm birth	PE	Cesarean section	Neonatal hypoglycemia
	-Suggestive tendency in SCII for a higher proportion of overweight or obesity -Other characteristics didn't differer	adjusted for age, race, PC BMI, parity, chronic hypertension, nephropathy, retinopathy, infant sex, education level and year of delivery	(0.56-1.47)		6.25)	
Żurawsa-Kliś2021	SCII were older, were diagnosed with T1DM at a younger age, had a higher rate of albuminuria and proteinuria and had more planned pregnancy PC HbA1c was insignificantly lower in SCII, prepregnancy daily dose of insulin body weight and BMI did not differ between the groups.	LGA MDI=20% vs SCII = 41% p=0.316 Macrosomia MDI = 20% vs SCII= 26.3% p =0.326	MDI = 29.4% vs SCII= 29.8% p=0.955	not assessed	MDI = 75% vs SCII= 73% p=0.347	MDI = 7.3% vs SCII = 10.3% p=0.492
Ogassavara 2023	SCII had longer duration of diabetes but similar rates of retinopathy and nephropathy but same preconceptional BMI	LGA MDI= 19.3 vs SCII = 26.5% p= 0.175	(34-37 week) MDI= 41.5% vs SCII= 51.4% p= 0.573 (<34 week) MDI = 13% p = 0.573 vs SCII = 11.4%	PE MDI = 18.4% vs SCII 16.7% p = 0.146 OR	C section MDI = 75.4% p 0.017 vs SCII = 94.1% aOR = 2.67 (0.52-13.67)	
Cyganek 2017	In the macrosomia group, mothers were slightly younger, had lower prevalence of retinopathy but diabetes duration, BMI, rate of pregnancy planning did not differ	in SCII : macrosomia = 67.9% vs no macrosomia =56,4% did not found any differences in offspring size related to SCII use	not assessed	not assessed	macrosomia = 63.1% vs no macrosomia = 68.0%	

IV. ARTICLE

Subcutaneous continuous insulin infusion vs multiple daily injection in pregnant women with type 1 diabetes : maternal and fetal outcomes.

INTRODUCTION

With the growing incidence of type 1 diabetes (25) we cannot ignore the impact that this increase will have on our healthcare systems (26). However, pregnancy in women with type 1 diabetes is still associated with a rate of maternal and fetal complications not comparable to the general population(1), despite an overall improvement in glycemic control and management of diabetes-related complications (2).

Type 1 diabetes offsprings present more large-for-gestational-age (LGA), preterm birth, neonatal hypoglycemia than in non-diabetic women(5) which are non exhaustive complications that require specialized medical support with logistical and institutional cost for both the mother and newborn. For example, LGA predisposes offsprings to childhood obesity then to metabolic syndrom (8,9) and neonatal hypoglycemia can have long-term developmental and intellectual consequences (15) Since type 1 diabetic patients are not exempt from the growing health burdens due to sedentary lifestyle in the general population (18), these risk factors for complicated pregnancies and deliveries may overlap with pregnancy linked complications.

These complications occur despite overall advances in the daily management of diabetes (1,2) and the widespread use of advanced technologies such as continuous glucose monitoring systems (CGMS) and subcutaneous continuous insulin infusion (SCII) therapy. Moreover, in adults, safety and better efficacy in glycemic control and hypoglycemia prevention (2) of pump has been proven, both insulin delivery mode SCIII or MDI has already been considered the gold standard for all age groups since 2018 in pediatric diabetology. With even preschoolers being treated with SCII, as this generation of type 1 diabetic children will soon reach childbearing age, the pump has not yet proven superiority in preventing pregnancy-related complications (2) partly because of the potential selection bias of observational studies, hence the lack of randomized trials.

In pregnancy, SCII or MDI treatment is recommended in the same way by the ADA (2) the introduction of SCII is often left to the discretion of the physician based on the patient's desire and assessment of their ability to manage such a system. Many practitioners like to introduce SCII women of child-bearing age or in their preconception check-up, as this physiological stage requires frequent titrations of insulin therapy to adapt to variations in insulin sensitivity while achieving more demanding glycemic targets (ADA). Having women already trained in the management and daily use of the pump is way more attractive as new technologies involving pumps are very promising (27,28) such as closed-loop insulin delivery.

The aim of our study is then to compare the fetal and maternal outcomes in women with type 1 diabetes treated either by MDI or SCII in a large french cohort.

MATERIAL AND METHODS

RESEARCH DESIGN

This retrospective, single-center, observational study was conducted among pregnant women with type 1 diabetes who were followed by the "Diabetes and Pregnancy" unit at the tertiary care center of the University Hospital of Lille, France.

Data were collected from archived and computerized records including maternal characteristics, obstetrical follow-up, delivery and newborn pediatric characteristics data.

All patients were informed of the possible use of their personal anonymized medical data for research purposes only, unless they opted out, as expected under French law,

The database was declared to the French data protection authority called CNIL for "Commission Nationale de l'Informatique et des Libertés".

We included all singleton pregnant women with type 1 diabetes followed by the Diabetes and Pregnancy Unit and whose delivery occurred at the University Hospital of Lille, France, between 1997 and 2023.

Women were excluded if they were younger than 18 years, had multiple pregnancies, were lost to follow-up, or delivered outside the University Hospital of Lille.

Other types of diabetes weren't included, such as monogenic, type 2, gestational or secondary diabetes, monogenic diabetes, doubtful cause of diabetes, latent autoimmune diabetes in adults (LADA), type 1 diabetes diagnosed during pregnancy, and diabetes treated with a closed-loop insulin pump.

We excluded pregnancies that resulted in spontaneous abortion (before 22 weeks of amenorrhea), miscarriage, and stillbirth (fetal death after 22 weeks of amenorrhea).

DATA COLLECTION

Maternal medical and demographic characteristics, as well as obstetric and diabetes outcomes, were collected from maternal records obtained either from standard diabetologic and obstetric routine visits and twice-weekly calls from our specialized nurses from the Pregnancy and Diabetes Unit.

All women performed self-monitoring of glycemic outcome either from capillary glycemic lector or continuous interstitial glucose monitoring system with a fasting and before meals target of < 0.95 g/l (<5.3 mmol/L) besides <1.40 g/L and < 1.20 g/l 1 hours and 2 hours after the beginning of the meal respectively, as recommended by the French Society of Diabetology (1) and American Diabetology Association (2). CGMS targets are Time in Range (between 0.63 -1.40 g/L) >70%, Time above range (>1.40 g/L) <25%, Time below 0.63 g/L <4% and below 0.54 g/L <1% (2).

Patients were treated with either multiple daily subcutaneous insulin infusions or a continuous subcutaneous insulin pump. The choice of insulin mode was made by a diabetologist and the

patient based on their preference and ability to use a SCIII. Patients treated with a pump prior to pregnancy maintained this insulin regimen during pregnancy, and some patients treated with an MDI may switch to SCIII early in pregnancy.

The type of insulin, treatment, and self-monitoring device used before pregnancy were continued during pregnancy, unless decided otherwise by the diabetologist.

MATERNAL DATA

We recorded age, year of diagnosis of diabetes, duration of diabetes and pre gestational diabetes complications such as history of retinopathy (defined by the results of the last preconception fundus), of maculopathy, of nephropathy (defined by pathological albuminuria >30 mg/24h or renal insufficiency (1)of neuropathy, of high blood pressure (>140/90 mmHg or anti-hypertensive treatment), of angina.

Body mass index (BMI) in kg/m2 was calculated from pregestational weight and height (weight/height2).

Concerning their past obstetrical history, we reported their parity, gravidity, history of miscarage and macrosomia.

We assessed pregestational and during pregnancy smoking status as well as pregregnancy laser treatment of ophthalmologic diabetes linked complications.

DIABETES DATA

During pregnancy, the evolution of their complications of diabetes was assessed by trimestrial fundus to screen the stability or progression of retinopathy and maculopathy (1).

We monitored monthly the worsening of proteinuria and hypertension during pregnancy (1).

The onset of pre-eclampsia was defined by the presence of arterial hypertension and proteinuria greater than 300 mg/24h after 20 weeks of gestation (29).

Pregestational HbA1c, defined as the last known HbA1c before pregnancy, trimestral and postpartum HbA1c were collected.

HbA1c targets is <6–6.5% in early gestation then individualized goal <6% or <7% according to the risk of hypoglycemia (2).

Data on ketoacidosis decompensation, maternal intensive care unit transfer during pregnancy were collected.

OBSTRETRICAL DATA

Obstetric outcomes included mode of delivery (vaginal or cesarean), mode of labor (induced or spontaneous), and need for obstetric devices during vaginal delivery.

The degree of urgency (planned or emergency) of the cesarean section was recorded.

We reported postpartum hemorrhage (defined as bleeding > 500 ml in the case of vaginal delivery or > 1000 ml in the case of cesarean section, within 24 hours of delivery).

NEONATAL DATA

Neonatal outcomes were collected from obstetric and pediatric records: sex, birth height, head circumference, birth weight (BW), neonatal status (alive or intrauterine fetal death, defined as death after the fetal viability threshold of 22 weeks of amenorrhea), Apgar scores at 1, 5, and 10 minutes (with a score < 7 indicating poor adaptation to extrauterine life), acute respiratory distress, indication for intubation, and transfer to a neonatal intensive care unit.

Birth weight percentiles were sorted according to the Audipog formula. Macrosomia was defined as a birth weight greater than 4,000 grams (60)

Large for gestational age (LGA) was defined as weight greater than 90th percentile and small for gestational age (SGA) was defined as weight < 10th percentile, both according to the Audipog formula.

We collected data on neonatal hypoglycemia, defined as a blood glucose level of less than 0.35 g/dL within the first forty-eight hours of life or less than 0.40 g/dL forty-eight hours after birth or the use of glucose infusion according to an expert consensus (2).

STATISTICAL ANALYSIS

Qualitative data are presented in numbers and percentages. In the case of a Gaussian distribution, quantitative data are expressed as mean and standard deviation, otherwise by the median and interquartile range (25th and 75th percentiles). The normality of numerical parameters was verified graphically and by the Shapiro-Wilk test.

Patient characteristics, maternal, obstetric and neonatal outcomes were were compared between the two treatment groups (multiple daily injection (MDI) or subcutaneous insulin infusion (SCI) using the Chi-square test (or Fisher's exact test in case there were fewer than five cases) for qualitative variables and Student's t-test for quantitative Gaussian variables, or the Mann-Whitney U test for non-Gaussian quantitative variables

Associations between the studied complications (LGA, prematurity, preeclampsia, mode of delivery, emergency caesarean section, neonatal hypoglycemia within twenty four first hours, neonatal intensive care transfer and macrosomia) and the treatment group were compared using logistic regression models with and without adjustment for predefined confounders based on literature (Mathiesen's article). These selected confounders were pregestational data measured before the start of pregnancy and are: duration of diabetes (<=20 vs. > 20 years), BMI (<=25 vs. >25 kg/m2), history of hypertension, history of retinopathy, history of nephropathy, parity (nulliparous vs. primiparous and above) and smoking status before pregnancy.

Odds ratios are represented as measures of effect size, with their 95% confidence intervals.

The significance threshold was set at 5%. Statistical analysis was carried out using SAS software, version 9.4 (SAS Institute, Cary, NC, USA) by the Biostatistics Unit of Lille University Hospital.

RESULTS

MATERNAL CHARACTERISTICS

We included 835 pregnant women with type 1 diabetes, of whom 323 were treated with multiple daily subcutaneous injections and 510 were treated with a subcutaneous insulin infusion therapy (SCII).

There were some important statistically significant differences in maternal characteristics in the SCII group, who were on average older (30.0 years ± 4.8 vs 28.6 years ± 5.1 p <0.001), had a higher mean pre-gestational MBI (24. 4 kg/m2 (21.9; 28.1) vs 23.2 kg/m2 (21.1; 26.0) p<0. 001). SCII users were significantly more often nulliparous (20(3.9%) vs. 1(0.3%) p = 0.001), but we did not describe a statistical difference in the history of macrosomia (81(16%) vs. 40 (12.4%) p = 0.16) and miscarriage (0.3 ± 0.7 vs. 0.4 ± 0.8 p= 0.19).

Women in the SCII group had a significantly longer duration of diabetes (16.6 years ± 7.5 vs 12.2 years ± 7.9 p <0.001) and were therefore more likely to have pregestational diabetic complications (173 (34.0%) vs 71(22.1%) p<0.001) such as retinopathy (29. 6% vs 19.2% p<0.001), nephropathy (8.2% vs 4.6% p = 0.045)), pregestational hypertension (4.5% vs 1.5% p = 0.021), and were also more likely to have smoked before (23.9% vs 31.3% p -0.037) and less during pregnancy (11.7% vs 20.6% p = 0.002).

Mean pre pregnancy HbA1c was 7.8 ± 1.9% in MDI users and 7.4 ± 1.1% in SCII users (p=0.21), with no significant differences, although MDI users were significantly more likely than SCII users to be below the recommended pre-pregnancy goal of HbA1c <6.5% (97 (20.0%) vs. 80 (29.6%) p=0.003)).

In our study, we did not observe significant differences in gestity (2.1 ± 1.2 vs. 2.2 ± 1.3 p 0.72), parity (1.6 ± 0.9 vs. 1.7 ± 1.0 p= 0.74), history of neuropathy (20 (3.9) vs. 9 (2.8) p=0.39), and angina (2 0.4%) vs. 1 (0.3)).

GLYCEMIC OUTCOMES

In both groups, as expected, mean HbA1c improved during the first (7.0 ± 1.2 vs 6.8 ± 0.9 p=0.049) and second trimesters (6.5 ± 0.9 vs 6.4 ± 0.7 p=0.56) compared to preconception HbA1c (7.8 ± 1.9 vs 7.4 ± 1.1) but increased in the third trimester.

Mean HbA1c was significantly lower in the SCII group than in the MDI group during the first trimester (6.8 ± 0.9 % vs. 7.0 ± 1.2 % p=0.049), but the differences weren't statistically significant during the second (6.4 ± 0.7 % vs. 6.5 ± 0.9 % vs. p=0.56) and third (6.5 ± 0.7 % vs 6.6 ± 0.9 % p=0.52) trimesters. Nevertheless, mean HbA1c increased in the third trimester in both groups.

The proportion of women achieving the recommended therapeutic goal decreased with each trimester but the comparison between the two groups was not significant.

In the first and the second trimesters, more women treated with SCII achieved the target HbA1c than women treated with MDI (38,8% vs 42% at T1 p= 0.39 and 31,1% vs 28,7% at T2 p= 0.47) but the trend reversed in the third trimester with a higher proportion of women treated with MDI achieving the target HbA1c than in the SCII group (27% vs 23,3% p= 0.26). The decrease in HbA1c levels from preconception to the third trimester differs between the two groups in favor of the SCII users (-1.6 ± 1.6 vs -1.2 ± 1.1 p= 0.027).

MATERNAL OUTCOMES

The rate of vaginal deliveries (247(48.5%) vs. 176(54.7%) p=0.85) and therefore instrumental assisted deliveries (100 (40.5%) vs. 70 (41.7%) vs p=0.81) were not significantly different.

No statistical differences were described in cesarean deliveries rate (262 (51.5%) vs (146 (45.3%) p=0.085) while there were proportionally more emergency cesarean deliveries in the MDI group (172 (66.2%) vs. 100 (69.9%) p=0.44) still with no statistical differences.

There were no disparities in induced labor (303 (78.1%) vs. 187 (74.8%) p=0.34) and shoulder dystocia, with this event complicating 45 deliveries (16.2%) in the SCII users compared to 23 deliveries (12.2%) in the MDI users (p=0.23).

There were no significant differences in postpartum hemorrhage during both vaginal (27 (12.3%) vs. 13 (10.4%) p= 0.60) and cesarean delivery (35 (14.6%) vs. 16(14%) p=0.89), either from delivery hemorrhage or operative hemorrhage greater than 1000 ml.

The number of maternal transfers to intensive care units was encouraging, with 5 transfers (1%) in the pump group and 4 transfers (1.2%) in the daily injection group (p=0.74) with an insignificant difference.

Regarding the development of diabetic complications during pregnancy, we did not observed a difference in a worsening of chronic hypertension (87(17.2%) vs. 43(13.4%) p=0.15), retinopathy (118(23.3%) vs. 74(23.1%) p=0.93) and proteinuria (114(22.5) vs 75 (23.4%). p=0.75) in both groups. Preeclampsia complicated 60(11.9%) pregnancies in SCII group and 30 (9.4%) in MDI group (p= 0.25).

There were no statistical difference in both groups in mean gestational weight gain (13.8 kg +/- 5.4 kg vs 14.5 kg +/- 5.3 kg p= 0.082) and in pre-eclampsia, that occurred in 60 (11.9%) pump users and 30 (9.4%) daily injectors (p=0.25).

NEONATAL OUTCOMES

The majority of offspring were born alive in both groups (505 (99.2%) vs. 319 (99.1%)), but we regret 3 stillbirths in each group and 1 death during delivery in the SCII group.

Gestational age was essentially the same in both treatment groups with a mean gestational age of 37.5 weeks amenorrhea in the SCII groups and 37.4 weeks in the MDI group (p=0.79).
Preterm delivery complicated pregnancy in 61(12%) pump users and 45(14%) daily injectors (p=0.41), proportionally but not significantly more often in the MDI group.

The median birth weight is significantly higher in the SCII groups than in the MDI groups (3610 (3250-3980) g vs 3500(3103-3900) g p=0.011).
According to the AUDIPOG formula, there was no differences in LGA rate ((269(54.7%) vs (124(54.5%) p=0.25) thus 124 SCII infants (24.5%) and 61 MDI infants (19.1%) were considered macrosomic (p=0.070).
SGA occurred in 8 (1.6%) SCII-treated pregnancies and in 6 (2%) MDI-treated pregnancies (p=0.72).

Babies born to MDI mothers were more likely to have an Apgar score < 7 at five minutes (10(3.1%) vs. 6(1.2%) p=0.047) indicating poor adaptation to extrauterine life, but there was no statistical disparity at one minute (36(11.3) vs. 47(9.3) p=0.34).

Congenital defects were described in 34 (6.7%) and 23 (7.2%) of the offspring in the SCII and MDI groups, respectively (p=0.81).
Respiratory distress syndrome affected 45 (9.1%) infants in the SCII user group, of whom 10 (23.3%) required intubation, and 27 (8.6%) infants in the MDI group, of whom 8 (27.6%) required intubation; both results were not statistically significant.

Neonatal transfer to NICU was equally frequent in both groups (59 (11.7%) vs. 42 (13.1%) p=0.5383),
Neonatal hypoglycemia was described in 153 (48.4%) of the offspring in the MDI group and 230 (46.4%) of the offspring in the SCII group (p=0.57) with no statistical differences, as well as the

exact incidence of neonatal hypoglycemia within the first 3 hours, 12 hours, 24 hours, 48 hours, and 72 hours.

Glucose perfusion was required in same proportion in borth groups with 44 (14%) MDI births and 60 (12.1%) SCII births (p=0.44).

Neonatal jaundice complicated 203 (40,9%) postpartum hospitalisations in the SCII group and 127(40,3%) in the MDI group. Phototherapy was statistically more often required in 147(72,4%) SCII babies and 109 (85,8%) MDI babies (p=0.004).

MULTIVARIATE ANALYSIS

After analysis with literature selected confounding factors such as duration of diabetes, BMI, history of hypertension, history of retinopathy, history of nephropathy, parity and smoking status before pregnancy, we still did not find significant association between treatment mode and feto-maternal complications rates.

In logistic regression analyses, no treatment was significantly associated with more cesarean section (adjusted OR = 1.096 [0.783-1.535] p= 0.5934) , LGA (adjusted OR= 1.170 [0.837; 1.634] p = 0.3588), macrosomia (adjusted OR = 1.155 [0.769 ; 1.734] p=0.4882), preeclampsia (adjusted OR =1.061 [0.610; 1.846] p= 0.8350), respiratory distress (adjusted OR =0.864 |0.464 ; 1.607] p= 0.643), neonatal hypoglycemia (1. 086 [0.600 ; 1.968] p=0,7847) either in crude nor adjusted on confounding factors analysis .

DISCUSSION

Our study aimed to compare maternal and fetal outcomes in pregnant women with type 1 diabetes treated with either multiple daily insulin injections (MDI) or continuous subcutaneous insulin infusion (CSII) in a monocentric retrospective cohort of 833 French women.

Our analysis revealed significant differences in patient characteristics between the two groups. Women using CSII were generally older, had a longer duration of diabetes and were more likely to

have pre-existing diabetic complications. Despite these differences, both groups achieved comparable glycemic control throughout pregnancy except in the first trimester when the women treated with SCII had a lower HbA1c.

The mean birth weight was significantly higher in the CSII group, although no statistically significant differences were observed in the rates of large-for-gestational-age (LGA) infants or macrosomia. Furthermore, our study revealed no notable differences in the incidence of neonatal hypoglycemia, respiratory distress syndrome, NICU transfers, or intubation between the two groups. Additionally, the mode of delivery, rates of emergency cesarean section, labor induction, and postpartum hemorrhage were comparable between the two groups. Moreover, there were no notable discrepancies in the exacerbation of pre-gestational diabetes complications, such as chronic hypertension, proteinuria, or retinopathy, between CSII and MDI patients.

Two recent studies challenge the commonly held belief that PSC is superior in improving pregnancy outcomes for women with DT1. However, there is still no consensus among the literature on this topic.

The 2024 large prospective international cohort by Thorius and colleagues included 723 women treated with insulin pumps and 1,280 with MDI (3). The results indicated that SCII users were associated with a LGA (adjusted odds ratio [OR] 1.36) and preterm delivery (adjusted OR 1.46). This suggests that SCII did not lead to improved pregnancy outcomes in terms of reducing preterm births or fetal overgrowth. These results remained significant even after adjusting for factors such as diabetes duration, history of hypertension, of retinopathy, of nephropathy, nulliparity, maternal BMI at enrollment, educational level, smoking, HbA1c at baseline, HbA1c at delivery, and gestational weight gain.

The results of this study align with the existing literature on the higher prevalence of LGA or macrosomia among SCII (19,30,31). However, other studies have not identified any significant differences between the treatment groups, as observed in our study (4,32–34).

Furthermore the LGA prevalence observed in our study aligns with the literature, which describes both higher (3,4,31,34) and lower LGA rates (19,32,33,35) in type 1 diabetes pregnancies. A secular trend towards increased LGA rates in type 1 diabetic offspring has been reported in countries such as Scotland (12-13) and Sweden. It is postulated that improved glycemic control during the preconception and early pregnancy periods may facilitate placentation, resulting in a larger, more efficient placenta that supports increased fetal growth (36). One study also indicated that normal serum markers of early placentation might predict macrosomia , while others describe a positive association between placental weight and neonatal outcomes (37).

The CONCEPTT trial is an international randomized study designed to evaluate the security and efficacy of CGMS. One of the prespecified analyses aimed to compare glycemic control, quality of life and pregnancy outcomes between SCII and MDI users.

The trial did not identitfy any significant differences in the rates of LGA and preterm birth. However, SCII users had a higher prevalence of hypertensive disorders (30.6% vs. 15.5% for MDI; P = 0.011), largely driven by increased gestational hypertension (14.4% vs. 5.2%; P = 0.025). Additionally, SCII offspring demonstrated a higher incidence of neonatal hypoglycemia (31.8% vs. 19.1% for MDI; P = 0.05). (4)

Our study revealed that women using CSII tend to have longer durations of diabetes and more frequent preconceptional occurrences of retinopathy and nephropathy. This may lead to more complex diabetes management, (32) as longer diabetes durations are linked to elevated risks of microangiopathic and obstetric complications (7).

The maternal characteristics in Thorius and al. 2024 differ between the groups, aligning with the literature. It is often described that women using CSII tend to have a longer history of diabetes (3,18,29,29–34) and report higher rates of preconceptional microvascular complications in these patients (3,30,32). In our experience, CSII is typically introduced in the preconception period for

women who fail to meet recommended preconception HbA1c targets, occasionally at the beginning of the pregnancy. Our study yielded comparable results to those of Thorius and al. 2024, indicating that individuals utilizing SCII exhibited prolonged diabetes duration, elevated baseline BMI, and increased retinopathy prevalence.

The maternal characteristics in CONCEPTT study demonstrated no statistical differences, as the randomization process stratified women based on HbA1c levels and the method of insulin delivery. In the Thorius and al. study, HbA1c levles were found to be lower in SCII users compared to MDI users, both in pregestational and first trimester. Consequently,no significant difference in HbA1c levels was observed between the two groups in the second and third trimesters.

Our study demonstrated that the pregestational HbA1c levels were not statistically different between the two groups. Consequently, a significant higher proportion of women in the MDI group achieved the pregestational target of HbA1c <6,5%. The first trimester HbA1c was significantly lower in the PSC group. However, there was no difference between the two groups in the second and third trimesters, with a median third trimester HbA1c of 6.5 (Q1;Q3 (5.9;7.0))% in the MDI group and 6.4 (Q1;Q3 (6.0;6.9))% in the SCII group. This indicates that at least 75% of the women studied in both groups achieved a third trimester HbA1c below or equal to 7%.

CONCEPTT described that the HbA1c levels at randomization were comparable between the two groups, in line with the pre-established stratification. Furthermore, the MDI group exhibited superior glycemic control, with a higher proportion of MDI users achieving the target level at 24 and 34 weeks of gestation.

Our study found no significant differences in glycemic outcomes between CSII and MDI

users. The mean HbA1c levels in the second and third trimesters, as well as the proportion of women

achieving target HbA1c levels, were found to be similar between the two groups. While some studies indicate superior glycemic control with CSII (1,30,33,38)without exposing them to more frequent severe hypoglycemia or diabetes ketoacidosis (30), these finding are not universally

replicated as other studies have not identified a significant difference in HbA1c levels across trimesters (19,39–41).

Hauffe et al. (19) postulated that excess gestational weight gain is a contributing factor to LGA. Their findings indicated a higher prevalence of LGA, greater gestational weight gain, and more frequent excessive weight gain in CSII users. It is already established that pre-gestational BMI is a risk factor for excess gestational weight gain and LGA in the general population. However, it tends to be higher in women with type 1 diabetes in childbearing age. The data from the American National Health Interview Survey (2016-2021) indicate that the prevalence of overweight and obesity in women with type 1 diabetes is comparable to that of the general population (18), which increases the risk of insulin resistance and metabolic complications.

The study revealed that women using CSII had a higher pregestational BMI. However, there was no significant difference in gestational weight gain or better glycemic control observed in these women. Other studies have reported similar gestational weight gain between CSII and MDI groups (30,34,39), with some describing slightly greater weight gain with CSII therapy (19,40). In contrast, a 2022 study by Wang et al. (31) revealed a higher prevalence of LGA among CSII users, despite superior glycemic control. Furthermore, the association between SCII and LGA persisted even after adjusting for gestational weight gain, indicating that the link between fetal growth and SCII is independent of gestational weight gain.

CSII's flexibility in managing macronutrient intake is often cited as a potential contributor to weight gain. However, an additional subanalysis of the CONCEPTT trial (42) study found no significant difference in total energy intake, sugar consumption, or snacking behaviors between the CSII and MDI groups. In a further analysis of the data, Hill et al. (43) examined dietary data from 547 pregnant women with type 1 diabetes and found a positive correlation between HbA1c and carbohydrate consumption in the latter stages of pregnancy. This finding is consistent with other studies that have linked carbohydrate intake to higher HbA1c levels (44).

Carbohydrate counting, a requirement for functional insulin therapy (FIT), was more common among CSII users, as recommended before transitioning to CSII due to evidence towards a lower HbA1c levels (45). However, clinical practice shows that CSII users may be more prone to correcting hyperglycemia, which can lead to subsequent hypoglycemia and correction with high glycemic index foods, potentially contributing to weight gain (46).

Cyganek et al. (40) discovered that even HbA1c levels as low as 4.5% are still linked to an increased risk with macrosomia. Their findings indicate a linear correlation between third-trimester HbA1c and macrosomia risk between 5.5 and 7%. Reducing HbA1c levels below 6% can reduce the risk of macrosomia, but it does not eliminate it entirely. Furthermore, pursuing even lower targets may not be feasible without increased risks.

The study revealed that women who gave birth prematurely were more likely to have pre-existing kidney disease, higher gestational weight gain, and similar early pregnancy HbA1c levels compared to those who gave birth at term. It is widely acknowledged that pre-existing kidney disease, preeclampsia, gestational weight gain, ultrasound-estimated fetal overgrowth, and poor glycemic control (HbA1c >7%)in late pregnancy are considered significant predictors of preterm birth (47).

In regards to cesarean delivery rates, the Thorius and al (2024) study indicates a lower rate of cesarean sections among SCII users, primarily due to reduction in the number of planned cesarean sections. Other studies have reported similar rates of cesarean delivery between the two insulin modes, which aligns with our findings. The global rate of cesarean sections was approximately 21% in 2018, with a consistent increase over the past 30 years. Our cesarean section rate was lower than in many comparable studies, with a consistent ratio of two-thirds emergency to one-third planned cesarean sections in both groups, and a consistent prevalence of preeclampsia.

It is well-established that maternal age, higher pre-pregnancy BMI, and an increased prevalence of LGA are significant predictors of cesarean delivery. Planned cesarean sections are often influenced by poorer glycemic control and ultrasound estimates of fetal overgrowth (48), while emergency cesarean sections are more frequently associated with acute obstetric complications, including suspected fetal asphyxia or hypertensive disorders (49)

The study revealed that women using CSII were generally older and had higher BMIs. However, there were no significant differences in the rates of LGA and glycemic control were similar between the groups, and the cesarean section rates were comparable. This could indicate a potentially beneficial effect of CSII in managing these risk factors. However, making direct comparisons of cesarean section rates are challenging due to the complex interaction of non-medical factors that can influence the mode of delivery. These include clinical judgment and practical considerations from both the mother and healthcare providers (35). Therefore, the potential for unidentified confounding factors to impact our findings cannot be completely eliminated.

The results of our study indicate that the incidence neonatal hypoglycemia in both the MDI and SCII groups is significantly high, with rates of 48.3% and 46.4%, respectively. This may be attributed to the composite nature of our hypoglycemia criterion, which encompasses both the ADA definition of hypoglycemia persisting throughout hospitalization and the need for glucose infusion (1,2). A broad definition may result in an overestimation the incidence of clinically significant hypoglycemia. Additionally, factors such as aggressive screening protocols or variations in institutional definitions of hypoglycemia could potentially influence the results.

The comparable obstetrical and neonatal outcomes in women with different pregestational characteristics despite comparable glycemic controle indicate that HbA1c may not be the most effective marker of glycemic control in pregnancy. HbA1c targets may not be sufficient to prevent diabetic-specific pregnancy complications.

HbA1c is a widely used and comparable variable in the literature however its lack of ability to distinguish the propensity for glycemic excursions patterns of glucose excursions. It is a weak point when considering the safety of CGMS and its efficacy in improving glycemic and neonatal outcomes in pregnant women with type 1 diabetes, as demonstrated in the CONCEPTT trial. In the aforementioned trial, 68% of CGMS users spent time in the recommended target range, compared to 61% of those using only capillary glucose monitoring. This means CGMS users spent an average of one whole hour less per day in hyperglycemia (23). The authors therefore propose that CGMS data on maternal time spent in hyperglycemia may be a more relevant factor for neonatal outcomes. In light of the literature indicating that late pregnancy glycemic excursions can predict LGA (38) and that an almost normal HbA1c can still indicate that women spent a substantial amount of time above the glycemic target. Unfortunately, these data were not available for our study.

STRENGTHS

The size of our cohort and the large number of patients treated with SCII represent a significant advantage. Outpatient management, as recommended by the SFD (58), and the uniformity of the specialized diabetes nurse team that called the pregnant women twice a week undoubtedly made data collection easier. The multidisciplinary team recorded the same information on internal, specific hospital protocols, thus ensuring the reliability of this retrospective data collection.

LIMITATIONS

Due to the absence of randomization to the SCII and MDI groups and the retrospective nature of the study, there is a risk of section bias, which makes it challenging to establish a direct causal link between the variables under investigation.

The recruitment methos, which was conducted at a single center and a regional centralized tertiary center, the length of the enrollment period, which saw progressive changes in clinical practices in line with professional societies' guidelines and the government funding of access to the pump due to the French healthcare system, make it difficult to draw generalizations.

Since 1999, there have been notable advancements in recommendations for glycemic control, as well as in the types of pumps and methods of daily glycemic monitoring (1). Therefore, the recent widespread use of CGMS may also have an impact. To increase internal validity, it would have been beneficial to analyze subgroups according to the date of publication of the French recommendations.

We weren't able to analyse preconceptional and first trimester HBA1C, gestational weight gain in linear regression analysis.

For women with type 1 diabetes, pregnancy represents a significant opportunity to enhance their engagement with daily diabetes management. Unfortunately, the rate of planned pregnancy remains undocumented in our study as previous research indicates that women who plan their pregnancies are more likely to achieve preconception and first trimester HbA1c targets. Some authors described a lack of pregnancy planning and high HbA1c levels in the first trimester are identified as risk factors for LGA and macrosomia (32).

CONCLUSION

The objective of our study was to compare maternal and neonatal outcomes in pregnant women with type 1 diabetes who were either using insulin pumps or multiple daily injections (MDIs).

Our findings revealed notable discrepancies in maternal characteristics with comparable maternal and neonatal outcomes between the two groups even after adjusting for potential confounding variables and maintaining comparable glycemic control in both treatment modes.

Despite the prevalence of obstetric complications such as large for gestational age (LGA), prematurity, and neonatal hypoglycemia, our results highlight the necessity for further research to identify predictors of these common obstetric complications. The use of more modern outcomes, such as continuous glucose monitoring system, may prove beneficial.

The higher rates of diabetes-related antepartum complications, higher BMI and longer duration of diabetes in the SCII group indicate that the lack of significant differences in maternal and neonatal outcomes may be attributed to the beneficial effect of the pump.

Our findings highlight the necessity for further research to ascertain predictors of these prevalent obstetric and neonatal complications, with the objective of implementing preventive measures. goal of prevention.

TABLES & FIGURES

Figure 1 : Flow chart

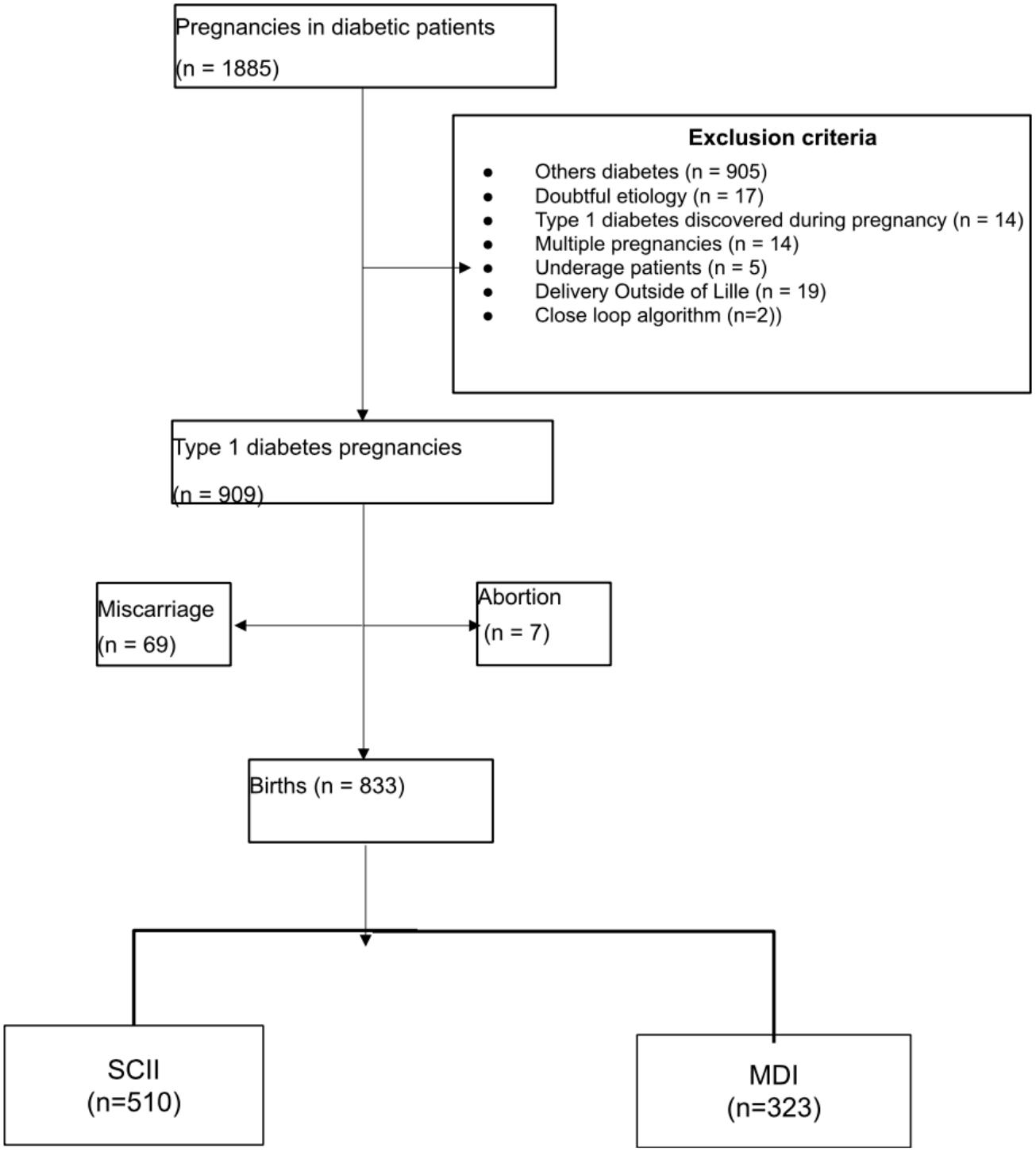

Table 1 : Maternal characteristics in treatment groups

	Treatment				*p-value*
	MDI N = 323	***n***	**SCIII N=510**	***n***	
Age (years), mean ± SD	**28.6 ± 5.1**	**323**	**30.0 ± 4.8**	**510**	**<0.001**
Pregestational weight (kg), median (IQR)	**63.0 (57.0 ; 70.0)**	**314**	**66.3 (59.5 ; 76.0)**	**502**	**<0.001**
Pregestational BMIl (kg/m2), median(IQR)	**23.2 (21.1 ; 26.0)**	**308**	**24.4 (21.9 ; 28.1)**	**495**	**<0.001**
Duration of diabetes (years), mean ± SD	**12.2 ± 7.9**	**321**	**16.6 ± 7.5**	**510**	**<0.001**
Nulliparity, n(%)	**1 (0.3)**	**323**	**20 (3.9)**	**508**	**0.001**
Parity (n), mean ± SD	1.7 ± 1.0	322	1.6 ± 0.9	508	0.74
Gestity (n), mean ± SD	2.2 ± 1.3	322	2.1 ± 1.2	508	0.72
History of macrosomia, N(%)	40 (12.4)	322	81 (16.0)	507	0.16
History of miscarriages (n), mean ± SD	0.4 ± 0.8	323	0.3 ± 0.7	509	0.19
Smoking before pregnancy, N(%)	78 (31.3)	249	98 (23.9)	410	0.037
Smoking during pregnancy, N(%)	**50 (20.6)**	**243**	**46 (11.7)**	**393**	**0.002**
Pregestational diabetic complication, N(%)	**71 (22.1)**	**321**	**173 (34.0)**	**509**	**<0.001**
Diabetic retinopathy	**62 (19.2)**	**323**	**151 (29.6)**	**510**	**<0.001**
Laser photocoagulation, N (%)	18 (5.6)	323	37 (7.3)	510	0.34
Diabetic nephropathy, N (%)	**15 (4.6)**	**323**	**42 (8.2)**	**510**	**0.045**
Diabetic neuropathy, N(%)	9 (2.8)	321	20 (3.9)	509	0,39
History of hypertension, N (%)	**5 (1.5)**	**323**	**23 (4.5)**	**510**	**0.021**
History of angina, N (%)	1(0.3)	321	2 (0.4)	509	number <8
FIT, N(%)	**32 (9.9)**	**323**	**238 (46.8)**	**509**	**<0.001**
Pregestational HbA1c, mean(SD)	7.8 ± 1.9	270	7.4 ± 1.1	485	0.21
Pregestational HbA1c <6,5%, N(%)	**80 (29.6)**	**270**	**97 (20.0)**	**485**	**0.003**

Table 2 : Glycemic outcomes by treatment group

	Treatment				
	MI N=323	**N**	**SCIII N=510**	**N**	**p-value**
T1 HbA1c <6.5 %, N(%)	109 (38.8)	281	199 (42.0)	474	0.39
T2 HbA1c <6 %, N(%)	92 (31.1)	296	139 (28.7)	485	0.47
T3 HbA1c <6 %, N(%)	74 (27.0)	274	103 (23.3)	443	0.26
Mean HbA1c, mean(SD)	6.7 ± 0.9	239	6.5 ± 0.7	416	0.15
T1 HbA1c %, mean(SD)	**7.0 ± 1.2**	**281**	**6.8 ± 0.9**	**474**	**0.049**
T2 HbA1c %, mean(SD)	6.5 ± 0.9	296	6.4 ± 0.7	485	0.56
T3 HbA1c %, mean(SD)	6.6 ± 0.9	274	6.5 ± 0.7	443	0.52
T3 HbA1c %, median(Q1-Q3)	6.5 (5.9 ; 7.0)	274	6.4 (6.0 ; 6.9)	443	0.52
Change from preconception to the third trimester, mean (SD)	-1.6 ± 1.6	266	-1.2 ± 1.1	481	0.027

T1 HbA1c: HbA1c at first trimester ; T2 HbA1c: HbA1c at second trimester; T3 HbA1c: HbA1c at third trimester

Figure 2 : Proportion of on-target HbA1c in SCII and MDI during pregnancy

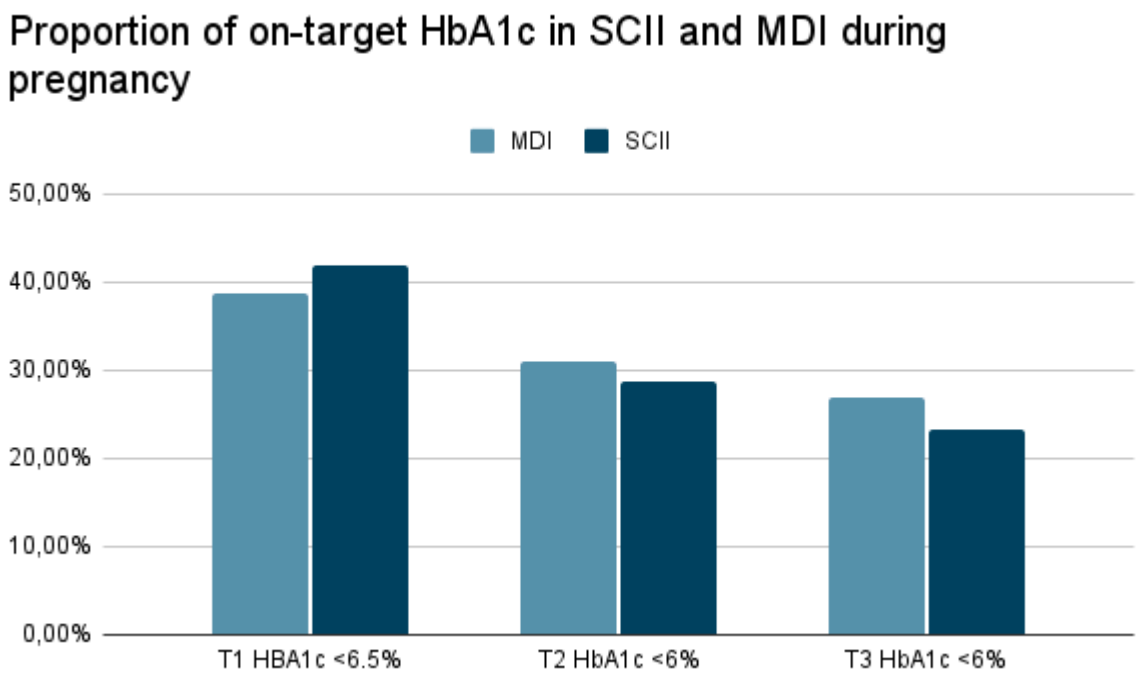

Figure 3 : Mean HbA1c in MDI and SCII during pregnancy

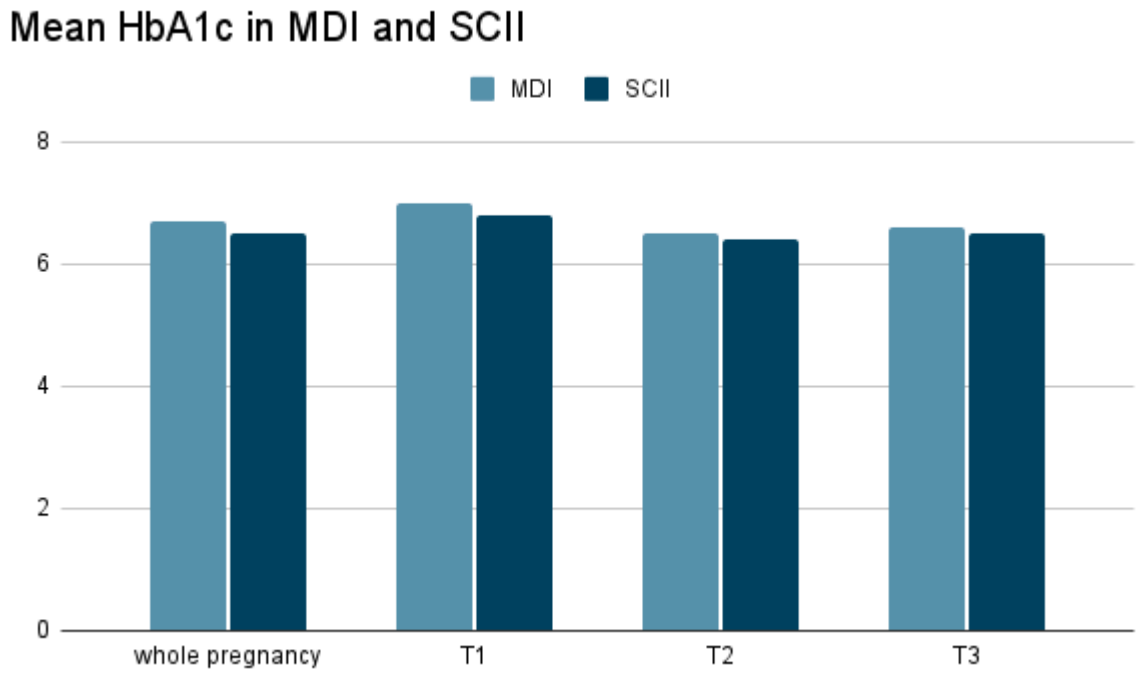

Table 3 : Maternal outcomes by treatment group

	Treatment				
	MDI N=323	**N**	**SCIII N=510**	**N**	**p-value**
Vaginal delivery, N(%)	176 (54.7)	322	247 (48.5)	509	0.085 *
Instrumental assistance for vaginal delivery, N(%)	70 (41.7)	168	100 (40.5)	247	0.81
Cesarean delivery, N(%)	146 (45.3)	322	262 (51.5)	509	0.085*
Planned cesarean delivery, N(%)	43 (30.1)	143	88 (33.8)	260	0.44
Emergency Cesarean delivery, N(%)	100 (69.9)	143	172 (66.2)	260	0.44
Spontaneous labor, N(%)	63 (25.2)		85 (21.9)		0.34 **
Induced labor, N(%)	187 (74.8)	250	303 (78.1)	388	0.34 **
Mother transfer to ICU, N(%)	4 (1.2)	323	5 (1.0)	510	0.74
Postpartum hemorrhage among vaginal deliveries, N(%)	13 (10.4)	125	27 (12.3)	220	0.60
Postpartum hemorrhage during cesarean delivery, N(%)	16 (14.0)	114	35 (14.6)	240	0.89
Estimated blood loss, mean(SD)	681.6 ± 217.1	31	802.3 ± 319.8	77	0.033
Preeclampsia, N(%)	30 (9.4)	320	60 (11.9)	503	0.25
Shoulder dystocia, N(%)	23 (12.2)	188	45 (16.2)	277	0.23
Worsening chronic hypertension, N(%)	43 (13.4)	320	87 (17.2)	506	0.15
Worsening of proteinuria, N(%)	75 (23.4)	320	114 (22.5)	507	0.75
Worsening of retinopathy, N(%)	74 (23.1)	321	118 (23.3)	506	0.93
Weight gain in pregnancy, mean(SD)	14.5 ± 5.3	264	13.8 ± 5.4	435	0.082

ICU : intensive care unit

Table 4 : Neonatal outcomes by treatment group

	Treatment				
	MDI N=323	**N**	**SCII N=510**	**N**	**p-value**
Living birth, N(%)	319 (99.1)		505 (99.2)		effectif < 8
Intrauterine foetal death, N(%)	3 (0.9)		3 (0.6)		
Death during delivery, N(%)	0 (0.0)	322	1 (0.2)	509	
Birth weight, median(Q1;Q3)	3500 (3103;3900)	320	3610(3250 ; 3980)	507	0.011
Macrosomia, (N(%)	61 (19.1)	320	124 (24.5)	507	0.070
LGA Audipog, N(%)	154 (50.5)	305	269 (54.7)	492	0.25
SGA Audipog, N(%)	6 (2.0)	305	8 (1.6)	492	0.72
Birth defect, N(%)	23 (7.2)	320	34 (6.7)	504	0.81
1-min Apgar < 7, N(%)	36 (11.3)	318	47 (9.3)	507	0.34
5-min Apgar inferior < 7, N(%)	10 (3.1)	318	6 (1.2)	507	0.047
10-min Apgar inferior < 7, N(%)	1 (0.3)	316	1 (0.2)	499	effectif < 8
Emergency transfer, N(%)	42 (13.1)	320	59 (11.7)	505	0.54
Resuscitation center, N(%)	27 (64.3)	42	39 (65.0)	60	0.94**
NICU, N(%)	15 (35.7)	42	21 (35.0)	60	
Respiratory distress, N(%)	27 (8.6)	314	45 (9.1)	497	0.82
Intubation, N(%)	8 (27.6)	29	10 (23.3)	43	0.68
Neonatal jaundice, N(%)	127 (40.3)	215	203 (40.9)	496	0.86
Phototherapy, N(%)	109 (85.8)	127	147 (72.4)	203	0.004
Neonatal hypoglycemia, N(%)	153 (48.4)	316	230 (46.4)	496	0.57
Perfusion of glucose solution,N(%)	44 (14.0)	315	60 (12.1)	495	0.44
NNH within the first 3 hours, mean(SD)	0.5 ± 0.8	316	0.5 ± 0.9	496	0.26
NNH within the first 12 hours, mean(SD)	0.5 ± 1.1	315	0.5 ± 1.0	495	0.99
NNH within the first 24, mean(SD)	0.2 ± 0.7	315	0.2 ± 0.8	496	0.55
NNH within the first 48 hours, mean(SD)	0.1 ± 0.4	315	0.1 ± 0.4	496	0.20
NNH within the first 72 hours, mean(SD)	0.1 ± 0.6	315	0.1 ± 0.5	496	0.20
Term,mean (SD)	37.4 ± 2.1	322	37.5 ± 1.9	509	0.79
Preterm birth, N(%)	45 (14.0)	322	61 (12.0)	508	0.41

Table 5 : multivariate analysis by treatment group

Variable	MDI	SCII	p-value	adjusted p-value*	Crude OR(95% CI)/ Adjusted OR (95% CI) *	
LGA, N(%)	154 (50.5)	269 (54.7)	0,2503	0.3588	Crude OR	1.183 [0.888 ; 1.575]
					Adjusted OR	1.170 [0.837; 1.634]
Macrosomia, N(%)	61 (19.1)	124 (24.5)	0.0704	0.4882	Crude OR	1.375[0.974 ; 1.940]
					Adjusted OR	1.155 [0.769 ; 1.734]
Preterm birth, N(%)	45 (14%)	61 (12%)	0.4084	0.158	Crude OR	0.840[0.556; 1.270]
					Adjusted OR	0.694 [0.418; 1.153]
Preeclampsia, N(%)	30 (9.4)	60 (11.9)	0.2537	0.8350	Crude OR	1.309 [0.824; 2.079]
					Adjusted OR	1.061 [0.610; 1.846]
Cesarean section, N(%)	146(45.3)	262(51.5)	0.0852	0.5934	Crude OR	1.279 [0.966-1.692]
					Adjusted OR	1.096 [0.783-1.535]
Planned C section, N(%)	43 (30.1)	88 (33.8)	0.4390	0.694	Crude OR	1.190 [0.766;1.848]
					Adjusted OR	1.115 [0.648; 1.917]
Emergency Cesarean section, N(%)	100(69.9)	172 (66.2)	0.439	0.6947	Crude OR	0.840 [0.514-1.305]
					Adjusted OR	0.897 [0.522-1.543]
Respiratory distress, N(%)	27 (8.6)	45 (9.1)	0.824	0.643	Crude OR	1.058 |0.642 ; 1.744]
					Adjusted OR	0.864 |0.464 ; 1.607]
Neonatal hypoglycemia before 24h, mean(SD)	0.2 ± 0.7	0.2 ± 0.8	0.5015	0,7847	Crude OR	0,842 [0.509 ; 1.391]
					Adjusted OR	1. 086 [0.600 ; 1.968]
Neonatal reanimation or NICU transfert	42 (13.1)	59 (11.7)	0.5383	0,2082	Crude OR (95% CI)	0.876 [0.574 ; 1.337]
					Adjusted OR (95% CI)	0.717 [0.427 ; 1.204]

**Adjusted for diabetes duration exceeding 20 years, history of hypertension, history of retinopathy, history of nephropathy, nulliparity, preconceptional BMI exceeding 25 kg/m2 and smoking status before pregnancy.*

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AUTEURE : Nom : BIROTA **Prénom** : Ameline
Date de soutenance : 01/10/2024
Titre de la thèse : Pompe sous cutanée d'insuline ou multi-injections au cours de la grossesse diabétique de type 1: résultats maternels et foetaux.
Thèse - Médecine - Lille 2024
Cadre de classement : Diabétologie
DES : Endocrinologie-Diabétologie-Nutrition
Mots-clés : pompe, multi-injection, grossesse, diabète de type 1, complications obstétricales, complication néonatales

Résumé :

CONTEXTE ET OBJECTIFS : Pendant la grossesse de la femme diabétique de type 1, les deux modes d'administration d'insuline (multi-injections et les pompes à insuline sous cutanées (2)) sont préconisés au meme plan par l'ADA 2024. Or la pompe n'a pas encore fait la preuve de sa supériorité dans la prévention des complications materno-foetale chez la patiente DT1 comme en témoigne des études récentes retrouvant une prévalence plus élevée de LGA et prématurité chez les patientes traitées par pompe. Le but de cette étude est donc de comparer l'efficacité des deux méthodes de traitement, pompe à insuline et multi-injection, en terme de réduction des complications chez les femmes enceintes diabétiques de type 1.

MÉTHODE : étude rétrospective, observationnelle incluant 834 patientes DT1 ayant accouché au CHU de Lille entre 1997 et 2023. Les données cliniques (caractéristiques pré gestationnelles, les différentes complications maternelles et fœtales) ont été comparées en fonction de leur groupe de traitements.

RESULTATS : Caractéristiques maternelles : Les utilisatrices de SCIII étaient plus âgées (30.0 ans ± 4.8 vs 28.6 ans ± 5.1 p <0.001), avaient un diabète plus ancien (16.6 ans ± 7.5 vs 12.2 ans ± 7.9 p <0.001), un IMC plus élevé et davantage de complications liées au diabète (173 (34.0%) vs 71(22.1%) p<0.001.

Contrôle glycémique : L'HbA1c était significativement plus basse dans le groupe SCII au 1er trimestre (6.8 ± 0.9 % vs 7.0 ± 1.2 % p=0.049) mais similaire par la suite.

Résultats maternels : Aucune différence significative n'a été observée entre les deux groupes en termes de césarienne (262 (51.5%) vs (146 (45.3%), de pré-éclampsie (60(11.9%)vs. 30 (9.4%)p= 0.25), d'aggravation d'hypertension chronique (87(17.2%) vs. 43(13.4%) p=0.15), de néphropathie (114(22.5%) vs 75 (23.4%). p=0.75) ou de rétinopathie ((118(23.3%) vs. 74(23.1%) p=0.93),de prise de poids gestationnelle (13.8 kg +/- 5.4 kg vs 14.5 kg +/- 5.3 kg p= 0.082).

Résultats néonataux : La SCII a été associée à un poids de naissance plus élevé (3250-3980) g vs 3500(3103-3900) g p=0.011) mais aucune différence significative n'a été mis en évidence pour les LGA (269(54.7%) vs (124(54.5%) p=0.25), la macrosomie (124 (24.5%) vs 61(19.1%) p=0.070), la prématurité (61(12%) vs. 45(14%)p=0.41)), la détresse respiratoire (45 (9.1%)vs. 27 (8.6%) p=0.82) et l'hypoglycémie néonatale (230 (46.4%) vs. 153 (48.4%) p=0.57).

Les analyses multivariées n'ont pas révélé d'association significative entre le mode de traitement (SCII vs MDI) et les complications fœto-maternelles, même après ajustement pour divers facteurs de confusion reconnu dans la littérature (durée du diabète, l'IMC et les antécédents de complications)

CONCLUSION : Les traitements par SCIII et MDI ont montré des résultats de complications maternelles et néonatales similaires malgré des caractéristiques maternelles différentes en période pré gestationnelle.

Composition du Jury :
Président : Pr Damien SUBTIL
Assesseurs : Docteur RAZKA Thameur
Docteur LEMAITRE Madleen
Directrice de thèse : Pr Anne VAMBERGUE