PP 01
Is there a difference in pregnancy and glycemic outcome in patients with type 1 diabetes on insulin pump with constant or intermittent glucose monitoring?

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**Background:** The aim of the study is to describe glycemic and insulin outcomes by trimester, maternal and fetal outcome in patients with type 1 diabetes using insulin pump with constant (CGM) or intermittent glucose monitoring (IGM).

**Methods:** Twenty five women with type 1 diabetes with newly diagnosed pregnancy were treated with insulin pump therapy (Medtronic 722) for at least one year. Insulin pump and CGM (Medtronic PRT) were implemented at least 3 months before conception. Patients were randomized in two groups: CGM group, twelve patients on insulin pump with glucose sensor, 24h per day and IGM group, thirteen patients on insulin pump with intermittent glucose sensor, 14 days per month. The following parameters were analyzed HbA1c, mean blood glucose, insulin requirement IU/kg/day, weight gain, severe hypoglycemic events, DKA, macrosomia, cesarean section and neonatal hypoglycemia.

**Results:** Both groups achieved good glucose control during their pregnancies (p<0.05): 6.78%±1.3 and 6.92%±0.9 at the beginning of the study with 6.14%±0.9 (CGM group) and 6.23%±0.6 (IGM group) at the end of the study, (last HbA1c before delivery). There was no significant decrease of HbA1c between groups. The CGM group had significantly lower A1c in first trimester comparing IGM group. Maternal and fetal outcome did not show significant difference between both groups.

**Conclusion:** Insulin pump therapy together with constant or intermittent glucose monitoring can improve diabetes control and pregnancy outcome in type 1 diabetes. The quality of glucose profile in the moment of conception was the important factor for pregnancy outcome.

PP 02
Usefulness of Glycated Albumin (GA) as a Marker of Mother’s Blood Glucose Control – Report of the Japan GA Study Group

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**Background:** HbA1c, which every doctor knows as a glucose control marker, is to combine glucose at the amino terminal valine of the B-chain of Hemoglobin. GA is to combine glucose at the lysine–525 among types of lysine. The half-life of albumin is shorter than HbA1c, about 17 days. As GA has been able to be measured by enzymatic method using autoanalyzer taking only 3 minutes, developed from the assay using HPLC, I would like to introduce the usefulness of GA as a blood glucose control marker during pregnancy.

**Subjects** were 676 normal pregnant women for estimation of the changes of GA levels during pregnancy. GA in 136 diabetic pregnant women (type 1 and type 2) was measured during pregnancy.

Subjects of normal and diabetic pregnant women were collected throughout Japan. Plasma
Glucose levels were measured at each hospital visit, GA by enzymatic method (ASAHI KASEI reagent) every two weeks and HbA1c every month. **Results:** The range of GA and HbA1c in normal pregnant women were 15.7 ~11.5% and 5.7 ~ 4.5% (JDS) respectively, the same as in non-pregnant women. The range of GA in diabetic pregnant women could be kept under control during pregnancy from 20% to 14.5% the same as HbA1c. There were several newborn complications although not serious, hypoglycemia had the highest rate at 22.6%. **Conclusion:** We recommend the use of GA accompanied by HbA1c, random blood glucose and SMBG at home before and during pregnancy in order to maintain the best control.

**PP 03**

The incidence of severe hypoglycaemia in pregnant women with Type 1 Diabetes can be reduced with unchanged HBA1C levels and pregnancy outcomes in a routine care setting

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**Background and aims:** Severe hypoglycaemia is the main limiting factor for further optimization of glycaemic control in pregnant women with type 1 diabetes and occurs in up to 45% of all women, with an incidence in first trimester 5-fold higher than in the year preceding pregnancy. We investigated whether the incidence of severe hypoglycaemia in pregnant women with type 1 diabetes can be reduced without deteriorating HbA1c levels or pregnancy outcomes in a routine care setting.

**Materials and methods:** Two cohorts of pregnant women with type 1 diabetes were compared. The first cohort (2004-2006) consisted of 108 women and the second cohort (2009-2011) consisted of 104 women. In between the cohorts a focused intervention including education of caregivers and patients in the prevention of severe hypoglycaemia in pregnancy was implemented. Women entered the study at median 8 (range 5-13) weeks. Severe hypoglycaemia (requiring assistance from others) was prospectively reported in structured interviews. **Results:** In the first vs. second cohort, severe hypoglycaemia during pregnancy occurred in 45% (n=49) vs. 23% (n=24), p=0.0006. The incidence of severe hypoglycaemia during pregnancy was reduced by 36%, from 2.5 events/patient-year in the first cohort to 1.6 events/patient-year in the second cohort, p=0.04. Two or more events with severe hypoglycaemia during pregnancy occurred in 31% (n=33) vs. 11% (n=11), respectively (p=0.0002). HbA1c at inclusion was comparable between the cohorts (6.6% (4.9-10.5) vs. 6.7% (5.4-10.0); 49 mmol/mol (30-91) vs. 50 (36-86), p=0.48). Insulin dose at inclusion in women on multiple daily injections was lower in the second cohort (0.77 IU/kg (0.4-1.7) vs. 0.65 (0.2-1.4), p=0.0006), but similar in women on insulin pumps (0.59 IU/kg (0.3-0.9) vs. 0.51 IU/kg (0.3-1.1), p=0.49). A higher proportion of women in the second cohort was on insulin analogues (rapid-acting 44% vs. 97%, p<0.0001; long-acting 6% vs. 76%, p<0.0001) and insulin pumps (5% vs. 23%, p<0.0001). Prevalence of large for gestational age infants (>90th percentile) (47% vs. 40%, p=0.48) and other pregnancy outcomes were similar in the two cohorts. **Conclusions:** Using a multifactorial approach in a routine care setting, a clinically significant 36% reduction of the incidence of severe hypoglycaemia in pregnant women with type 1 diabetes was observed. The number of
women experiencing two or more severe hypoglycaemic events was reduced, from a third of all women in
the first cohort to one tenth in the second cohort. Importantly this reduction in the incidence and severity
of severe hypoglycaemia occurred with unchanged HbA1c levels and pregnancy outcomes. Improved
insulin therapy with lower insulin dose and increased use of insulin analogues and insulin pumps may
contribute.

PP 04
A Deadly Mother Instinct
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Realtime-continuous glucose monitoring (RT-CGM) is the most recent development in glucose
monitoring. The main features of RT-CGM are directly visible glucose values and alarm thresholds which
can be set individually. In non-pregnant patients current evidence indicates clear benefits; a decrease in
hyperglycaemic exposure without an increase in hypoglycaemic events and improvement in patient
satisfaction. Implementation of RT-CGMs in clinical practice generally requires continuous subcutaneous
insulin infusion (CSII) treatment, good compliance and support of an experienced diabetes team. Less
experience is available about the effect on glycaemic profiles in the individual pregnant woman with type
1 diabetes. Since pregnant patients differ from the studied patients in the trials and hypoglycaemia is a
frequent complication in the first trimester, we have to analyse individual data and behaviour very
carefully during treatment. We would like to draw attention to a phenomenon we have seen in our
outpatient clinic of pregnant diabetic women which we illustrate with an example of a diabetic type 1
patient during her first trimester. She is a 35-year-old well-educated woman with type 1 diabetes for 31
years, not complicated by micro- or macrovascular complications.. Preconceptional HbA1c levels were
in the target range (HbA1c 34 mmol/mol) and she used RT-CGMs from the moment of positive testing in
this third pregnancy. However, during the first 12 weeks she experienced very frequently severe
hypoglycaemic events, several times requiring ambulance assistance because of unconsciousness and
even an epileptic episode. The use of RT-CGM clearly could not protect her from these dangerous events
but moreover, possibly even contributed to them. Namely by questioning and retrospective analysing her
glucose profiles and insulin bolus behaviour, it became clear that she so much focused on her glucose
values that she impatiently administered insulin for each elevated glucose value she saw on the monitor,
not taking insulin accumulation into account. This lead to very severe hypoglycaemic episodes. In our
opinion this is an example of a mother who shows extremely compliant behaviour in avoiding every
(small) hyperglycaemic value to protect her unborn child, thereby accepting the risk for (severe)
hypoglycaemic events. This fetus-protecting mother instinct, with care for herself coming second after
that for her child, can be very dangerous and potentially lethal.
The beneficial features of RT-CGM in this type of patients actually can become a trigger for events they
are meant to prevent. This important phenomenon of RT-CGM use in pregnancy underscores the
necessity of intensive support during the use of this device. Since this instinctive behaviour may be very
difficult to change, the diabetic team has to warn every pregnant patient for this phenomenon again and
again so the mother can try to act against her deadly mother instinct.
PP 05
Type 1 Diabetes and pregnancy: Continuous subcutaneous insulin infusion versus multiple daily injection therapy
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Background and aims: Intensive insulin therapy through multiple daily doses of insulin (MDI) or subcutaneous insulin infusion (CSII) contributes to obtain good metabolic control and thus decrease the risk of maternal and fetal complications during pregnancy in DM1. This study aims to evaluate and compare the CSII and MDI therapy during pregnancy. Material and methods: Retrospective analysis of data of pregnancies in women with type 1 diabetes followed in Endocrinology-Obstetrics Department since 2005 treated with CSII and MDI. We evaluated metabolic control (A1C), maternal and fetal outcomes. Statistical analysis program SPSS 18.0 was used. Results: We followed 18 pregnant women (19 pregnancies) treated with CSII and 65 with MDI, mean age 30.4±4.3years and 29.3±4.6years, respectively. Mean duration of diabetes 17±6.7years, with CSII, and 11.7±6years with MDI (p=.006). The pre-conception counseling was higher in the group with CSII (84.2% versus 51.6%, p=.02). No differences were observed in diabetic chronic complications (nephropathy and retinopathy). Prepregnancy A1C was similar in both groups (8%±1.5 in pump group and 7.9%±1.5 in MDI). The metabolic control was similar in the 2 groups, except for the 2nd trimester, when a significant improvement in the pump group was observed (7.1%±0.8 versus 7.3%±1.2, 6.2%±0.5 versus 6.7%±1, 6.7%±0.7 versus 6.6%±1). The pregnancy-induced hypertension was higher in pregnant women with pump (27.8% versus 5.3%, p=.007), the occurrence of preeclampsia was similar. Preterm delivery occurred in 52.6% of pregnant women with CSII versus 27.9% with MDI (p=.045). The percentage of caesarean sections was high in both groups and related to the longer duration of diabetes (p=.01); CSII 73.7% versus 60.7% (p=ns). Birth weight did not differ between groups (3563g±675 versus 3514g±513). Birth weight >4000g occurred in 26.3% in the pump group versus 13.1% (p=ns). These differences remained regardless of the duration of diabetes. The morbidity and neonatal malformations were similar in both groups. Conclusions: These data show that the metabolic control and fetal prognosis did not differ significantly with these two modalities of intensive insulin therapy. Both were effective in improving maternal glycemic control. However pregnancy-induced hypertension and preterm delivery were higher in women with CSII. The use of infusion pump in pregnancy should be decided on an individual basis taking into account not only the glycemic balance as well as other factors that may determine the maternal-fetal prognosis.

PP 06
Severe hypoglycaemia in pregnant women with Type 2 Diabetes
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Background and aims: With increasing prevalence of type 2 diabetes in women of fertile age, pregnancy in this patient group is becoming more frequent. Strict glycaemic control during pregnancy is important to reduce the risk of maternal and fetal complications, but the risk of severe hypoglycaemia (requiring
assistance from others) has not previously been quantified. Therefore, we investigated the occurrence of severe hypoglycaemia in pregnant women with insulin-treated type 2 diabetes and near-normoglycaemic control. **Methods:** Twenty-seven consecutive pregnant women with pregestational type 2 diabetes for median 4 (range 1-11) years and pregestational BMI of 31.2 (21-53) kg/m^2^ treated with insulin from early pregnancy were included. At 9, 13, 21, 27 and 33 weeks the women were asked into the occurrence of severe hypoglycaemia in structured interviews, and Hb1Ac, insulin doses and 8-point self-monitored plasma glucose (SMPG) profiles for 6 days were registered. Pregnancy outcomes were recorded. **Results:** At inclusion at 9 (5-13) weeks, HbA1c was 6.5% (5.3-9.0) (IFCC 48 (34-75) mmol/mol). Twelve (44%) women were on insulin therapy before pregnancy and 15 (56%) women had insulin therapy initiated before 13 weeks. The women were treated with either basal bolus therapy (n=15) or insulin aspart mix (n=12). Five (19%) women experienced in total 15 (range 1-7) episodes of severe hypoglycaemia between 8 and 36 weeks. Severe hypoglycaemia in the year prior to pregnancy occurred in one (3%) woman who also experienced severe hypoglycaemia in pregnancy. Structured interviews during pregnancy were obtained after 13 (87%) events with SMPG of 2.3 (1.9-3.8) mmol/l. Six (40%) events occurred during sleep. Unconsciousness or convulsions did not occur and all events were treated with oral carbohydrate solely. The recovery time was 30 (5-120) minutes. Women with severe hypoglycaemia had lower median 8-point SMPG profiles at 33 weeks (5.1 (4.6-5.4) vs. 6.1 (5.1-7.3) mmol/l, p=0.008) compared to women without severe hypoglycaemia. Median SMPG in early pregnancy (5.8 (5.4-6.5) vs. 6.5 (5.0-10.7) mmol/l, p=0.08) and HbA1c in late pregnancy (5.6 (5.1-7.0) vs. 5.9 (5.3-6.8) %, p=0.13) (IFCC 38 (32-53) vs. 41 (34-51) mmol/mol) also tended to be lower in women with severe hypoglycaemia, but the differences did not reach statistical significance. Insulin dosages were similar between the groups throughout pregnancy. The prevalence of large for gestational age infants (40 vs. 27%, p=0.62) and other perinatal outcomes were comparable between women with and without severe hypoglycaemia. **Conclusions:** Strict glycaemic control in insulin-treated pregnant women with type 2 diabetes is associated with a clinically relevant risk of severe hypoglycaemia.

**PP 07**

**Diabetic retinopathy of twin pregnancy in Japanese patients**

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**Background and aim:** Pregnancy may worsen retinopathy in diabetic patients. Twin pregnancy could be potentially associated with the progression of diabetic retinopathy due to a higher circulating blood volume and larger placental mass than observed in a single pregnancy. Thus, we aimed to investigate diabetic retinopathy and its association with clinical factors in Japanese patients with twin pregnancy. **Subjects and methods:** Ten diabetic women with the following demographic characteristics had a twin pregnancy between 1977 and 2010: age, (mean [SD]) 29.5 (3.3) years; duration of diabetes, 11.6 (8.9) years; height, 153 (6.3) cm; pre-pregnancy body mass index (BMI), 22.2 (3.5) kg/m². Seven women had type 1 and 3 women had type 2 diabetes. They were evaluated by ophthalmologists and classified as having no, simple, preproliferative, or proliferative retinopathy. The incidence rate of deterioration in retinopathy was compared with 20 control patients with single pregnancy matched for diabetes type, age and retinopathy in early pregnancy (age, 29.9 (3.6) years; pre-pregnancy BMI, 22.2 (2.9) kg/m²). The
clinical risk for diabetic retinopathy was also assessed. **Results:** In the early pregnancy, 5 patients had simple retinopathy, 1 patient had proliferative retinopathy and the others had no retinopathy. In 4 patients, retinopathy deteriorated during pregnancy: from no retinopathy to simple retinopathy in 1 patient, from simple to preproliferative in 1 patient, and from simple to proliferative in 2 patients. Three women were treated with photocoagulation during pregnancy and after delivery. There was no significant difference in the rate of deterioration in retinopathy as compared with control patients with single pregnancy (40% vs. 20%). In twin pregnancy, the pre-pregnancy BMI in patients with deterioration in retinopathy was higher than that in patients without deterioration (25.6 [3.0] vs. 20.0 [1.5] kg/m$^2$, p < 0.05). The rates of rapid tightening of glycemic control and unplanned pregnancy were higher in patients with deterioration than in those without deterioration (75% vs. 0%, p < 0.05, 100% vs. 50% p = 0.076, respectively). While, in single pregnancy, there were no significant differences in clinical factors between patients with and without deterioration. **Conclusion:** This study did not show that twin pregnancy is a risk factor for the progression of retinopathy during pregnancy. Pre-pregnancy BMI and rapid improvement of glycemic control were associated with deterioration in retinopathy. Further studies involving a large number of patients are needed to clarify the association between twin pregnancy and deterioration in retinopathy.

**PP 08**
**CHO/I in pregnancy**
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**Aim:** trends of measured CHO/I (gold standard) and comparison of with the ones calculated by standardized coefficients, throughout pregnancy.  **Materials and methods:** multicenter, retrospective, observational study (2006-2012). 101 Caucasian pregnant women age 31.6±5.4 years, affected by T1DM, all under CSII, diabetes duration 15.3±8.67yrs, pregestational HbA1C 7.3%±0.9, pregestational BMI 24.34 kg/m$^2$ (18.7-40.5), delivery week 36.8±1.7 and birth weight 3.56±0.68 kg.

CHO/I ratio was measured dividing CHO grams of each meal by insulin unit injected (registered in patients’ diary) to get and maintain the following glycemic targets: Fasting ≤90; 1hr postprandial ≤130mg/dl. Simultaneously, CHO/IRI indexes were calculated through ‘500/24hr-insulin need’ ratio, ‘300/24hr-insulin need ratio’, and of ‘weight x 6.17/correction factor’ being CF= 1800/24hr-insulin need. Education and management before and during pregnancy were in agreement with ADI-AMD-SID recommendations. Data were processed by ‘Stat View’ and presented as mean±SD or as median +range according to their distribution. **Results:** CHO/I ratio measured decreased from 10 to 4.6 at breakfast, from 11.6 to 8.45 at lunch, from 12.5 to 6.13 at dinner. The difference between calculated (C) values and measured (M) were significant as follows: using **500 rule**, C vs M at breakfast always significant a part from very early and late pregnancy, at lunch significant from 9° to 28° week; at dinner from 17° to 28° week. Using **300 Rule** C vs M ratio: at breakfast significant until 16° week, at lunch as well as at dinner during all pregnancy. Using **Weight rule**, C vs M, at breakfast significant in the second and third trimester from the 15° week except 33°, 34°, 35°, 36° weeks; at lunch never significant; at dinner
significant by 9° to 12° week. **Conclusion:** Using standard coefficient taken from the literature out of pregnancy, at the first trimester the weight rule seems to be more appropriate for breakfast and lunch whilst ‘the 500 rule’ is for dinner; At the second and third trimester, the ‘300 rule’ is more appropriate for breakfast, while the ‘weight rule for lunch and dinner. Finally, at the third trimester the ‘500 rule’ can be also applied at lunch and dinner. In synthesis, the always effective criterion is the one calculated by the ‘weight rule’.

**PP 09**

**To Pump or Not to Pump in Type 1 Diabetes Pregnancy: Cambridge Experiences during 2006-2012**

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**Background:** We previously described better glycaemic control but more emergency CS, preterm deliveries and neonatal care admissions in offspring of women (n=38) using CSII compared to MDI during 2006-09. The aim of this study was to compare maternal fetal outcomes of CSII and MDI pregnancies during 2010-12. **Demographics:** Of 70 consecutive pregnancies, 37(53%) were managed using CSII, of whom 10 started post-conception (27%), and 33 (47%) were managed on MDI. Microvascular complications (nephropathy/retinopathy) were present in 8.1% vs. 15.2% and 59.5% vs. 67.3% of CSII vs. MDI users respectively. Diabetes duration and booking BMI were comparable but with more pre-pregnancy care among CSII users (49% vs. 18%; p=0.019). **Results:** CSII users had better glycaemic control during the second and third trimesters (table 1). Despite this improvement, the rates of obstetric and neonatal complications were comparable between CSII and MDI users.

Table 1: Figures represent n (%). Statistical analysis performed using analysis of variance and Fishers exact test.

<table>
<thead>
<tr>
<th></th>
<th>CSII (n=37)</th>
<th>MDI (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Diabetes (yrs)</td>
<td>17 ± 8</td>
<td>16 ± 8</td>
<td>0.70</td>
</tr>
<tr>
<td>BMI kg/m2</td>
<td>25 ± 3.3</td>
<td>25.8 ± 3.7</td>
<td>0.40</td>
</tr>
<tr>
<td>HbA1c prepregnancy mmol/l (%)</td>
<td>61 ± 16 (7.8 ± 1.5)</td>
<td>70 ± 2 (8.6 ± 2.1)</td>
<td>0.12</td>
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<tr>
<td>HbA1c booking mmol/l (%)</td>
<td>57± 16 (7.4 ± 1.5)</td>
<td>65 ± 21 (8.1 ± 1.9)</td>
<td>0.12</td>
</tr>
<tr>
<td>HbA1c trimester 2 mmol/l (%)</td>
<td>46 ±10 (6.3 ± 0.9)</td>
<td>53 ± 15 (7.1 ± 1.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>HbA1c trimester 3 mmol/l (%)</td>
<td>47 ±10 (6.5 ± 0.9)</td>
<td>53 ± 12 (7.0 ± 1.1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Gestation at Delivery (wks)</td>
<td>36.9 ± 2.1</td>
<td>36.5 ± 2.5</td>
<td>0.42</td>
</tr>
<tr>
<td>Preterm (&lt;37 wks)</td>
<td>11 (30)</td>
<td>11 (23)</td>
<td>0.80</td>
</tr>
<tr>
<td>Preterm (&lt; 34 wks)</td>
<td>3 (8)</td>
<td>3 (9)</td>
<td>1.0</td>
</tr>
<tr>
<td>Wt at Delivery (g)</td>
<td>3407 ± 727</td>
<td>3291 ± 741</td>
<td>0.52</td>
</tr>
<tr>
<td>Customised Birth Weight Centile</td>
<td>77.8 ± 24.2</td>
<td>72 ± 27.6</td>
<td>0.40</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>16 (43)</td>
<td>10 (30)</td>
<td>0.65</td>
</tr>
<tr>
<td>SGA</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>0.47</td>
</tr>
<tr>
<td>Inductions of labour</td>
<td>10 (27)</td>
<td>12 (36)</td>
<td>0.70</td>
</tr>
<tr>
<td>Elective C-Sectons</td>
<td>11 (30)</td>
<td>9 (27)</td>
<td>0.68</td>
</tr>
<tr>
<td>Emergency C-Sectons</td>
<td>11 (23)</td>
<td>13 (39)</td>
<td>0.35</td>
</tr>
<tr>
<td>Neonatal care admission</td>
<td>16 (34)</td>
<td>11 (33)</td>
<td>0.46</td>
</tr>
</tbody>
</table>
Conclusions: Maternal glucose control was improved, both in the current and previous cohorts, but without documented benefits on maternal/fetal outcomes. Pre-pregnancy care remains poor among MDI users. CSII and MDI alone are inadequate for optimal glucose control and pregnancy outcomes. CGM and/or closed-loop may be needed.