

RCTs on pregnant DM patients

Study name registration number Design	Setting Place, setting and time	Population Inclusion / Exclusion criteria Characteristics	Intervention vs. Control Description with duration	Outcomes Primary and secondary	Results Longest follow-up period with intervention effects (IG vs. CG) with SD, 95%- CI or p value	Study name registration number Design
Strategies to increase physical activity						
Embaby 2016 RCT	Egypt, urban, 07/2014- 02/2015	at increased risk for GDM due to obesity (BMI \geq 30 kg/m ²), age: $>$ 25 yrs, 20-24th gestational wks, multigravida, physically active with \geq 1 of the following 3 characteristics: history of macrosomia, abnormal glucose tolerance during previous pregnancy or first grade relative with DM2 no hypertension, GDM, medications that affects insulin secretion, serious pulmonary disease, cardiac, renal impairment and malignancy	n=40 100% female age (yrs): 29.2 \pm 3.8 BMI (kg/m ²):28.7 \pm 1.3 fasting glucose (mmol/l): 6.5 \pm 0.9 fasting insulin (IU/l): 15.78 \pm 1.58	<u>IG:</u> aerobic exercise program (walking on treadmill) three times weekly until the end of 37 wks of gestation + diet control. vs. <u>CG:</u> diet control with usual care given by obstetricians and midwives. <u>Duration:</u> appr. 4 months	Fasting plasma glucose, Insulin level	Change to 37 th week of gestation: <u>FPG (mmol/l)</u> Benefit for IG: 4.26 \pm 0.67 vs. 5.07 \pm 0.54 (p=0.0001) <u>Fasting insulin (IU/l):</u> Benefit for IG: 10.59 \pm 1.10 vs. 12.43 \pm 1.44 (p=0.0001)
Other non-pharmacological therapies						
El-Shamy 2018 RCT	Egypt, urban 12/2016- 05/2017	GDM, age: 20-30 yrs, gestational age: 24-26 wks, BMI \leq 30 kg/m ² , singleton live fetus no high-risk pregnancy, bad obstetric situations or diseases, smoking, oral sedatives	n=30 100% female age (yrs): 24.2 \pm 2.8 75 g OGTT (mg/dl): • fasting glucose: 129.05 \pm 0.6 • 2h postprandial: 146 \pm 1.65 BMI (kg/m ²): 27 \pm 1.5	<u>IG (n=15):</u> acupressure + standard antenatal care vs. <u>CG (n=15):</u> standard antenatal care only <u>Duration:</u> 12 weeks	Primary: glycemic control, requirement for insulin, insulin resistance Secondary: neonatal outcomes	Change over 3 months: 75 g OGTT (mg/dl): Fasting: 116.1 \pm 0.1 vs. 118.2 \pm 0.7 2h postprandial: 125.3 \pm 1.2 vs. 127.3 \pm 0.9 Complication (%): 5-min Apgar-Score < 7: 6.7 vs. 6.7 %

Utz 2018 NCT02979756	Marocco, urban / rural, primary care,	Health centres with ≥ 30 monthly antenatal care consultations and all pregnant women with newly diagnosed GDM	20 health centres n= 215 age (yrs):27.6 \pm 6.6 urban (%): 38.5 rural (%): 61.5	20 clinics were randomized \rightarrow 10 in each group <u>IG (n=120):</u> first screening for GDM \rightarrow positive tested women received counselling on nutrition and exercise <u>vs.</u> <u>CG (n=95):</u> routine practice	Primary: birthweight Secondary: maternal weight gain, glucose control, pregnancy complications.	Follow-up visits: 7.5 \pm 4.9 vs. 3.8 \pm 3.3 (p=0.001) FBG within the norm: better with IG <1/3 of all values: 7.6 vs. 32.6 % 1/3-2/3 of all values: 17.8 vs. 32.6 % >2/3 of all values: 74.6 vs. 34.8 % Macrosomia (birthweight>4000 g): 3.5 vs. 18.4 % (p<0.001)
Pharmacological strategies						
Ashoush 2016 RCT	Egypt, urban, tertiary care	GDM, mothers with 26–32- week GDM (oral 2-h 75 G glucose tolerance test) singleton pregnancies, failure of satisfactory glycemic control despite adequate diet and exercise for ≥ 1 wk no fetal anomalies on ultrasonography, other pregnancy complications, known intolerance to metformin or risk factors for lactic acidosis	n=95 100% female age (yrs): 31.8 \pm 3 HbA1c (%): 5.75 \pm 0.55 75g OGTT (mg/dl) • fasting: 106.05 \pm 4.6 • 1h:310.25 \pm 11.6 • 2h:176.65 \pm 9.4 BMI (kg/m ²): 31.2 \pm 1.4	<u>IG (n = 47):</u> metformin (initial total dose 1000 mg/d with meals, increase by 500 or 850 mg every 1 or 2 wks toward target or up to a maximum dose of 2500 mg/d until delivery, addition of insulin if needed) <u>vs.</u> <u>CG (n = 48):</u> <u>regular insulin + neutral</u> <u>protamine Hagedorn (3:7)</u> <u>(starting dose 0.7 units</u> <u>/kg*d, adjusted to</u> <u>achieve adequate</u> <u>glycemic control at</u> <u>increments of 1</u> <u>unit/10 mg glucose</u> <u>higher than the desired</u> <u>cut-off, short action</u> <u>insulin whenever needed)</u> <u>Duration: until delivery</u>	Primary: successful maternal glycemic control Secondary: maternal BMI, glycemic control parameters, maternal weight gained during pregnancy, side effects to metformin, mode of delivery, gestational age at delivery, neonatal birthweight, macrosomia, neonatal hypoglycemia, neonatal death, congenital anomalies, admission to neonatal intensive care unit	Until delivery: fasting glucose during treatment (mg/dl): better with IG: • during the last wk: 78 \pm 3.1 vs. 79.9 \pm 3.7 (p=0.008) • during the last 2 wks: 78.9 \pm 3.5 vs. 80.8 \pm 4.7 (p=0.029) maternal hypoglycaemia (%): no difference: 6.25 vs. 12.5 (p=0.254) neonatal hypoglycaemia (%): 12.8 vs. 14.6 (p=0.791) Maternal weight gain (Kg): 4.4 \pm 0.6 vs. 5.1 \pm 0.8 (p=0.001) neonatal congenital anomalies (%): 2.1 vs. 2.1 p= 0.747 headache (%): 27.3 (metformin+insulin) vs. 5.6 (metformin monotherapy) vs. 0% (insulin monotherapy) neonatal ICU admission (%): 8.5 vs. 10.4 (p= 0.514) Costs (Egyptian pounds): 89.66 \pm 0.96 vs. 174.9 \pm 11.1 (for monotherapies)

Beyuo 2015 ACTRN126140 00942651	Ghana, urban	pregnant women with DM2 or GDM (plasma glucose ≥ 7 mmol/l after an overnight fast or plasma glucose concentration ≥ 11.1 mmol/l 2 hours after a 75 g glucose drink), 20-30 wks gestation, age: 18-45yrs, eligible for insulin therapy	n= 104 100% female age (yrs): 33.3 \pm 4.6 fasting glucose (mmol/l): 8 2HPG (mmol/l): 10.5 BMI (kg/m ²): 3.1 \pm 6.6 type of diabetes: GDM (%): 65.9 DM2 (%): 34.0	<u>IG (n=52):</u> Metformin (starting with 500 mg / d, gradually increase over 2 wks to a maximum dose of 2500 mg/d, insulin was added if necessary) vs. <u>CG (n=52):</u> insulin treatment (daily dose 0.3 IU/kg, titrated to achieve the glycemic targets, if necessary, admission to the ward and therapy with soluble insulin) <u>Duration: until delivery</u>	Primary: 2-hour post prandial blood glucose (2HPG) Secondary: fasting glucose, 1HPG, maternal weight gain, pregnancy outcome and fetoneonatal outcomes.	Change from enrolment to delivery: glycemic control (mmol/l): fasting glucose: no difference: 6.42 \pm 0.98 vs. 6.62 \pm 1.57 (p=0.928) 1HPG: no difference: 8.95 \pm 1.27 vs. 9.62 \pm 1.44 (p=0.078) 2HPG: benefit for IG: 7.84 \pm 1.43 vs. 9.05 \pm 1.89 (p=0.004)
Ibrahim 2014 NCT01915550	Egypt, urban	GDM or pre-existing DM, gestational age 20-34 wks with insulin resistance No DM1, secondary diabetes or liver or renal impairment	n=90 100% female age (yrs): 29.8 \pm 5.4 BMI (kg/m ²):31.83 \pm 3.23 Gestational age: 28.7 \pm 3.7 wks GDM: 43.3 % Pre-existing DM: 56.7 % with median duration of 4 (1-15) yrs	<u>IG (n=46):</u> Metformin (1500 mg, raised to 2000 mg) without increasing insulin dose Patients switched to CG if treatment was not successful to control blood glucose concentrations <u>CG (n=44):</u> insulin dose was increased according to the standard protocol	Primary: maternal glycemic control (fasting glucose ≤ 95 mg/dl and 2-HPG ≤ 120 mg/dl) Secondary: maternal bouts of hypoglycemia, need for another hospital admission for uncontrolled diabetes during pregnancy, gestational age at delivery, mode of delivery, birth weight, birth trauma, congenital anomalies, Apgar score, neonatal hypoglycemia, need for neonatal intensive care unit admission, adverse neonatal outcomes	glycemic control: <ul style="list-style-type: none"> • better for CG: 76.1 vs. 100 % reached glycemic control (p=0.001) • 13 vs. 18.2 % had readmission for poor glycemic control • 6.5 vs. 22.7 % had bouts of maternal hypoglycaemia Complications: <ul style="list-style-type: none"> • 23.3 vs. 30.8 % had fetal macrosomia • 1 new-born in each group had congenital malformations • 7 vs. 38.5 % had neonatal hypoglycaemia • 18.6 vs. 41 % had NICU admission • 0 vs. 5.1 % had stillbirths • 11.6 vs. 25.6 % with respiratory distress syndrome

BMI: Body mass index; CG: Control group; CI: Confidence interval; DM: diabetes mellitus; DM2: type 2 diabetes; FPG: fasting plasma glucose; GDM: gestational diabetes; HbA1c: haemoglobin A1c; 1 / 2HPG: 1 / 2-hour post prandial blood glucose; IG: intervention group; n: number of participants; MD: mean difference; MDa: adjusted mean difference; OGTT: Oral glucose tolerance test; RCT: randomized controlled trial; RR: Relative risk; RRa: adjusted relative risk; SD: Standard-deviation; wks: weeks; yrs: years

Supplementary Table 4: Characteristics and results of studies on pregnant women with DM