J Endocrinol Invest (2017) 40:937–943
DOI 10.1007/s40618-017-0646-6

ORIGINAL ARTICLE

Analysis of the main risk factors for gestational diabetes diagnosed with International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria in multiple pregnancies

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Received: 24 January 2017 / Accepted: 17 February 2017 / Published online: 21 March 2017

Abstract
Introduction The aim is to investigate the proportion of multiple pregnancies with gestational diabetes mellitus (GDM) diagnosed using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria and to identify the impact of age, body mass index (BMI), and mode of conception on incidence of GDM.
Materials and methods This is a single center, retrospective cohort study on 656 multiple pregnancies screened for GDM with 75-g, 2-h oral glucose tolerance test at 24–28 weeks of gestation, between January 2010 and January 2016. The diagnosis of gestational diabetes mellitus (GDM) was reached through the IADPSG.
Results The incidence of GDM in our population was 15.1%. When patients who conceived through heterologous assisted reproduction technology were compared with those who conceived spontaneously, there was a significant difference for GDM (31.1 vs 13.6%, $p<0.001$, OR 2.86). A similar finding was also observed comparing egg donation IVF/ICSI patients with homologous IVF/ICSI patients (31.1 vs 14.8%, $p=0.006$, OR 2.59). Incidence of GDM was significantly higher in obese than in non-obese patients (42.5 vs 14.8%, $p<0.001$, OR 4.88) and in women over 35 compared to younger patients (18.4 vs 11.1%, $p=0.01$, OR 1.81). Logistic regression comparing the diabetes onset with conception mode gave a $p=0.07$. The calculation of the Chi-square and odds ratio for single mode of conception showed that homologous vs conceived spontaneously $p=0.90$, OR 0.97, heterologous vs homologous $p=0.01$ with OR 2.46, and heterologous vs conceived spontaneously $p=0.01$ with OR 2.39. Logistic regression showed that age and BMI are risk factors for developing GDM, respectively, $p=0.03$ with OR 1.4 and $p<0.01$ and OR 1.09.
Discussion The contribution our study can make is improved counseling about GDM risks for couples with multiple pregnancies. Our data support the role of age, BMI, and mode of conception as risk factors for GDM in multiple pregnancies.

Keywords Gestational diabetes mellitus · Multiple pregnancies · IADPSG criteria · Assisted reproduction technology

Introduction

Women with multiple pregnancies have an increased risk of maternal and neonatal complications including preterm birth, hypertensive complications, as well as fetal growth restriction [1, 2] but it is unclear whether gestational diabetes mellitus (GDM) is more common in twin or singleton pregnancies. Available data are conflicting and twin gestations have been found to be associated with GDM in some studies [3, 4] but not in others [5, 6].

The number of fetuses in multifetal pregnancies influences the incidence of GDM: it has been suggested that each additional fetus is associated with a 1.8-fold increased risk [7]. That finding supports the hypothesis that an

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increase in placental mass and, thus, an increase in diabetogenic hormones (human placental lactogen hormone, estrogens, progesterone and cortisol) play a role in the etiology of glucose intolerance. In fact, the main placental weight at term is double in twin pregnancies compared to that in singleton pregnancies, but the chorionicity does not seem to affect the change to develop abnormalities of glucose metabolism [8].

Others factors, regardless of the number of fetuses, can affect the risk of GDM, such as advanced maternal age, high pre-pregnancy BMI, smoking during pregnancy, parity, pre-existing hypertension, family history of diabetes, and assisted reproduction technology (ART) treatment [9–12].

Major risk factors like advanced maternal age, obesity, and polycystic ovary syndrome are conditions that often coexist in a significant proportion of women requesting in vitro procedures. Recent studies have shown that singleton and twin pregnancies conceived with ART have been associated with an increased risk of GDM [13] and this risk is two-fold higher in women with singleton pregnancies conceived following ART compared to women who conceived spontaneously [14].

Moreover, a study by Wang et al. found that multiple pregnancies resulting from ART can only partially explain the relationship between ART treatment and GDM; the odds of GDM was higher for mothers who have both twin and singleton pregnancies from ART procedures, than for non-ART mothers [15]. Therefore, other conditions may have a role in the increased likelihood of GDM in these patients, such as etiology of infertility, types of drugs used for ovulation induction and luteal phase support, changes in the hormonal environment due to increased hormone levels after ovulation induction and during early pregnancy, and the presence of underlying metabolic and vascular factors exacerbated during ovulation induction and IVF/ICSI procedures.

The aim of our study was to investigate the proportion of multiple pregnancies women with a diagnosis of GDM using the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, and therefore to identify the impact of age, body mass index, and mode of conception on incidence of GDM in this population.

Materials and methods

We performed a single center retrospective cohort study on all multiple pregnancies delivered at the Careggi Hospital in Florence, the Regional Reference Center for high-risk pregnancy, between January 2010 and January 2016. Eligibility criteria for the current study included multiple pregnancies screened for gestational diabetes with 75-g, 2-h oral glucose tolerance test (OGTT) at 24–28 weeks for patients who received prenatal care at our hospital from the first trimester to delivery.

The diagnosis of gestational diabetes mellitus (GDM) was reached through the International Association of Diabetes and Pregnancy Study Groups criteria (IADPSG) when one glucose value was greater than or equal to the established cut-off: fasting plasma glucose ≥5.1 mmol/L (92 mg/dL), 1-h ≥ 10 mmol/L (180 mg/dL), and 2-h ≥ 8.5 mmol/L (153 mg/dL) [16].

Exclusion criteria were

- maternal pre-gestational diabetes and hypertension or other chronic diseases (i.e., cardiovascular, autoimmune diseases, inherited and acquired thrombophilia)
- absence of the 75 g OGTT screening during pregnancy
- major fetal congenital anomalies
- twin-to-twin transfusion syndrome
- miscarriage or intrauterine fetal death before the OGTT

The study was exempt from Institutional Review Board approval because obstetric and neonatal outcomes were collected as part of clinical management. Patients signed an informed consent for the clinical investigations and the use of the results for scientific analysis according to privacy laws and human rights.

Information about pregnancy outcomes were obtained from the hospital's electronic medical records, according to criteria set forth on the standardized data collection form.

We collected data on maternal age, ethnicity, other demographic characteristics, reproductive history, pre-pregnancy diseases, delivery information, and neonatal outcomes.

We divided our study population into four categories of body mass index (BMI) as defined by the World Health Organization: underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), and obese (BMI ≥30 kg/m^2) patients [17].

BMI was calculated as weight in kilograms divided by height squared in meters. Because a considerable number of women did not have data on pre-pregnancy weight, we used BMI at the first prenatal visit (6–13 weeks gestation) as the pre-pregnancy BMI. We also collected data on mode of achieving the multiple pregnancy: naturally, ART with homologous oocyte or, heterologous ART with egg donation.

The newborns were evaluated on the basis of birthweight using the online calculator for multiple pregnancies available at http://medicinafetalbarcelona.org/calc/.

Birthweight was considered appropriate for gestational age (AGA) between the 10th and 90th percentile; the fetuses were otherwise categorized as small for gestational age, SGA (birthweight below 10th percentile) or

as large for gestational age, LGA (birthweight above 90th percentile).

Statistical methods

From the database percentages have been extrapolated. Shapiro Wilk test assessed the no normal distribution of the considered variables. The relationship between the variables with outcomes has been assessed using the Mann Whitney test for dichotomous variables, Kruskal–Wallis test for variables with more than two categories. χ^2 test and odds ratio were performed in order to identify any significant difference between the compared groups [18]. Logistic regression was used to evaluate the effect of the variables on the possible of gestational diabetes. The data were organized and statistical analyses were performed using SPSS for Windows 16.0 package (SPSS Inc., ©Copyright IBM Corporation 2010 IBM Corporation, Route 100 Somers, NY 10589). The level of significance was set at $p < 0.05$.

Table 1 Patient characteristics

Patient characteristics	Number	Percentage (%)
Ethnicity		
Caucasian	571	87.0
African	33	5.0
South-American	26	4.0
Asian	26	4.0
Age (years)		
<35	236	36.0
≥35 and <40	235	35.8
≥40	185	28.2
BMI (kg/m^2)		
<18.5	26	4.0
≥18.5 and <25	380	57.9
≥25 and <30	131	20.0
≥30	119	18.1
Previous pregnancies		
Nulliparity	481	76.7
Multiparity	146	23.3

Results

From 2010 to January 2016 at Careggi Hospital, 17,224 live births from 16,537 pregnancies were delivered; multiple pregnancies accounted for 3.97% of all deliveries. We obtained data on 656 multiple pregnancies that matched our inclusion criteria during the study period with 95.6% (n. 627) of twin pregnancies, 27 triplets, and 2 quadruplets.

Prevalent ethnicity of our sample was Caucasian (87.04%) and most of them were nulliparous (76.7% before the twin pregnancy). Patient characteristics are summarized in Table 1. There was a balanced distribution of patients in the three age groups with only 28.2% over 40 years old. Regarding BMI, more than half of the patients were normal weight (57.93%); 20% were overweight; 18.1% were obese; and only a minority (4.0%) was underweight.

All patients were screened for GDM with 75 g OGTT between 24 and 28 weeks of pregnancies. The incidence of GDM in multiple pregnancies referred to our hospital was 15.1% (n. 99). In particular, 15.0% of twin and 18.5% of triplet pregnancies were affected by GDM while no GDM was diagnosed in the two quadruplet pregnancies. The outcome of twin and triplet pregnancies affected by GDM is described in Table 2.

In 68.7% of cases (n. 68), an adequate diet for multiple pregnancy based on pre-pregnancy BMI was the only therapy, while in 31.1% (n. 31) insulin was combined with diet to obtain adequate glycemic control.

91.9% (n. 91) of women with multiple pregnancies underwent a cesarean section; 3.0% (n. 3) had a vaginal delivery with induction of delivery at term and 5.0% (n. 3) went into spontaneous with successful vaginal delivery. As for birthweight, more than half of the fetuses were AGA using customized centiles (71.7%), only 11.1% were SGA and 17.2% LGA, with a 56 average centile at birth.

We also analyzed the incidence of GDM regarding the mode of conception: 47.5% (group A, n.47) of women with multiple pregnancies who conceived spontaneously and 52.5% (n. 52) of pregnancies conceived by ART. The ART group was further subdivided into two groups based on egg donation: a subgroup of homologous IVF/ICSI (group B, n. 34) and a subgroup of heterologous IVF/ICSI (group C, n.18). No significant differences in BMI were found between them; however, the mean age in the two ART groups was higher, if compared with the spontaneous pregnancy group. The incidence of GDM was higher in all patients subjected to ART than in women who conceived spontaneously (18.2% vs 13.6%) although not statistically significant.

Comparing group C with group A, we identified a significant difference in incidence of GDM (31.1 vs 13.6%, $p < 0.001$) with an OR 2.86. A similar finding is also observed if we compare group C and B (31.1 vs 14.8%, $p = 0.006$, OR 2.59).

When we analyzed the incidence of GDM for BMI categories, we found that the incidence of GDM is significantly higher in obese women than in non-obese patients (42.5 vs 14.8%, $p < 0.001$). The obesity increases risk of GDM (OR 4.88) (Fig. 1). Moreover, GDM in multiple pregnancies had an higher incidence in women over 35 years old compared to younger patients (18.4 vs 11.1%, $p = 0.01$, OR 1.81); this difference becomes more significant when we compared

Table 2 Outcome of multiple pregnancies with GDM

	Number	Percentage (%)
Incidence of GDM		
Multiple pregnancies	99	15.1
Twins	94	15.0
Triplets	5	18.5
Quadruplets	0	0
Therapy		
Diet	68	68.7
Diet + Insulin	31	31.1
Delivery		
C-section	91	91.9
Induced vaginal delivery	3	3.0
Spontaneous vaginal delivery	5	5.0
Pregnancy-induced hypertension	7	7.0
Preeclampsia	1	1.0
Birthweight		
Average weight (g)	3290	
Average centile weight	56°	
SGA	11	11.1
AGA	71	71.7
LGA	17	17.2

patients aged ≥40 to women <40 years old (23.1 vs 13.2%, $p=0.009$, OR 1.97) (Fig. 2).

Logistic regression comparing the diabetes onset with conception mode gave a $p=0.07$. The calculation of the Chi-square and odds ratio for single mode of conception showed that homologous vs conceived spontaneously $p=0.90$, OR 0.97, heterologous vs homologous $p=0.01$ with OR 2.46, and heterologous vs conceived spontaneously $p=0.01$ with OR 2.39. Logistic regression showed that age and BMI are risk factors for developing GDM, respectively, $p=0.03$ with OR 1.4 and $p<0.01$ and OR 1.09.

Discussion

The contribution our study can make is improved counseling about GDM risks for couples with multiple pregnancies. Our data support the relationships of age, BMI, and mode of conception with GDM in multiple pregnancies: if a wide range of clinical information can be collected, more accurate assessment can be offered to couples in order to define pregnancy outcome.

Multiple gestation has become increasingly common and is often associated with an increased risk of GDM [19],

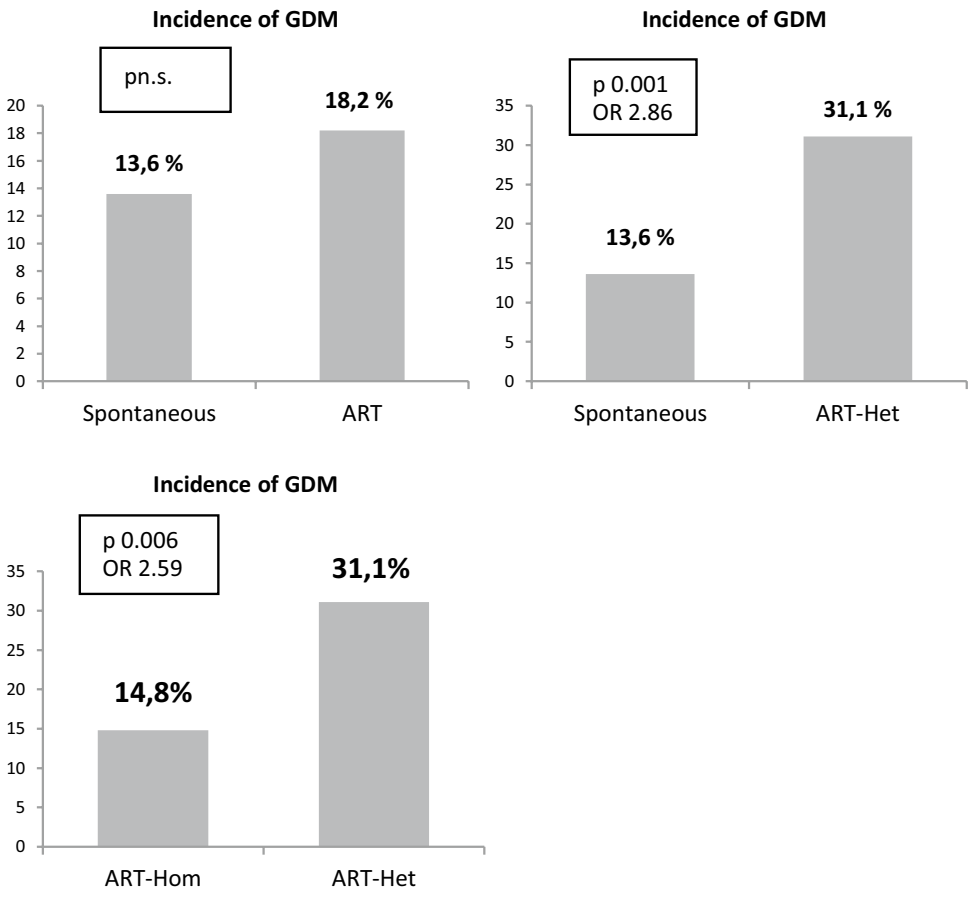

Fig. 1 Differences in incidence of GDM in groups based on mode of conceiving

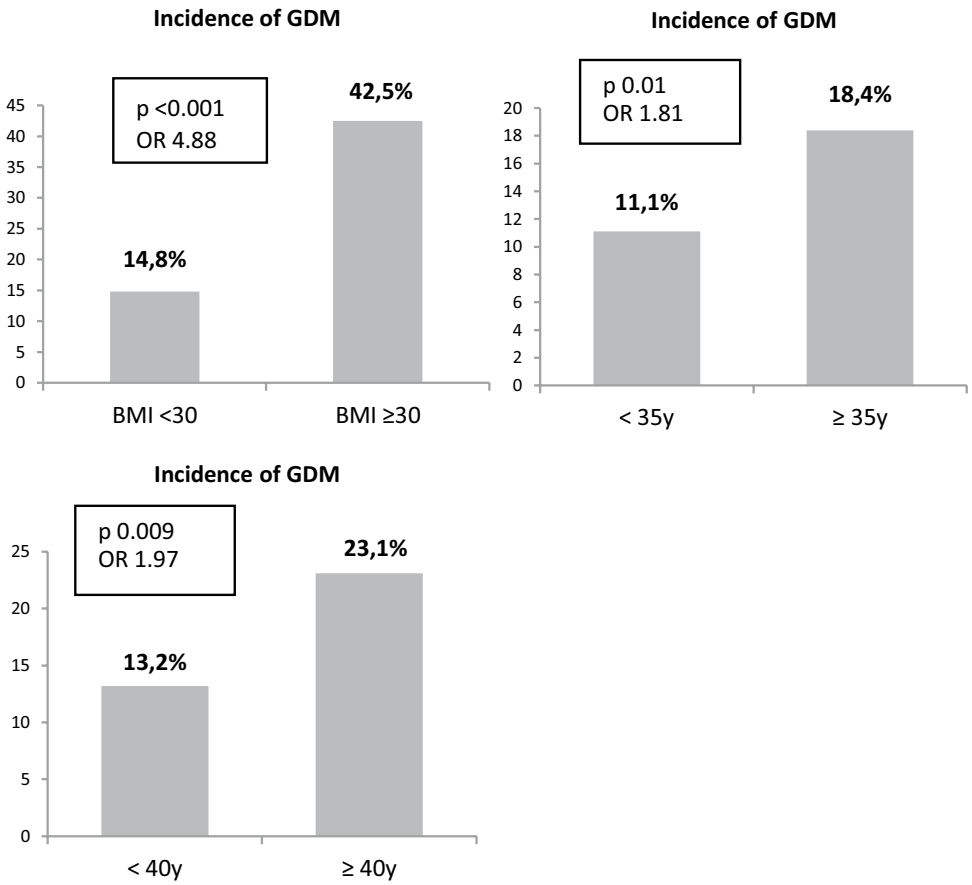

Fig. 2 Differences in incidence of GDM in the groups based on age or BMI

even if literature presents conflicting data [20]. This ambiguous information can be attributed to differences in study design and the definition of positive screening test and GDM diagnosis among different studies. However, multiple pregnancies are characterized by advanced maternal age [21] since they are often related to ART procedures. In fact, in recent years, older women who become pregnant are more often at first pregnancy and of higher socioeconomic status than in the past, when they were more often multiparous and of low socioeconomic status [22, 23]. Since advanced maternal age and increased maternal weight gain are known risk factors for GDM [10, 11], in association with a higher level of hormones that modify insulin sensitivity [24], and since they are all typical of multiple pregnancies, we expect higher incidences of GDM in these pregnancies.

Alptekin et al. recently proposed a model for the early diagnosis of GDM, in the first prenatal visit to the patients who had a history of GMD, a BMI >30 kg/m^2 or with an alteration in glucose metabolism. The authors concluded that screening of diabetes can be performed in the first trimester using anthropometric measurements and the homeostasis model assessment-insulin resistance (HOMA-IR) and weight gained during pregnancy, identifying values above which the risk of GDM was more high [25].

The IADPSG has recently recommended new universal screening and diagnosis criteria based on the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [26]. Overall, using the proposed criteria, 17.8% of the HAPO population would be identified as having GDM.

The prevalence of GDM in twin pregnancies using the IADPSG screening protocol is still unclear. Dinhams et al. in their study showed that the rate of gestational diabetes diagnoses in women with a twin pregnancy increased threefold with a change in screening, and that women with gestational diabetes and their infants had poorer perinatal outcomes than those without gestational diabetes. A better detection of GDM led to a reduction in large for gestational age infants. However, it is still debateable if it is a meaningful clinical outcome in twin pregnancies [27].

Liu et al. [28] found that the incidence of GDM in twin pregnancies using the IADPSG and two-step screening groups was 20.4 and 7.0%, respectively. After adjustment for maternal age, insurance status, pre-pregnancy BMI, education, type of conception, and chorionicity, the OR for GDM was 3.22 (95% CI 2.30–4.52), using the IADPSG screening protocol compared to the two-step screening protocol. ORs for GDM were similar in both spontaneous and assisted conceptions (3.55 and 3.16, respectively) using the new approach. In our study, population incidence of GDM

is 15.1%, lower than Liu et al. report. In our study, we considered an additional datum that could influence the incidence of GDM that was the impact of conception mode.

As reported by other studies, pregnancies obtained through ART tend to have generally poor outcomes [13, 29]; these findings were explained by correlation with etiology of infertility, with types of drugs used for ovulation induction and luteal phase support, with changes in the hormonal environment due to increased hormone levels after ovulation induction and during early pregnancy, and with the presence of underlying metabolic and vascular factors exacerbated during ART procedures [30]. In our study, 47.5% of the multiple pregnancies were conceived spontaneously and 52.5% were conceived through ART. As well as other studies in literature [31], the incidence of GDM in our patients subjected to ART was higher than in women who conceived spontaneously (18.2 vs 13.6%) but this difference was not statistically significant. However, patients who conceived with heterologous ART (group C) had a significantly higher incidence of GDM (31.1 vs 13.6%, $p<0.001$, OR 2.86) compared to group A (patients who conceived spontaneously). A similar finding is also observed if we compare group C with patients who conceived using homologous ART (31.1 vs 14.8%, $p=0.006$, OR 2.59). Our study confirms that (heterologous) ART is a relevant risk factor for GDM. However, it should be considered that group C patients are significantly older, and the effect of age should not be ignored despite no differences in terms of BMI being identified. Indeed, our results confirmed the role of advanced maternal age as a relevant risk factor for GDM in multiple pregnancies: if age is greater than or equal to 35 years, the OR of GDM is 1.81 and it increases to 1.97 if we chose 40 years as cut-off. However, the most relevant risk factor for GDM in our population of multiple pregnancies is a BMI greater than or equal to 30. This information must be taken into account when interpreting the impact of heterologous ART on GDM, which remains relevant because patients did not differ in BMI as previously specified. Logistic regression showed that age and BMI are risk factors for developing GDM, respectively, $p=0.03$ with OR 1.4 and $p<0.01$ and OR 1.09, and confirmed that the patients with egg donation showed more risk of GDM.

The main limitations of our study are its retrospective design and the lack of information on potential confounders such as data regarded the presence of polycystic ovary syndrome, history of diabetes type 2 in the family, and gestational weight gain. Among the different causes of infertility, women with polycystic ovary syndrome (PCOS) have shown higher physiological risk factors for pregnancy-induced peripheral insulin resistance. Holst et al. in our study demonstrated that fertility problems were associated with a modest statistically significant increased risk of GDM among women without PCOS (OR 1.33, 95% CI 1.25–1.42), but the association between fertility problems and risk of GDM was more pronounced among women with PCOS (OR 2.09, 95% CI 1.38–3.15). In these analyses, the association between fertility problems and risk of GDM was significantly modified by maternal age, parity, and PCOS, whereas no significant effect modification was observed for pre-pregnancy BMI, parental history of diabetes, or maternal smoking during pregnancy [32].

The strengths include the use of objective criteria (IADPSG) for GDM screening, which are usually offered in our area to all pregnant women, and the lack of similar reports for the Italian obstetric population.

In conclusion, our data highlighted the relationships of age, BMI, and mode of conception with GDM in multiple pregnancies: a right collection of clinical and personal information is therefore fundamental to better define pregnancy outcomes, and an improved counseling about GDM risks should be implemented and offered to all couples with multiple pregnancies.

Compliance with ethical standards

Conflict of interest All authors declare that they do not have conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Rossi AC, D'Addario V (2011) Neonatal outcomes of assisted and naturally conceived twins: systematic review and meta-analysis. J Perinat Med 39(5):489–493
2. Campbell DM, MacGillivray I (1999) Preeclampsia in twin pregnancies: incidence and outcome. Hypertens Pregnancy 18:197–207
3. Wein P, Warwick MM, Beischer NA (1992) Gestational diabetes in twin pregnancy: prevalence and long term complications. Aust NZ J Obstet Gynaecol 32:325–327
4. Dwyer PL, Oats JN, Walstab JE (1982) Glucose intolerancein twin pregnancy. Aust NZ J Obstet Gynaecol 22:131–135
5. Naicker RS, Subrayen KT, Jialal I (1983) Carbohydrate metabolism in twin pregnancy. S Afr Med J 63:538–544
6. Buhling KJ, Henrich W, Starr E, Lubke M, Bertram S, Siebert G, Dudenhausen JW (2003) Risk for gestational diabetes and hypertension for women with twin pregnancy compared to singleton pregnancy. Arch Gynecol Obstet 269(1):33
7. Schwartz DB, Daoud Y, Zazula P, Goyert G, Bronsteen R, Wright D, Copes J (1999) Gestational diabetes mellitus:

metabolic and blood glucose parameters in singleton vs twin pregnancies. Am J Obstet Gynecol 181(4):912–914
8. Bishop KC, Goetzinger KR, Tuuli MG, Cahill AG (2015) The impact of chorionicity on maternal pregnancy outcomes. Am J Obstet Ginaecol 213(3):390.e1-7
9. Hedderson MM, Ferrara A (2008) High blood pressure before and during early pregnancy is associated with an increased risk of gestational diabete mellitus. Diabetes Care 31:2362–2367
10. .Alshami HA, Kadasne AR, Khalfan M, Iqbal SZ, Mirghani HM (2011) Pregnancy outcome in late maternal age in a high-income developing country. Arch Gynecol Obstet 284(5):1113–1116
11. Baci Y, Üstüner I, Keskin HL, Ersoy R, Avşar F (2013) Effect of maternal obesity and weight gain on gestational diabetes mellitus. Gynecol Endocrinol 29(2):133–136
12. Jones BJ, Zollner J, Haynes S, Cheng F, Dornhorst A (2013) In vitro fertilization treatment influences glucose tolerance in multiple pregnancy. Diabet Med 30:252–254
13. Grady R, Alavi N, Vale R, Khandwala M, McDonald SD (2012) Elective single embryo transfer and perinatal outcomes: a systematic review and meta-analysis. Fertil Steril 97:324–331
14. Ashrafi M, Gosili R, Hosseini R, Arabipoor A, Ahmadi J, Chehrazi M (2014) Risk of gestational diabetes mellitus in patients undergoing assisted reproductive techniques. Eur J Obstet Gynecol Reprod Biol 176:149–152
15. Wang YA, Nikravan R, Smith HC, Sullivan EA (2013) Higher prevalence of gestational diabetes mellitus following assisted reproduction technology treatment. Hum Reprod 28(9):2554–2561
16. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiler JL, Lowe LP, McIntyre HD, Oats JJ, Omori Y, Schmidt MI (2010) International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 33(3):676–682
17. BMI Classification (2006) Global database on body mass index. World Health Organization, Geneva
18. Levorato S, Bocci G, Troiano G, Messina G, Nante N (2017) Health status of homeless persons: a pilot study in the Padua municipal dorm. Ann Ig 29(1):54–62
19. Rauh-Hain JA, Rana S, Tamez H, Wang A, Cohen B, Cohen A, Brown F, Ecker JL, Karumanchi SA, Thadhani R (2009) Risk for developing gestational diabetes in women with twin pregnancies. J Matern Fetal Neonatal Med 22(4):293–299
20. Yogev Y, Eisner M, Hiersch L, Hod M, Wiznitzer A, Melamed N (2014) The performance of the screening test for gestational diabetes in twin versus singleton pregnancies. J Matern Fetal Neonatal Med 27(1):57–61
21. Beemsterboer SN, Homburg R, Gorter NA, Schats R, Hompes PG, Lambalk CB (2006) The paradox of declining fertility but increasing twinning rates with advancing maternal age. Hum Reprod 21(6):1531–1532
22. Carolan M, Frankowska D (2011) Advanced maternal age and adverse perinatal outcome: a review of the evidence. Midwifery 27(6):793–801
23. Chan BC, Lao TT (2008) Effect of parity and advanced maternal age on obstetric outcome. Int J Gynaecol Obstet 102(3):237–241
24. Kazer RR, Cheng ER, Unterman TG, Glick RP (1991) Maternal plasma concentrations of insulin-like growth factor-I (IGF-I) and human placental lactogen (hPL) in twin pregnancies. Acta Genet Med Gemellol 40(3–4):383–387
25. Alptekin H, Çizmecioğlu A, Işık H, Cengiz T, Yildiz M, Iyisoy MS (2016) Predicting gestational diabetes mellitus during the first trimester using anthropometric measurements and HOMA-IR. J Endocrinol Invest 39:577–583
26. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS, Sacks DA (2008) Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 358(19):1991–2002
27. Dinham GK, Henry A, Lowe SA, Nassar N, Lui K, Spear V, Shand AW (2016) Twin pregnancies complicated by gestational diabetes mellitus: a single centre cohort study. Diabet Med 33(12):1659–1667
28. Liu X, Chen Y, Zhou Q, Shi H, Cheng WW (2015) Utilization of International Association of Diabetes and Pregnancy Study Groups criteria vs a two-step approach to screening for gestational diabetes mellitus in Chinese women with twin pregnancies. Diabet Med 32(3):367–373
29. Jackson RA, Gibson KA, Wu YW, Croughan MS (2004) Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Obstet Gynecol 103:551–563
30. Szymanska M, Horosz E, Szymusik I, Bomba-Opon D, Wielgos M (2011) Gestational diabetes in IVF and spontaneous pregnancies. Neuroendocrinol Lett 32:885–888
31. Pandey S, Shetty A, Hamilton M, Bhattacharya S, Maheshwari A (2012) Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis. Hum Reprod Update 18(5):485–503
32. Holst S, Kjær SK, Jørgensen ME, Damm P, Jensen A (2016) Fertility problems and risk of gestational diabetes mellitus: a nationwide cohort study. Fertil Steril 106(2):427–434.e1