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BRIEF COMMUNICATION

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Follow-up of offspring and mothers with gestational diabetes treated with metformin or glibenclamide: A randomized controlled trial

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Treatment options for moderate gestational diabetes mellitus include metformin and glibenclamide.[1,2] A randomized controlled trial[3] performed 9 years ago comparing the use of metformin and glibenclamide showed significantly better neonatal outcomes with the use of metformin. The present study followed up 78 (49%) of 159 women that were randomized, along with their offspring, to compare adiposity, anthropometric measurements, and prevalence of diabetes between the two treatment groups. Informed consent and ethical approval from the institutional review board of Christian Medical College, Vellore, India, were obtained for this study. To show a 2% difference in mean body fat percentage between the offspring of the two treatment groups, and a standard deviation of 4 with 80% power and 5% level of significance, we needed a sample size of 63 in each group. However, the sample size was not achieved.

Data from the original study[3] showed that women who were not followed up were more likely to have a family history of diabetes (48/81 [55.8%] vs 38/78 [44.2%]) (P=0.045), than those who were followed up. Other variables were similar. The 37 women who received glibenclamide (Sanofi-Aventis, Paris, France) and 41 women who received metformin (Franco-Indian Pharmaceuticals, Mumbai, India) and their offspring had a detailed history and demographic profile, blood pressure check, anthropometric examination, nutritional assessment using a 3-day recall method, physical activity assessment using a global physical activity questionnaire, biochemical tests, and dual energy X-ray absorptiometry (DEXA) for body fat, regional fat, and lean mass composition.

Among the anthropometric measurements, body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters), waist circumference, hip circumference, waist–hip ratio, triceps, biceps, subscapular skin fold thickness, and mid-arm circumference were measured for both mothers and offspring. All statistical analyses were performed using software STATA version 16 (StataCorp, College Station, TX, USA). P<0.05 was considered statistically significant.

Baseline characteristics from the original study (3) of followed-up mothers with the two modes of treatment were similar, except that the first-hour glucose tolerance test (GTT) value in the group treated with metformin was significantly higher when compared to the group treated with glibenclamide (mean [SD]; 12.3 [1.9] mmol/L vs 11.3 [1.9] mmol/L, P=0.025), and there were higher triglyceride levels in the group treated with metformin (median [IQR]; 2.7 [2.1, 3.3] mmol/L vs 2.4 [1.9, 2.7] mmol/L, P=0.047) (data not shown in table).

Nutritional and physical activity assessment, anthropometric measurements were similar in both the mother and offspring of both treatment groups (data not shown). The current health status of mothers and their offspring are elaborated in Table 1. Most outcomes were

TABLE 1 Comparison of current health status of mothers and offspring at follow-up according to treatment groups

Characteristics	Offspring			Mother		
	Glibenclamide (n = 37)	Metformin (n = 41)	*P* value	Glibenclamide (n = 37)	Metformin (n = 41)	*P* value[a]
Age (years)	9.6 (0.8)	9.7 (0.8)	0.538	39.1 (4.7)	38.8 (4.9)	0.779
BMI (kg/m^2)	18.1 (3.4)	18.2 (4.5)	0.902	28.7 (4.7)	28.1 (4.6)	0.608
Waist circumference (cm)	63.3 (9.4)	62.0 (12.3)	0.599	91.7 (10.7)	91.1 (12.7)	0.813
Hip circumference (cm)	73.9 (8.1)	72.5 (12.6)	0.564	104.0 (10.4)	102.7 (12.0)	0.628
SBP (mm Hg)	101.8 (8.8)	102.4 (10.5)	0.776	123.5 (16.8)	124.2 (16.7)	0.863
DBP (mm Hg)	60.7 (7.4)	60.7 (7.1)	0.999	77.1 (8.9)	72.0 (11.7)	0.035
Serum fasting glucose (mmol/L) level[b]	4.75 (4.5, 5.1)	4.67 (4.5, 4.9)	0.498	9.2 (7.3, 12.6)	7.2 (6.1, 8.4)	0.019
Serum fasting insulin (mIU/mL) level	7.1 (3.5)	8.2 (6.3)	0.319	NA	NA	—
Cholesterol (mmol/L)	3.81 (0.8)	3.85 (1.2)	0.531	4.6 (0.9)	4.3 (1.1)	0.190
Triglyceride (mmol/L)[b]	0.75 (0.6,1.0)	0.88 (0.7,1.3)	0.030	1.6 (1.2, 2.4)	1.5 (0.9, 2.0)	0.512
HDL (mmol/L)	1.15 (0.2)	1.23 (0.5)	0.392	1.1 (0.2)	1.0 (0.2)	0.673
LDL (mmol/L)	2.43 (0.7)	2.38 (0.8)	0.762	3.1 (0.7)	2.8 (0.8)	0.106
DEXA						
Total fat[b]	10.7 (7.5, 15.5)	10.1 (6.1, 15.9)	0.948	37.8 (6.5)	39.0 (5.1)	0.384
Abdominal fat[b]	4.1 (2.4, 6.0)	3.3 (2.1, 6.6)	0.940	36.4 (6.3)	37.4 (5.3)	0.424
Lean body mass[b]	20.3 (18.3, 23.8)	20.6 (18.8, 23.2)	0.885	16.1 (4.3)	16.3 (2.6)	0.800
Diabetic status, n (%)[c]						
Prediabetic	3 (8.3)	4 (10.0)	0.844	7 (18.9)	16 (39.0)	0.120
Diabetic	1 (2.8)	0	—	28 (75.7)	22 (53.7)	—

Abbreviations: DBP, diastolic blood pressure; DEXA, dual energy X-ray absorptiometry; NA, not available; SBP, systolic blood pressure.
Data are expressed as mean (SD) unless otherwise specified.
[a]*P* value obtained using student's *t*-test or Wilcoxon rank-sum test and Chi-square test or Fisher's exact test.
[b]Median (IQR) and n (%).
[c]One offspring measurement missing in each group.

similar except for triglyceride levels in the offspring of mothers treated with metformin, which was higher. Additionally, diastolic blood pressure and fasting blood glucose levels were higher in the mothers of the group treated with glibenclamide. The average BMI of the offspring was 18, similar in both groups. The body fat composition using DEXA were similar in both groups for the women and the offspring. Virtually all women were either diabetic or prediabetic 9 years later.

To our knowledge, this is the only study that compared long-term outcomes in women and their offspring treated with metformin and glibenclamide, though there have been studies that have followed up and compared metformin with insulin.[4,5] From the information in this study, we would still favor the use of metformin for the treatment of moderate hyperglycemia in pregnancy.

AUTHOR CONTRIBUTIONS

PP, LP, AA, HY, and JEM were involved in the conception and designing of the study. BM, TVP, and NT were involved with the execution of the study, along with the above authors. SP and BA, along with the other authors, were involved with the analysis, critical evaluation, and drafting of the manuscript.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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