THE METABOLIC GLOBAL APPROACH: A MULTIDISCIPLINARY PROGRAM DEVELOPED TO ASSESS METABOLIC RISK OF OBESE WOMEN BEFORE ASSISTED REPRODUCTIVE TECHNOLOGIES

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INTRODUCTION

Obesity is one of the major concern in fertility clinics since more than half of reproductive-age women are now overweight or obese and increased body mass index (BMI) seems to be associated to lower pregnancy and live birth rates. Maternal obesity is correlated to many metabolic complications, including detrimental effect on female reproductive health, that can largely differ for the same BMI between subjects. Metabolic parameters other than weight need to be evaluated to assess maternal risk before assisted reproductive technologies (ART) in order to try to improve pregnancy outcome.

OBJECTIVE

To evaluate the impact of a metabolic global approach of obesity on female reproductive capacity and pregnancy rate.

METHODS

The metabolic global approach was developed by endocrinologist at the CHUM fertility clinic to guide the evaluation of obese women before ART. This individualized intervention is based on patient's BMI and specific metabolic parameters. At first visit, if initial BMI is ≥30 kg/m2, a 75g oral glucose tolerance test (OGTT) and an individual nutritional counselling are scheduled before going through ART.

If BMI is ≥35 kg/m2, a consultation with an endocrinologist is added and work-up is completed by lipid profile, liver function, and blood pressure (BP). ART can be reconsidered when women are metabolically stable meaning that all the following goals are achieved:

1. Weight lost of at least 5 to 10%,
2. Normal OGTT or, if impaired glucose tolerance (IGT)/diabetes was diagnosed, this condition is now controlled (HbA1c < 7%, ideally < 6%),
3. Triglycerides levels <1.7mmol/L
4. Controlled BP ≤130/85 mmHg
5. Normal liver function (AST/ALT within normal range)
6. Adoption of healthier lifestyle such as smoking cessation and regular physical activity.

Throughout the process, patients are followed by a registered dietician who recommends an energy-reduced balanced diet (45% carbohydrates, 25% proteins, 30% fat) and regular physical activity (minimum 150 min/wk). During follow-up, waist circumference, evaluation of body composition by bioimpedance and a complete survey around personal health practice and lifestyle are performed. We also ensured that current drugs are safe for pregnancy. Weight loss and stabilization of the different metabolic parameters were required before initiation of fertility treatment.

RESULTS

A sample of 42 infertile obese women were randomly selected from our cohort since the beginning of the program in 2011. Mean BMI at program entry and at last weighing were respectively, 40.3 and 37.5 kg/m2, representing a mean weight loss of 7.0% (Table 1). Majority of patients (88.1%) exceeded the imposed 5% minimum loss of their total body weight (Table 2).

Table 1 : Age, weight and BMI at initial and last visit

	Baseline	Final	Difference
Age (yrs)	31.8 ± 4.8		
Weight (kg)	104.0 ± 15.4	96.8 ± 15.5	7.2 ± 6.0
BMI (kg/m²)	40.3 ± 9.4	37.5 ± 9.3	2.21 ± 0.69

Table 2: Categories of weight loss

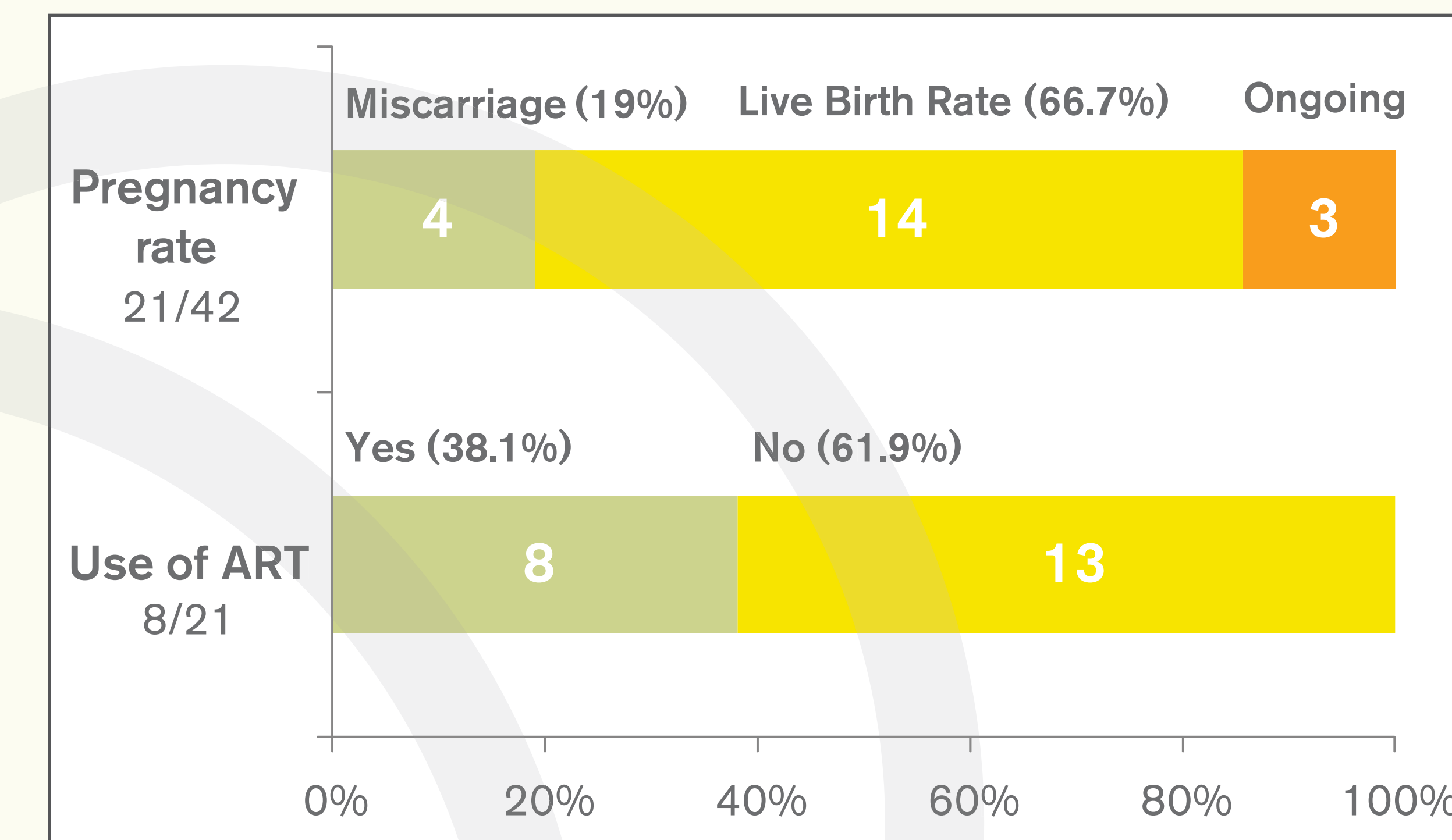| Weight Loss	n	%
< 5%	5	11.9
Between 5-10%	24	57.1
> 10%	13	31.0

Half of patients were classified as metabolically unstable based on at least one abnormal parameter at first evaluation (Graphic 1). Most unstable subjects had more than 2 abnormal metabolic parameters at assessment.

Graphic 1: Metabolic parameters of unstable patients (n=21)

- IGT 26.2%
- T2D 4.8%
- Hypertriglyceridemia 23.8%
- HBP 14.3%
- Abnormal liver function 4.8%
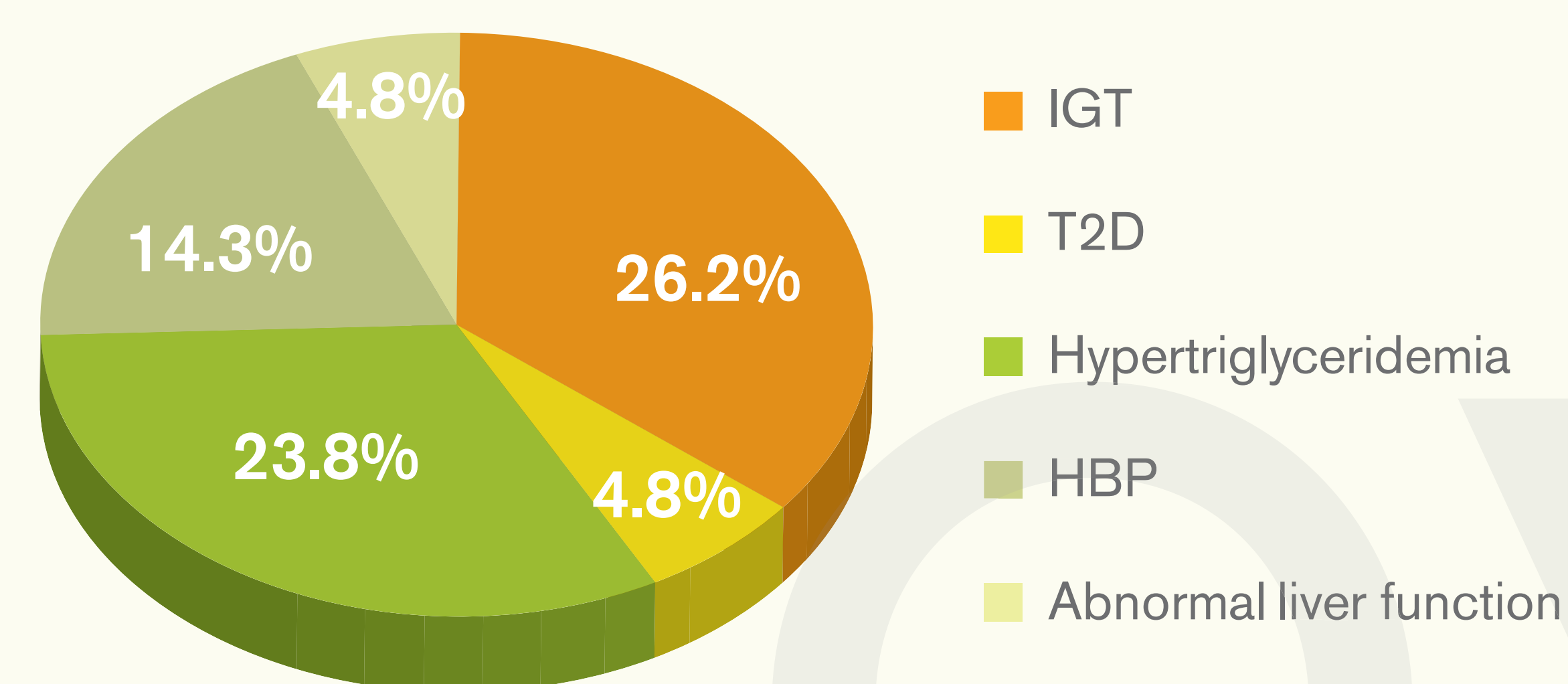
Pregnancy rate was 50% after a mean follow-up of 6.6 months (2.5-11.8 months). Over 60% became pregnant spontaneously or simply with oral ovulation-stimulating drugs (metformin and/or clomiphene citrate). Subsequent miscarriages were noted in 4 subjects but 14 women had a normal term delivery and 3 are actually entering second trimester (Graphic 2).

Graphic 2: Details on pregnancy rate, use of ART and outcomes

Pregnancy rate 21/42 — Miscarriage (19%): 4 | Live Birth Rate (66.7%): 14 | Ongoing: 3

Use of ART 8/21 — Yes (38.1%): 8 | No (61.9%): 13

We compared metabolically stable and unstable women and there were no statistical difference regarding age, weight and BMI. Weight loss was similar in both groups as were use of ART, pregnancy and miscarriage rates (Table 3), reinforcing the fact that all women received, as planned, similar care and nutritional advice.

Table 3: Comparison between metabolically stable and unstable patients

Metabolically	Stable (%)	Unstable (%)	CI (95%)	p
n	21 (50.0)	21 (50.0)		
Age (yrs)	32.2	31.3	(-2.10-3.91)	0.55
Initial Weight (kg)	99.6	108.4	(-18.07-0.62)	0.07
Final Weight (kg)	93.4	100.2	(-16.38-2.77)	0.16
Weight Loss (kg)	-6.2 (6.2)	-8.2 (7.6)	(-1.79-5.63)	0.30
Initial BMI (kg/m²)	39.8	40.8	(-6.99-4.85)	0.72
Final BMI (kg/m²)	37.3	37.8	(-6.35-5.40)	0.87
Pregnancies (n)	9 (42.9)	12 (57.1)	(-0.44-0.16)	0.34
Miscarriages(n)	1 (11.1)	3 (25.0)	(-0.46-0.18)	0.42
Term (n)	6 (66.7)	8 (66.7)	(-0.41-0.41)	1.00
After ART (n)	5 (55.6)	3 (25.0)	(-0.10-0.71)	0.15
No ART (n)	4 (44.4)	9 (75.0)	(-0.71-0.10)	0.15

Moreover, no statistical difference was noted between subgroups of pregnant and not pregnant women regarding maternal profile and metabolic parameters, suggesting that by addressing and treating metabolic comordities of obesity, risks and outcomes of metabolically unstable subjects tend to be similar to the ones of stable women initially classified as healthy obese (Table 4).

Table 3: Comparison between metabolically stable and unstable patients

	Pregnancy (%)	No pregnancy (%)	CI (95%)	p
n	21 (50.0)	21 (50.0)		
Age (yrs)	30.8	32.8	(-4.91-1.00)	0.19
Initial Weight (kg)	104.9	103.1	(-7.86-11.61)	0.70
Final Weight (kg)	97.8	95.7	(-7.72-11.87)	0.67
Weight Loss (kg)	-7.1 (6.8)	-7.4 (7.2)	(-3.56-3.96)	0.92
Initial BMI (kg/m²)	41.5	39.1	(-3.53-8.23)	0.42
Final BMI (kg/m²)	38.7	36.3	(-3.46-8.20)	0.42
IGT (n)	6 (28.6)	5 (23.8)	(-0.15-0.24)	0.74
Type 2 Diabetes (n)	1 (4.8)	1 (4.8)	(-0.09-0.09)	1.00
Hypertriglyceridemia (n)	6 (28.6)	4 (19.0)	(-0.10-0.19)	0.80
Hypertension (n)	3 (14.3)	3 (14.3)	(-0.14-0.14)	1.00
Abnormal liver function (n)	1 (4.8)	1 (4.8)	(-0.09-0.09)	1.00

CONCLUSIONS

Those preliminary data suggest that the metabolic global approach is an effective way to evaluate the heterogeneous metabolic profile of obese women before ART and consequently, after metabolic stabilization and a modest weight loss, could reduce need for ART and enhance female reproductive capacity and pregnancy rate. We believe that this program, in delay for most that do not postponed excessively ART, could improve ART and pregnancy outcomes and limit maternal and fetal risks of obese infertile women in a way that prevent stigmatization and weight discrimination. Further analysis with a larger cohort is needed.

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