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P-415 Wednesday, October 19, 2016

IMPACT OF METFORMIN ON IN VITRO FERTILIZATION OUTCOMES IN OVERWEIGHT AND OBESEPOLYCYSTIC OVARY SYNDROME WOMEN: A PROSPECTIVE COHORT STUDY. O. S. Abdalmageed,[a] T. A. Farghaly,[b] A. M. Ismail,[c] W. W. Hurd.[d] [a]Assiut University IVF Center, Assiut, Egypt; [b]Obstetrics and Gynecology, Assiut University IVF Unit, Assiut, Egypt; [c]Obstetrics and Gynecology, Women's Health Hospital, Assiut, Egypt; [d]Obstetrics and Gynecology, Duke University, Durham, NC.

OBJECTIVE: To determine the impact of short-term metformin therapy on in vitro fertilization-embryo transfer (IVF-ET) outcomes in overweight and obese women with polycystic ovary syndrome (PCOS).

DESIGN: A prospective cohort study

MATERIALS AND METHODS: This prospective cohort study was performed at a University IVF Center. The study population was composed of 102 overweight and obese women (BMI>24 kg/M^2) with PCOS who were undergoing their first fresh autologous IVF-ET cycle with intracytoplasmic sperm injection (ICSI). The study population was composed of two groups according to whether or not they received metformin during the IVF cycle treatment (51 patients in each group). The metformin-treated group received metformin (1,000 mg per day orally) starting from onset of ovarian stimulation therapy and continued until the day of the pregnancy test. For women with a positive pregnancy test, the patients continued metformin until the end of the 12th week of gestation. The primary outcome measures were the number of retrieved oocytes, the number of the fertilized oocytes (two pn oocytes), fertilization rate, implantation rate, clinical pregnancy rate and miscarriage rate.

RESULTS: Both the metformin-treated group and the control group were comparable in terms of the age, BMI, duration of infertility, basal FSH, and AFC . The metformin-treated group demonstrated a decreased number of the retrieved oocytes and 2pn oocytes ($p < 0.01$). There was no difference between the two groups regarding the fertilization rate, implantation rate, multiple pregnancy rates, miscarriage rate or life birth rate (Table2). There were no cases of ovarian hyperstimulation syndrome in either group.

CONCLUSIONS: Short-term administration of Metformin to overweight and obese women with PCOS women decreases the number of oocytes retrieved, but otherwise does not affect IVF outcomes.

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OBESITY AND METABOLISM

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ASSOCIATION OF INSULIN SENSITIVITY (IS) WITH AGE AT MENARCHE (AAM) IN GIRLS WITH TYPE 1 DIABETES (T1D): SEARCH FOR DIABETES IN YOUTH STUDY. H. Borg,[a] W. Lang,[b] R. D'Agostino,[b] S. L. Young,[a] J. Lawrence,[c] C. Pihoker,[d] G. Kim,[d] P. Wadwa,[e] W. Tamborlane,[f] E. Mayer-Davis.[a] [a]University of North Carolina, Chapel Hill, NC; [b]Wake Forest School of Medicine, Winston-Salem, NC; [c]Kaiser Permanente, Pasadena, CA; [d]University of Washington, Seattle, WA; [e]University of Colorado, Aurora, CO; [f]Yale University, New Haven, CT.

OBJECTIVE: Abnormal timing of menarche is a predictor of many pathological conditions. Those pathologies include reproductive dysfunctions, metabolic disorders and cardiovascular diseases. It has been reported that early AAM is associated with lower IS and increased risk of type 2 diabetes. However, the association of IS with AAM in girls with T1D has not been studied. We have previously demonstrated that in girls with T1D, poor glycemic control correlates with delayed AAM, while obesity - reflected by Body Mass Index (BMI) correlates with earlier AAM. In this study, we examine the association of IS with the AAM.

DESIGN: The SEARCH for Diabetes in Youth study comprises the largest contemporary cohort of youth with diabetes in the US, inclusive of youth diagnosed with diabetes younger than age 20 years whose diabetes was prevalent in 2001, or incident in the years thereafter.

MATERIALS AND METHODS: Participants included in our analyses were girls (n=379) diagnosed with T1D from 2002-2005. Their mean age at diagnosis was 9.6 ± 2.7 years and T1D duration 9.8 ± 6.1 months. All subjects had a baseline visit prior to menarche and ≥1 follow-up visits. Their A1c was 7.8 ± 1.4 % and BMI 18.5 ± 3.4 kg/m^2. This cohort included 71% of non-Hispanic Whites, 12% African-Americans, 8% Hispanics, and 9% others. IS was determined using the IS score validated by euglycemic-hyperinsulinemic clamp studies [1]. A series of multiple linear regression (MLR) models with AAM as the outcome variable was fitted to examine the confounder-adjusted impact of IS (measured at each visit) on AAM, including linear and non-linear terms.

RESULTS: Unadjusted MLR models demonstrated neither linear nor quadratic effects of IS as significant predictors for AAM (p=NS). However, when adjusted for the potential confounders, including duration of T1D, BMI, race, and socioeconomic status - IS had a significant negative linear effect (β=-0.09; $p<0.01$), and a significant quadratic effect ($p<0.01$) on AAM. This pattern was opposite to the one seen in girls without T1D.

CONCLUSIONS: In our cohort of girls with T1D, lower IS is associated with later AAM after the adjustment for potential confounders. This pattern is the opposite of that seen in girls without T1D. The reversal of pattern may be secondary to pathological processes underlying T1D such as autoimmunity. Further studies are needed to better understand the impact of IS on reproductive system, including functionality of hypothalamic-pituitary-gonadal axis of women with T1D.

Reference:

1. Dabelea D, D'Agostino RB Jr, Mason CC, et al. Development, validation and use of an insulin sensitivity score in youths with diabetes: the SEARCH for Diabetes in Youth study. Diabetologia 2011;54:78-86.

Supported by: SEARCH is funded by the Centers for Disease and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

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HIGH C-REACTIVE PROTEIN LEVELS IN WOMEN UNDERGOING IVF ARE ASSOCIATED WITH LOW QUALITY EMBRYOS. E. Haikin Herzberger, N. Miller, Y. Ghetler, R. Tamir Yaniv, K. Amichay Keren, A. Shulman, A. Wiser. IVF Unit, Department of Obstetrics and Gynecology, Meir Medical Center, Kfar-Saba, Israel.

OBJECTIVE: This study investigated the physiology of CRP during the IVF cycle in obese and non-obese women and evaluated the effect of CRP on IVF outcomes.

DESIGN: A Prospective study was conducted between 4-8/2014. Patients who underwent IVF treatment were recruited .The patients were divided into two groups: normal/overweight (BMI <30 kg/m2) or obese (BMI ≥30 kg/m2).

MATERIALS AND METHODS: IVF Patients, ages 18-42 years were enrolled. Those with chronic inflammatory diseases or with an acute illness were excluded. A total of 31 patients were included in analysis, 17 with BMI <30 kg/m2 and 14 patients with BMI ≥30 kg/m2. CRP levels were measured at three points: 1) before starting ovarian stimulation (lowest E2 level), 2) on day of HCG administration (maximal E2 level), and 3) on day of ovum pick-up (OPU), in both serum and follicular fluid. A basic hormonal profile was also obtained at each point. Linear regression was used to evaluate the effect of the different variables on embryo quality. Pearson and Spearman correlations were used for CRP concentrations and other relevant parameters.

RESULTS: The serum CRP levels were significantly higher in obese women at all 3 time points compared to those with BMI<30. A positive correlation was found between basal estradiol (E2) and basal CRP (r=0.71, P<0.05). However, no specific pattern of CRP level was detected at the different time points during the IVF cycle. A positive correlation was found between serum and follicular CRP levels during the day of ovum pick-up (r=0.74, P<0.05). The serum CRP level on the day of OPU had a negative effect on embryo quality (P=0.056). Patients were divided according to CRP level <0.5 mg/dL and ≥0.5 mg/dL. Patients with CRP ≥0.5 had lower quality embryos (2.6±0.3 vs. 3.3±0.3, P=0.04).

CONCLUSIONS: High serum CRP level on OPU day has a negative effect on embryo quality. CRP level can be considered as a predictive marker for IVF outcome.

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DOSE OF HUMAN CHORIONIC GONADOTROPIN TO TRIGGER FINAL OOCYTE MATURATION. M. Irani,[a] R. Setton,[b] V. Gunnala,[c] I. Kligman,[d] D. E. Goldschlag,[e] Z. Rosenwaks.[f] [a]Reproductive Endocrinology and Infertility, Weill Cornell Medicine, New York, NY; [b]Department of Obstetrics and Gynecology, Weill Cornell Medical College, New York, NY; [c]OB/GYN, REI Fellow, New York, NY; [d]Weill Cornell Medical College, New York, NY; [e]Obstetrics, Gynecolology and Reproductive Medicine, Weill Cornell Medical Center, Manhattan, NY; [f]Weill Cornell Medicine - Center for Reproductive Medicine, 1305 York Avenue, New York, NY.

ASSOCIATION OF INSULIN SENSITIVITY WITH AGE AT MENARCHE IN GIRLS WITH TYPE 1 DIABETES: SEARCH FOR DIABETES IN YOUTH STUDY

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ABSTRACT

Our group has previously reported that in girls with type 1 Diabetes (T1D) poor glycemic control correlates with delayed Age at Menarche (AAM), and obesity correlates with earlier AAM [1]. In this study, we examined the association of Insulin Sensitivity (IS) with AAM in the same cohort (n=379). The IS score used (see below) was validated by euglycemic clamps [2]. To examine the confounder adjusted impact of IS on AAM we have fitted a series of multiple linear regression models with AAM as the outcome variable, including linear and non-linear terms. Unadjusted models showed that neither linear nor quadratic effects of IS are significant predictors for AAM (p=NS). After adjusting for the potential confounders (duration of T1D, BMI, race, socioeconomic status) IS had a significant negative linear effect (β=-0.09; p<0.01), and a significant quadratic effect (p<0.01) on AAM. This pattern was reverse to the one typically seen in girls without T1D [3]. Therefore, it appears that pathologies underlying T1D may alter the way in which IS impacts AAM.

OBJECTIVES

Abnormal timing of menarche is a predictor of many pathological conditions. Those pathologies include reproductive dysfunctions, metabolic disorders and cardiovascular diseases. It has been reported that early AAM is associated with lower IS and increased risk of type 2 diabetes [4]. However, the association of IS with AAM in girls with T1D has not been studied. We have previously demonstrated that in girls with T1D, poor glycemic control correlates with delayed AAM, while obesity - reflected by Body Mass Index (BMI) - correlates with earlier AAM.

In this study, we examined the association of IS with AAM in T1D.

DESIGN & METHODS

The SEARCH for Diabetes in Youth study comprises the largest contemporary cohort of youth with diabetes in the US, inclusive of youth diagnosed with diabetes younger than age of 20 years, whose diabetes was prevalent in 2001, or incident in the years thereafter. Participants included in our analyses were girls (**n=379**) diagnosed with T1D from 2002-2005. Their mean age at diagnosis was **9.6±2.7** years and T1D duration **9.8±6.1** months. All participants had a baseline visit prior to menarche and ≥1 follow-up visits. At the baseline visit, their mean A1c was **7.8±1.4** % and BMI **18.5±3.4** kg/m2. This cohort included **71%** of non-Hispanic Whites, **12%** African-Americans, **8%** Hispanics, and **9%** others. IS was determined using the IS score formula validated by euglycemic clamp studies [2], as follows:

IS=exp [4.6472520 - 0.02032 x (**A**-0.0977) x (**B**-0.00235) x **C**],

where **IS**= Insulin Sensitivity; **A**=waist (cm); **B**=HbA1c (%); **C**= Triglycerides (mg/dL).

A series of multiple linear regression (MLR) models with AAM as the outcome variable was fitted to examine the confounder-adjusted impact of IS (measured at each visit) on AAM, including linear and non-linear terms.

RESULTS

In our analyses, the unadjusted MLR models demonstrated that neither linear nor quadratic effects of IS are significant predictors for AAM (p=NS). When adjusted for potential confounders, including duration of T1D, BMI, race, and socioeconomic status - IS had a significant negative linear effect (**β=-0.09; p<0.01**), and a significant quadratic effect (**p<0.01**) on AAM. Unexpectedly, this pattern is opposite to the one observed in girls without T1D [3]. However, as expected Body Mass Index z-score (BMIz) had a significant negative correlation with IS (**Spearman's Rho =-0.41, p<0.0001**).

FIGURES

Fig. 1: Association of Insulin Sensitivity with Age at Menarche

Fig. 2: Correlation between Insulin Sensitivity and Body Mass Index z-score

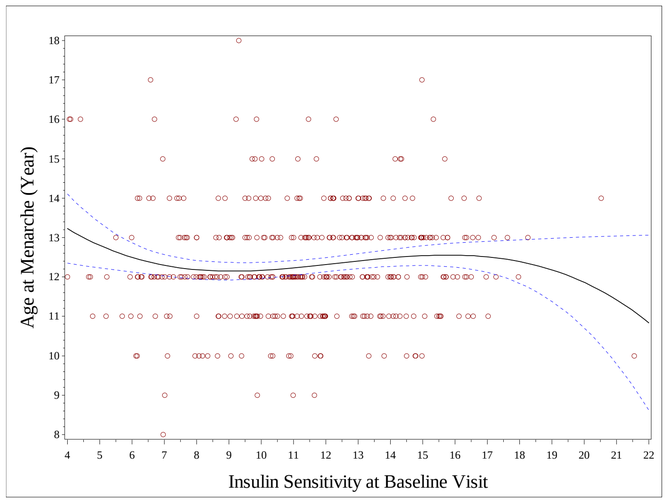

Fig.1

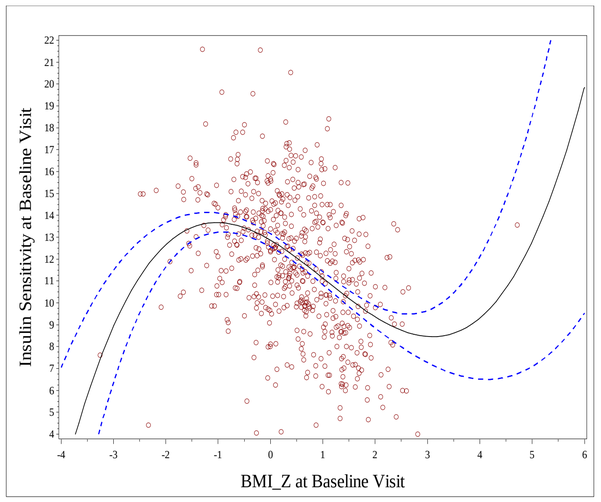

Fig.2

CONCLUSIONS

- **In our cohort of girls with T1D, *lower IS* is associated with *later AAM* after the adjustment for potential confounders.**
- **This pattern is the opposite of the one seen in girls without T1D.**
- **The reversal of pattern may be secondary to pathological processes underlying T1D.**
- **Further studies are needed to better understand the impact of IS on reproductive system.**

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3. Lim SW, Ahn JH, Lee JA, et al. Early menarche is associated with metabolic syndrome and insulin resistance in premenopausal Korean women. Eur J Pediatr. 2016;175(1):97-104. doi:10.1007/s00431-015-2604-7.
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The SEARCH for Diabetes in Youth Study is funded by the Centers for Disease Control and Prevention (RFA-DP10-001) and supported by the National Institute of Diabetes and Digestive and Kidney Diseases. www.searchfordiabetes.org