Polycystic ovarian syndrome: New light on its causes and its effect on brothers

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Researchers have found evidence that chronic disease in either a mother or father can create unfavourable conditions in the womb that are associated with the development of polycystic ovarian syndrome (PCOS) in daughters. In another study, researchers found that brothers of women with PCOS and insulin resistance are themselves at greater risk of developing insulin resistance or diabetes, suggesting that factors associated with the condition can be passed down to sons as well as daughters.

The two studies were presented to the 25th annual meeting of the European Society of Human Reproduction and Embryology in Amsterdam heard today.

Associate Professor Michael Davies told a news briefing: "We already know from clinical studies of women with reproductive problems that foetal growth restriction is associated with the development of PCOS symptoms in daughters, and that problems during pregnancy and in the way the mother adapts to the metabolic challenge of pregnancy can indicate the future cardiovascular health of both the mother and the child. What we don't know is whether giving birth to a daughter who later develops PCOS is associated with increased, long term cardiovascular disease risk in the mother. Nor do we know whether conditions underlying chronic disease in the father increases the risk of PCOS in the daughter."

Prof Davies, co-director of the Research Centre for the Early Origins of

Health and Disease at the University of Adelaide (Australia), looked at records for all female babies who were born and survived between 1973-1976 at The Queen Elizabeth Hospital in Adelaide. He and his colleagues interviewed the daughters to build up a picture of their health and any history of chronic disease in their parents. So far, 998 (63%) have responded, and Prof Davies reported preliminary data up to mid-1975 to the conference.

Sixty-two daughters (6.2% of the group) had a pre-existing diagnosis of PCOS. Mothers of these women tended to have elevated blood pressure during pregnancy. Daughters were nearly eight times as likely to have PCOS if their mothers had it, and they had a slightly higher risk if their mothers smoked during pregnancy. Mothers were 1.6 times as likely to have high blood pressure in later life if their daughters developed PCOS. If their fathers had heart disease or stroke, the daughters also had a higher risk of PCOS: double and three times the risk respectively. A history of diabetes in either parent was not significant.

Prof Davies said: "These findings suggest a new pathway for the development of PCOS. We think that factors associated with the pre-existence of cardiovascular dysfunction in the mother or the father, and which operate during pregnancy, may create adverse conditions for the foetus, which alter the metabolic profile of offspring, leading to insulin resistance and reproductive consequences, such as PCOS, for daughters. A family history of diabetes is, therefore, not essential to observe an insulin resistance-related disease in offspring."

He said it was still unclear exactly how the cardiovascular risk in the father affected the daughter. "We firstly need to consider the potential role of a common environment; for instance, that families with high levels of obesity (and therefore cardiovascular disease) will also tend to have heavy daughters who are thereby more likely to be affected by PCOS. However, the paternal effect that we saw was independent of the

daughter's weight, maternal age, socioeconomic status, maternal smoking, and country of birth, which suggests either a direct genetic effect on the daughter, or an effect of paternal genetic factors that are expressed during pregnancy."

Dr Verena Mattle told the news briefing that her study was the first to show that brothers of women who had PCOS and insulin resistance were themselves more likely to develop insulin resistance or even diabetes or dyslipidaemia (a disruption in the levels of lipids (or fats) in the blood).

"Until now, it was not clear whether the male relatives of women with PCOS were at increased risk for the metabolic disorders associated with PCOS," said Dr Mattle, who is chief resident at the University Clinic of Gynecological Endocrinology and Reproduction Medicine in Innsbruck (Austria).

Dr Mattle and her colleagues conducted oral glucose tolerance tests on 15 brothers of sisters with PCOS and insulin resistance (group 1). They also performed a serum analysis to determine lipid levels. As a control, nine brothers of sisters with PCOS but without insulin resistance were included in the study (group 2).

The researchers found that in the first group eight brothers showed an insulin resistance, one was diagnosed with diabetes and six had a normal glucose tolerance test. All nine affected brothers had a body mass index (BMI) between 19-31 kg/m2 and had elevated cholesterol and triglyceride levels. The six unaffected brothers had a BMI between 23-29, and none had high levels of cholesterol or triglycerides. In the second group, no insulin resistance was diagnosed. BMI was between 18-27 and two brothers had elevated cholesterol levels. Although there was a trend towards higher BMI in the first group, Dr Mattle said there was no statistically significant difference in BMIs between the two groups.

Dr Mattle said: "These results mean that we should pay attention to the health not only of women with PCOS but also to their brothers as they seem to have an increased risk for the medical problems that make up the metabolic syndrome, such as insulin resistance, diabetes and cardiovascular disease. Our findings are also in accordance with the hypothesis that not only is PCOS is a heritable disease, but that factors associated with it, such as insulin resistance, can be passed down to the next generation of either sex."

She said that it could not be the case that the high BMI by itself could have caused the insulin resistance and diabetes in the affected brothers. "There must be a correlation between PCOS and insulin resistance because we could only find brothers with insulin resistance in the group that had sisters with PCOS and insulin resistance, but we couldn't find brothers with insulin resistance in the group that had sisters with PCOS and no insulin resistance. It is known that about 50% of women with PCOS are insulin resistant and also that lean PCOS patients are insulin resistant. The BMI of insulin-resistant and non-resistant brothers were not statistically different."

Dr Mattle and her colleagues are continuing to test brothers of women with PCOS for insulin resistance and lipid levels to collect more data from a larger group. "At this stage we would hesitate to say that a genetic inheritance is definitely playing a role in the increased risk of insulin resistance and other, related conditions in these brothers. We need to explore the possible effect of conditions in the womb and also the role of the environment. However, we think our data strongly support the view that brothers of women with PCOS and insulin resistance may have an increased risk of insulin resistance, diabetes and other, adverse metabolic conditions," she concluded.

Source: European Society for Human Reproduction and Embryology (news : web)