

PCOS is linked to increased risk of neuropsychiatric disorders in offspring

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Children born to mothers with polycystic ovary syndrome (PCOS) are at greater risk of a wide range of psychiatric and neurodevelopmental disorders, according to new research published today in *Human Reproduction*, one of the world's leading reproductive medicine journals.



Researchers in Sweden, China and Finland found that the <u>increased risk</u> existed for children born to mothers who had PCOS alone, but was further increased if PCOS was combined with mothers being obese, having gestational diabetes, a caesarean delivery, or if there were other medical problems for the mothers or babies around the time of birth.

The study is the first to show links between PCOS and such a wide range of disorders, which include emotional and <u>behavioural problems</u>, delayed development, learning, speech and language problems, autism and <u>attention deficit hyperactivity disorder</u> (ADHD). It is the largest study to date, including over one million babies born in Finland between 1996 and 2014 and followed up until the end of 2018.

PCOS is a common hormonal disorder in which there is an excess of male hormones and the ovaries do not function correctly. It is the most common cause of anovulatory infertility, when the ovaries do not release eggs during the menstrual cycle, and it is estimated to affect between 6-20% women of reproductive age. Women with PCOS may experience irregular menstrual cycles, higher incidence of miscarriage and other health problems such as hirsutism, acne, obesity and diabetes.

The researchers, led by Catharina Lavebratt, an associate professor at the Karolinska Institutet, Stockholm, Sweden, compared data from 24,682 (2.2%) children born to mothers with PCOS or anovulatory infertility with 1,073,071 (97.8%) children born to mothers without PCOS. A total of 105,409 (9.8%) children were diagnosed with a neurodevelopmental or psychiatric disorder during the follow-up period.

Professor Lavebratt said: "We found that children born to mothers with PCOS have an increased risk of neurodevelopmental or <u>psychiatric</u> <u>disorders</u>. The higher risk applied to a number of psychiatric diagnoses, including mood, anxiety, eating and sleeping disorders, intellectual disabilities, specific developmental, autism spectrum, attention deficit



hyperactivity, conduct and tic disorders, and other behavioural and emotional disorders. This is the first study to report an increased risk of a wide range of neuropsychiatric disorders in offspring exposed to maternal PCOS, indicating a broad adverse effect of PCOS on neurodevelopment. In addition, the risk is increased independent of the babies' sex and maternal obesity."

The risk of being diagnosed with any psychiatric disorder increased 1.3-fold among children of mothers with PCOS. In particular, the risk of sleeping disorders increased 1.5-fold, ADHD, conduct and tic disorders 1.4-fold, intellectual disabilities and autism spectrum disorders 1.4-fold, developmental and eating disorders nearly 1.4-fold, anxiety disorders 1.3-fold, mood disorders nearly 1.3-fold and other behavioural and emotional disorders nearly 1.5-fold.

Prof Lavebratt said: "During the follow-up period, 2532 out of 24,682 children—10.3% - born to mothers with PCOS were given a neuropsychiatric diagnosis compared to 102,877 out of 1,073,071 children—9.6% - born to mothers without PCOS. The risk of neuropsychiatric disorders was 1.3 times higher in children with PCOS exposure compared to those without. This means that 700 more children per 100,000 are born with any sort of mental health problems due to maternal PCOS."

When the researchers analysed the risks according to the mothers' body mass index (BMI), they found that the risk of being diagnosed with any neuropsychiatric disorder among offspring of normal weight women with PCOS increased 1.2-fold compared to those without PCOS, but more than doubled in offspring of PCOS mothers who were severely obese. The risk also doubled in mothers with PCOS who experienced perinatal problems, and increased 1.7-fold in mothers who experienced gestational diabetes or had a caesarean delivery.



To check whether the increased risk of neuropsychiatric disorders could be due to perinatal problems, gestational diabetes, caesarean delivery or fertility treatment rather than to PCOS, the researchers analysed the data to exclude mothers with these conditions, but they still observed a 1.2- to 1.3-fold increased risk.

The first author of the paper, Xinxia Chen, is associate professor at Shandong University, Jinan, Shandong China, and also worked at the Karolinska Institutet in 2019. She said: "Although highly prevalent, PCOS remains one of the most poorly understood medical disorders for patients, doctors and scientists. In particular, the long-term health consequences of PCOS for both affected women and their families are less well known, although some previous epidemiological studies have reported an increased risk of autism spectrum disorders and ADHD. However, until now, it was not known whether PCOS was associated with a wide range of neuropsychiatric effects, and whether the effects were independent of other, common medical problems such as obesity, diabetes and infertility.

"Our study shows that children of mothers with PCOS are in need of psychological support and longer follow-up for mental health. Healthcare providers should consider that children born to mothers with PCOS are at high risk of mental health problems, even those born to normal-weight mothers. Counselling for women with PCOS and monitoring of their offspring should be offered routinely in order to help prevent these problems."

As the study is observational it cannot show with certainty that PCOS causes the psychiatric and neurodevelopment problems, only that it is associated with them. The researchers are planning further studies to confirm the results and investigate potential mechanisms. Other limitations include the fact that the prevalence of PCOS in the Finnish registries was lower than that reported elsewhere, suggesting that this



study might have captured only the most severe cases; bias might occur by combining diagnoses of PCOS with anovulatory infertility; it was not feasible to distinguish between different types of PCOS; other familial factors might affect the association between PCOS in mothers and problems in offspring; and the mothers' BMI was available only for children born between 2004-2014, and there was no information on weight gain during pregnancy.

More information: Xinxia Chen et al, Association of polycystic ovary syndrome or anovulatory infertility with offspring psychiatric and mild neurodevelopmental disorders: a Finnish population-based cohort study, *Human Reproduction* (2020). DOI: 10.1093/humrep/deaa192

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