Contraception use and pregnancy outcomes in women with polycystic ovary syndrome: data from the Australian Longitudinal Study on Women’s Health

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STUDY QUESTION: Do contraception use, pregnancy outcome and number of children differ in women with and without polycystic ovary syndrome (PCOS)?

SUMMARY ANSWER: Women with PCOS were less likely to report use of contraception and more likely to report a miscarriage, whilst number of children was similar between groups.

WHAT IS KNOWN ALREADY: The oral contraceptive pill is used in the management of PCOS, but the patterns of contraception use in women with PCOS is not known. In women with PCOS who undergo assisted reproduction, the risk of pregnancy loss appears higher, yet pregnancy loss and family size among community-based women with PCOS is not known.

STUDY DESIGN, SIZE AND DURATION: This is a cross-sectional analysis of a longitudinal cohort study. Mailed survey data were collected at five time points (years 1996, 2000, 2003, 2006 and 2009). Data from respondents to Survey 4 (2006), aged 28–33 (n = 9145, 62% of the original cohort aged 18–23 years) were analysed.

PARTICIPANTS/MATERIALS, SETTING, METHODS: This study was conducted in a general community setting. Data from participants who responded to the questions on PCOS, contraception and pregnancy outcome were analysed. The main outcome measures were self-reported PCOS, body mass index (BMI), contraception use, pregnancy loss and number of children.

MAIN RESULTS AND THE ROLE OF CHANCE: In women aged 28–33 years, women with PCOS were less likely to be using contraception (61 versus 79%, P < 0.001) and more likely to be trying to conceive (56 versus 45%, P < 0.001), compared with women not reporting PCOS. A greater proportion of women with PCOS reported pregnancy loss (20 versus 15%, P = 0.003). PCOS was not independently associated with pregnancy loss; however, BMI was independently associated with pregnancy loss in the overweight and obese groups (OR 1.2, 95% CI 1.04–1.4, P = 0.02 and OR 1.4, 95% CI 1.1–1.6, P = 0.001, respectively). Fertility treatment use was also independently associated with pregnancy loss (adjusted OR 3.2, 95% CI 2.4–4.2, P < 0.001). There was no significant difference in number of children between women with and without PCOS.

LIMITATIONS, REASON FOR CAUTION: PCOS, contraception use and pregnancy outcome data were self-reported. Attrition occurred, but is reasonable compared with similar longitudinal cohort studies.

WIDER IMPLICATIONS OF THE FINDINGS: This community-based cohort aged 28–33 years provides insights into the contraceptive use, pregnancy loss and family size of a large cohort of unselected women. Women reporting PCOS had lower rates of contraception use and were more likely to be currently trying to conceive, suggesting that they may be aware of potential fertility challenges, yet in those not planning to conceive, contraceptive use was low and further education may be required. Despite prior reports of higher rates of pregnancy loss in PCOS, usually from infertility services, in this community-based population, PCOS was not independently associated with pregnancy loss, yet independent risk...
Introduction

Polycystic ovary syndrome (PCOS) affects 6–21% of women of reproductive age, depending on the diagnostic criteria applied and population studied (Diamanti-Kandarakis et al., 1999; Asuncion et al., 2000; Azziz et al., 2004; March et al., 2010). PCOS diagnosis is based on oligo or anovulation, hyperandrogenism (clinical or biochemical), and polycystic ovaries on ultrasound (Group, 2004; Azziz et al., 2006). Insulin resistance and hyperandrogenism are the main hormonal abnormalities in PCOS (Diamanti-Kandarakis and Papavassiliou, 2006; Teede et al., 2010) and contribute to the reproductive (hyperandrogenism, menstrual irregularity, oligo or anovulation, infertility), metabolic (dyslipidemia, type 2 diabetes, cardiovascular risk factors) and psychological features (depression, anxiety and lower quality of life) (Group, 2004; Meyer et al., 2005; Teede et al., 2007).

The oral contraceptive pill (OCP) is one of the key medical therapies used in PCOS to regulate menstrual cycles, provide uterine endometrial protection and treat symptoms of hyperandrogenism including acne and hirsutism (Teede et al., 2010). The OCP has potential adverse effects including mood disturbance, possible weight gain and venous thromboembolism risk and there are some reports that the OCP may worsen insulin resistance (Meyer et al., 2007), a key factor in women with PCOS. The role for and safety of the use of the OCP in women with PCOS who are already at high risk of metabolic abnormalities remain unclear. Whilst there is some literature on the use of specific hormonal therapies in PCOS, there are few studies that have examined patterns of contraception use in women with PCOS.

Women with PCOS are thought to have 30–50% rates of first trimester pregnancy loss (Grundy, 1998, 1999, 2002), a 3-fold increased risk in comparison to women without PCOS (Jakubowicz et al., 2002). Whilst studies have investigated the prevalence of PCOS in women with recurrent miscarriage, many of these studies have defined PCOS using polycystic ovary morphology alone, not PCOS per se and have limited generalizability. There are many studies comparing miscarriage rates between groups treated with various medical fertility therapies in PCOS, but no studies analysing the background prevalence of miscarriage among women reporting PCOS in the community. Furthermore, the long-term reproductive outcome and live birth rates of pregnancies in community-based women reporting PCOS remain unclear.

In these analyses, we examine self-reported contraception use, attempts to conceive, pregnancy outcome and number of children in the large, prospective, community-based Australian Longitudinal Study on Women’s Health (ALSWH).

Methods

The ALSWH first collected mailed survey data from three age cohorts of Australian women in 1996. The current study utilized data collected from the cohort born 1973–1978 (n = 14 779 at Survey 1, age 18–23). The study’s primary aims were to examine the relationships between biological, psychological, social, lifestyle factors, women’s physical and mental health, and their use of and satisfaction with health care services (Lee, 2001; Lee et al., 2005). Women were randomly selected from the national health insurance scheme (Medicare) database which includes almost all people who are permanent residents of Australia (Lee et al., 2005). Women were recruited nationally with intentional over-sampling from rural and remote areas (Lee et al., 2005). Further details of the methods used by the ALSWH and characteristics of the sample have been reported elsewhere and are available at www.alswh.org.au (Brown et al., 1998; Lee, 2001; Powers and Loxton, 2010). The Human Research Ethics Committees of the University of Newcastle and the University of Queensland approved the study methods. With intensive tracking procedures and follow-up, retention of participants was 62% for Survey 4 (year 2006).

Outcome variables assessed in Survey 4

Contraception: Women were asked about current and past contraception use. Women could select any or all responses that applied and included the OCP, emergency contraception, implant (e.g. Implanon), condoms, withdrawal method, another method or no contraception. Women were also asked about their history of tubal ligation or hysterectomy or about vasectomy in their partner.

Attempts at pregnancy: Women were asked if they were currently trying to become pregnant.

Pregnancy outcomes: Women were asked to report all pregnancy outcomes including number of live full-term births, live pre-term births, stillbirths and miscarriages. The total number of children was calculated from adding the total number of live full-term births and live pre-term births. Pregnancy loss was defined as a history of one or more miscarriage or stillbirth.

Explanatory variables

Polycystic ovary syndrome: Women were asked if they had been diagnosed or treated for PCOS in the last 3 years (since the last survey).

Fertility treatment: Women were asked if they were currently using or had previously required fertility hormone treatment, which specified the use of clomid or in vitro fertilization (IVF).

Statistical analysis

Analysis of contraception use and attempts to conceive were performed in the group of women without a history of hysterectomy, tubal ligation or partner vasectomy and who were not currently or recently pregnant.
Continuous explanatory variables were summarized as means with standard errors. Categorical explanatory variables were reported as percentages. Differences in variables at baseline between subgroups of the study population were tested using survey weighted univariable regression or the $\chi^2$ test, as appropriate. To assess the relationships between PCOS and BMI with pregnancy loss at Survey 4, logistic regression analyses, adjusted for potential confounding covariates including age, type 2 diabetes (T2DM), hypertension, household income and smoking status, were performed. Two multivariable regression models were analysed; model 1 does not include fertility treatment, whereas model 2 includes fertility treatment. The selection of variables was based on identifying all measured clinical variables of known or suspected prognostic importance for the outcome of interest (and/or exhibiting a $P$-value of $<0.1$ in the univariate analysis). All analyses including calculations of proportions were survey weighted by area of residence to adjust for the deliberate over-sampling in rural and remote areas. All $P$-values were calculated from two-tailed tests of statistical significance with a type I error rate of 5%. All analyses were performed using Stata software version 11.0 (StataCorp, TX, USA).

**Results**

Cross-sectional data from all 8612 young women (aged 28–33) who completed Survey 4 and responded to the question on PCOS were analysed (Fig. 1). The cohort of 478 women reporting PCOS were similar in age to the 8134 not reporting PCOS (mean age 30.5 ± 0.1 years and 30.6 ± 0.02 years, respectively).

**Relationship between BMI and PCOS prevalence**

Overall, the mean BMI was significantly higher in women reporting PCOS ($27.8 ± 0.4$ kg/m$^2$) compared with women not reporting PCOS as previously reported ($24.8 ± 0.1$ kg/m$^2$) ($P < 0.001$) (Teede et al., 2013). Overall, 58% of women with PCOS were overweight or obese compared with 37% of women not reporting PCOS (Fig. 2).

**Contraception use**

Fewer women with PCOS (61%) were using contraception than women without PCOS (79%) ($P < 0.001$, Fig. 1). Among those women using contraception, OCPs or condoms were most common (Table I). The use of most forms of contraception was similar in both groups except for the OCP, which was used less by women with PCOS than without PCOS (35% compared with 44%, $P = 0.002$) (Table I).

**Attempts to conceive**

Of the women who were not currently or recently pregnant and with no history of hysterectomy, tubal ligation or partner vasectomy and not using any contraception, more women with PCOS were trying to conceive (56%) than women without PCOS (45%) ($P < 0.001$, Fig. 1). Of the women who were not using contraception but not trying to conceive, a similar proportion of women reported having male partners.
(39% of women with PCOS compared with 32% of women without PCOS, \( P = 0.31 \)).

**Pregnancy outcomes**

A similar proportion of women with PCOS (44%) and without PCOS (46%) reported having children \( (P = 0.43, \text{Table I}) \). A greater proportion of women with PCOS reported pregnancy loss (miscarriage or stillbirth) \( (20 \text{ versus } 15\%, \ P = 0.003) \) (Table I). Of the women without children, 11% of women with PCOS and 6% of women without PCOS had experienced pregnancy loss \( (P = 0.002) \).

**Multivariable analyses of factors associated with pregnancy loss**

PCOS was associated with pregnancy loss \( (\text{adjusted OR 1.4, 95\% CI 1.1–1.8, } P = 0.02) \) in a multivariable regression model (Table II). However when use of fertility treatment was included in the model (ovulation induction and/or IVF), PCOS was no longer related to pregnancy loss. Fertility treatment use was independently associated with pregnancy loss \( (\text{adjusted OR 3.2, 95\% CI 2.4–4.2, } P < 0.001) \). BMI was also independently associated with pregnancy loss in the overweight and obese groups \( (\text{OR 1.2, 95\% CI 1.04–1.4, } P = 0.02 \text{ and OR 1.4, 95\% CI 1.1–1.6, } P = 0.001, \text{ respectively}) \). There was no significant interaction between PCOS and BMI or PCOS and fertility treatment use observed for this outcome \( (P = 0.30 \text{ and } P = 0.47, \text{ respectively}) \) and therefore further sensitivity analyses were not performed. Age, gestational diabetes, hypertension in pregnancy and smoking were also independently associated with pregnancy loss (Table II). On analysis of miscarriage alone, results were found to be similar to that of a combined outcome of miscarriage and stillbirth.

**Discussion**

The current study of women aged 28–33 years is the first large community-based cohort study to focus on contraception use, pregnancy outcomes and number of children, in women with PCOS. At a mean age of 30.9 years, women reporting PCOS were less likely to be using contraception and more likely to be trying to conceive. Women with PCOS were more likely to report a pregnancy loss; however, PCOS was not independently associated with pregnancy loss. There was no significant difference between the groups in number of children.

Hormonal contraception offers effective therapy in PCOS, targeting irregular menstrual cycles, hirsutism and acne. Yet, we have observed lower rates of hormonal contraception use in women reporting PCOS when compared with women not reporting PCOS. A possible reason for this is that more women with PCOS were trying to conceive and/or had higher fertility concerns. A previous study has similarly reported that women with PCOS may not be concerned about unprotected sex, as they consider their likelihood of unplanned pregnancy to be low \( (\text{Jones et al., 2011}) \). Given that women with PCOS often retain fertility and can conceive spontaneously, it is important that these women are aware of the need for contraception, if pregnancy is not desired.

Many women underestimate the impact of age on fertility \( (\text{Daniluk et al., 2012}) \) and the value of planning earlier family initiation. Whilst infertility is a known complication of PCOS, there are limited large community-based studies exploring rates of trying to conceive.

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**Table I** Contraceptive use and pregnancy outcomes in relation to PCOS status.

<table>
<thead>
<tr>
<th>Contraceptive use</th>
<th>PCOS ( n = 309 ) (%)</th>
<th>Non-PCOS ( n = 5208 ) (%)</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral contraceptive pill</td>
<td>34.8</td>
<td>44.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Implant</td>
<td>3.2</td>
<td>4.4</td>
<td>0.34</td>
</tr>
<tr>
<td>Condoms</td>
<td>29.2</td>
<td>33.1</td>
<td>0.19</td>
</tr>
<tr>
<td>Withdrawal method</td>
<td>8.2</td>
<td>10.8</td>
<td>0.18</td>
</tr>
<tr>
<td>Emergency contraception</td>
<td>2.1</td>
<td>2.1</td>
<td>0.99</td>
</tr>
<tr>
<td>Another method</td>
<td>1.7</td>
<td>4.0</td>
<td>0.03</td>
</tr>
<tr>
<td>No contraception used</td>
<td>39.4</td>
<td>21.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pregnancy outcome</td>
<td>PCOS ( n = 478 ) (%)</td>
<td>Non-PCOS ( n = 8116 ) (%)</td>
<td>( P )-value</td>
</tr>
<tr>
<td>Miscarriages/stillbirths</td>
<td>103 (20.2)</td>
<td>1292 (14.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>Has children</td>
<td>222 (44.4)</td>
<td>4011 (46.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Number of live births</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>256 (55.7)</td>
<td>4105 (53.6)</td>
<td>0.75</td>
</tr>
<tr>
<td>1</td>
<td>103 (21.2)</td>
<td>1691 (21.0)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>72 (15.5)</td>
<td>1557 (17.4)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>32 (6.7)</td>
<td>574 (6.1)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>12 (1.6)</td>
<td>136 (1.4)</td>
<td></td>
</tr>
<tr>
<td>( \geq 5 )</td>
<td>2 (0.2)</td>
<td>49 (0.5)</td>
<td></td>
</tr>
</tbody>
</table>

Values are reported as proportions. All estimates are survey weighted to account for over-sampling of women from rural and remote areas.
In the current study, women aged 28–33 years with PCOS were more likely to be currently trying to conceive. Given that both PCOS and non-PCOS groups were similar in age, the difference in contraception use and proportion trying to conceive may encouragingly reflect that women with PCOS are aware of the risks of infertility and are proactive in planning earlier family initiation. In the setting of PCOS, it is important that women, their partners and clinicians are aware of fertility issues and that education and awareness include an emphasis on optimal timing of family initiation.

The higher prevalence of obesity, metabolic complications, infertility and use of fertility treatment may impact pregnancy outcomes in PCOS. Women with PCOS have previously been reported to have a 3-fold higher risk of early pregnancy loss compared with women without PCOS (Jakubowicz et al., 2002). The current study also suggests that a greater proportion of women with PCOS report pregnancy loss (miscarriage or stillbirth) (20 versus 15%, P = 0.003); however, we advance knowledge in this area by demonstrating that PCOS was not independently associated with pregnancy loss in multivariable regression analysis once BMI and fertility treatment use were taken into account. Also, the rates of early pregnancy loss in this community-based population were lower than previous studies of women selected from PCOS clinic populations or from women receiving treatment for infertility (Jakubowicz et al., 2002). Here, fertility treatment use was independently associated with pregnancy loss (adjusted OR 3.2, 95% CI 2.4–4.2, P < 0.001) and there was no interaction between PCOS and fertility treatment for this outcome.

The current study found that BMI was independently associated with pregnancy loss (adjusted OR 1.02 per BMI unit, 95% CI 1.01–1.03, P < 0.001) and there was no significant interaction between PCOS and BMI observed for this outcome. BMI was also independently associated with pregnancy loss in the overweight and obese groups (OR 1.2, 95% CI 1.04–1.4, P = 0.02 and OR 1.4, 95% CI 1.1–1.6, P = 0.001, respectively). Hence, in the current study, we provide novel insights into the apparent higher prevalence of pregnancy loss in women with PCOS, noting that it may be attributable to greater BMI and fertility treatment use in this population (Teede et al., 2013). Age, gestational diabetes, hypertension in pregnancy and smoking were also independently associated with pregnancy loss (Table II). Gestational diabetes risk is higher in PCOS and this risk factor also contributes to the apparent higher pregnancy loss rates in women with PCOS. Given the impact of BMI on the risk of gestational diabetes (Joham et al., 2013) and pregnancy loss, and the greater propensity for those with PCOS to be overweight, the argument for optimal lifestyle and reducing weight in overweight women with PCOS becomes even more compelling.

The current literature on reproductive outcomes in PCOS is mostly in relation to efficacy of infertility treatments; however, the natural reproductive history of women with PCOS from a community representative sample is not known. Our study shows that there is no difference in number of children between women with and without PCOS aged 28–33 years from our community-based population. Reassuringly, despite the greater need for fertility treatment (Wild et al., 2000; Roos et al., 2011), and increased BMI, women reporting PCOS had similar numbers of children to women not reporting PCOS. This may provide reassurance to those women with PCOS and their families who are likely to harbour concerns regarding fertility and family size.

The limitations of our study include reliance on self-reported data, although this is generic in large prospective community-based cohort studies with thousands of women over multiple time points. However we have previously validated self-reported PCOS diagnosis against menstrual cycle irregularity (Teede et al., 2013). Women with PCOS may have been undiagnosed and therefore included in the non-PCOS group. In the current study, the timing of PCOS diagnosis and timing of

<table>
<thead>
<tr>
<th>Table II</th>
<th>Univariable and multivariable regression analysis of risk of pregnancy loss.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariable regression</td>
</tr>
<tr>
<td></td>
<td>Odds ratio (95% CI) P-value</td>
</tr>
<tr>
<td>PCOS</td>
<td>1.4 (1.1–1.8) 0.003</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.02 (1.01–1.03) &lt;0.001</td>
</tr>
<tr>
<td>BMI &lt; 25a</td>
<td></td>
</tr>
<tr>
<td>BMI 25–29.9</td>
<td>1.3 (1.1–1.5) 0.001</td>
</tr>
<tr>
<td>BMI ≥ 30</td>
<td>1.4 (1.2–1.7) 0.001</td>
</tr>
<tr>
<td>Fertility treatment use</td>
<td>3.2 (2.5–4.1) 0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.2 (1.1–1.2) 0.001</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td>2.4 (1.7–3.4) 0.001</td>
</tr>
<tr>
<td>Type 2 diabetesa</td>
<td>0.3 (0.1–0.8) 0.01</td>
</tr>
<tr>
<td>Hypertension in pregnancy</td>
<td>1.9 (1.4–2.4) &lt;0.001</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>0.9 (0.6–1.4) 0.62</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.4 (1.2–1.6) &lt;0.001</td>
</tr>
</tbody>
</table>

*aReference category
All estimates are survey weighted to account for over-sampling of women from rural and remote areas. Bold indicates P value < 0.05.

*The validity of this result cannot be validated due to small numbers of women with type 2 diabetes.
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pregnancy loss were also not specifically ascertained. BMI from Survey 4 has been used for analysis, but may not correspond to the BMI at the time when a woman experienced pregnancy loss. It should be noted that not all women completing the survey responded to the PCOS question or completed all other questions on the survey. Missing data are noted in the results. However, the impact of attrition on associations between variables in this large cohort study has been found to be minimal (Powers and Loxton, 2010).

The strengths of the current study include the large, unselected community cohort with high baseline and ongoing participation rates; the use of prospective data with limited information bias and a focus on diagnosed PCOS, validated by correlations with PCOS symptoms. A comparison of women who participated in the baseline survey with data from women in the same age range from the Australian census of 1996 showed that the ALSWH participants were reasonably representative of the general population (Brown et al., 1998; Lee et al., 2005).

This is the first study of women with a reported diagnosis of PCOS in a representative, community-based, unselected population, to explore use of contraception and pregnancy outcomes. These data significantly advance our knowledge of the natural history of this common condition. Women with PCOS have lower rates of hormonal contraception use and are more likely to be currently trying to conceive. However, infertility is not universal in PCOS and contraception remains important for women not wishing to conceive. Reported pregnancy loss is higher in PCOS; however, we advance the field here by noting that this risk appears to be primarily related to risk factors for pregnancy loss including BMI, fertility treatment use and gestational diabetes, present in PCOS, rather than an independent effect of PCOS. Reassuringly, the number of children per woman is similar in PCOS and non-PCOS groups, albeit with higher rates of fertility treatment. Understanding the natural history of reproductive outcomes in PCOS is important and the apparent planned earlier family initiation is at the least already occurring in these women at a higher risk of infertility; however, a greater focus is needed on preventing, recognizing and treating risk factors for pregnancy loss in women with PCOS.

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Authors’ roles

H.J.T. was responsible for substantial contributions to the study conception and design, and acquisition of data. A.E.J., S.Z., J.A.B., S.R. and H.J.T. were responsible for the analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published.

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Conflict of interest

None declared.

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