inactivation, or interfere with chromosomal pairing during meiosis (Shelling, 2000).

Of interest is the lower copy number detection rate in our study (4%) compared with the detection rate of 48% in the recent publication by Quilter et al. (2010). Quilter et al. report that one of the 15 women with a CNV had primary amenorrhea. Possibilities to explain the differences in detection rate compared with this study may be differences in the age of onset of POF, or the presence of a positive family history of POF. Quilter et al. (2010) does not provide these demographic details. Further studies in larger numbers of POF patients clinically characterized by age of onset and the presence of a positive family history would help clarify the association between X chromosome CNV and POF.

Funding

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References


The study described by Dudding and colleagues confirms the results of our own work (Quilter et al., 2010), which suggested that submicroscopic copy number variants (CNVs) of the X chromosome may be of significance for the aetiology of premature ovarian failure (POF). They have used both an array of comparative resolution and a patient cohort of similar size to our study. The two micro-duplications they detected were in Xp22.33 and Xq13.3. Although the former is not consistent with our results it is within 5 Mb of one of our novel CNV at Xp22.31, present in two of our patients with micro-duplications. The latter is within another of our reported CNV at Xq13.3–Xq21.33, present in one patient with a micro-duplication. These findings are important as they support the need for more detailed future investigations of the contribution of CNV, and the candidate genes within them, to the development of POF.

The main difference between the two studies was that in ours the frequency of CNV detected was higher (48%) compared with Dudding’s (4%). Although this is a big difference we did carry out Q-PCR to validate our results. This frequency discrepancy may be attributed to differences between the two patient cohorts with ours coming from the UK and theirs from New Zealand. The majority of our patients came from a regional hospital covering a rural area, so it is possible that there may be ancestral relationships of which we are unaware and unfortunately access to family history or samples, was not available for our study. In a comparative unpublished study on a more diverse population carried out within our laboratory, we found 9 of 40 patients with CNV. Of these, six were considered to be non-polymorphic after comparison with the database of common variants and four were on the X chromosome. This illustrates that a more diverse population can give results that are comparable with Dudding et al. (2010) and Aboura et al.’s (2009) results, and is worth taking into consideration for any future studies. In addition, 6 of 42 of our patients had primary amenorrhea and 36 had secondary amenorrhea but further clinical information was limited. Dudding et al. were able to record more clinical details, including age of onset of POF and family history. We agree with these authors that any future studies on large numbers of POF patients should include the recording of extensive clinical details, including where possible family histories and samples, so that patients can be subtyped where necessary. It may then become clearer if a pattern emerges linking CNVs to certain subcategories of ovarian failure.

Funding

This work was funded by the Department for Environment, Food and Rural affairs (DEFRA).
No influence of body mass index on first trimester fetal growth

Sir,

We read with interest the recent article on the effect of obesity on first trimester fetal growth (Sarris et al., 2010). Using a univariate model, the BMI was found to be uncorrelated with first trimester growth. However, the authors did not examine potential interactions between other maternal characteristics in a multivariate model. BMI is a derived variable from maternal weight and height. Its correlation with body weight is 0.87 in women, although it is minimally correlated with height (Gallagher et al., 1996). Its correlation with percent body fat changes according to age and a formula is available to estimate the body fat percent from the BMI, age and sex (Deurenberg et al., 1991). Another potential confounding factor is the well-known correlation of high BMI with menstrual irregularities which may have a bearing on the gestational age assignment in obese women. Ideally, a multivariate analysis should have been performed in this study, which would have greater power to detect an effect of body mass index on early fetal growth.

The second issue is why a univariate (rather than a multivariate) analysis was performed. We have previously examined potential interactions between maternal characteristics other than BMI (maternal age, ethnicity, vaginal bleeding, parity, pain, previous miscarriage and anxiety) and early fetal growth (Bottomley et al., 2009) in univariate and multivariate models. The BMI was not available to us at that time and we obtained this later, and presented it in the current study. As univariate analysis showed no association between BMI and fetal growth, whether modelled using BMI as a continuous variable or as a categorical variable using the WHO criteria, we did not feel multivariate analysis was appropriate.


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<table>
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<tr>
<th>BMI group</th>
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<tr>
<td>&lt;18.50</td>
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The references for this reply are:


References


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Reply: No influence of body mass index on first trimester fetal growth

Sir,

We thank Drs Mongelli and Condous for their interest and comments on the reporting on the effect of BMI on first trimester fetal growth (Sarris et al., 2010).

In our study, women were only included if they had a known last menstrual period with a regular 26–30 day cycle. A review of the menstrual cycle length (in days) of the women within each BMI category showed that there were no significant differences in cycle length (table below, P = 0.86). This demonstrates that in our group of women there were no menstrual irregularities associated with higher BMI and menstrual cycle length was not a confounding factor.

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References

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