

# Effect of ethnicity on live birth rates after *in vitro* fertilisation or intracytoplasmic sperm injection treatment

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**Objective** To assess the relationship between the ethnicity of women and the clinical success of *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) treatment.

**Design** Observational cohort study.

**Setting** Nottingham University Research and Treatment Unit in Reproduction (NURTURE), UK.

**Sample** A total of 1517 women, of which 1291 were white Europeans and 226 belonged to an ethnic minority group. All the women were undergoing their first cycle of assisted reproductive technology (ART) between 2006 and 2011.

**Methods** All of the women underwent their first cycle of ART between 2006 and 2011.

**Main outcome measures** Live birth rates following IVF or ICSI treatment.

**Results** Although pre-treatment ovarian reserve variables [mean age, basal follicle stimulating hormone (FSH), and total antral

follicle count] were significantly favourable in the ethnic group, the live birth rates were significantly lower in this group (35%) compared with the white European group (43.8%) (relative risk 0.8; 95% CI 0.66–0.97). On logistic regression analysis, ethnicity was an independent predictor of live birth rate (OR 0.688; 95% CI 0.513–0.924). After controlling for the other independent variables (age and FSH), the significant association between ethnicity and live birth rate remained strong (OR 0.591; 95% CI 0.425–0.822) on multivariate logistic regression analysis.

**Conclusions** Live birth rates following IVF or ICSI treatment were significantly lower in the ethnic minority group compared with white European women, which suggests that ethnicity is a major determinant of live birth following IVF treatment.

**Keywords** ART births, assisted conception, embryo, ethnic background, ICSI, infertility, IVF.

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## Introduction

In the western world, ethnic minorities form a significant proportion of couples undergoing *in vitro* fertilisation (IVF) treatment. Whereas couples should be informed of their realistic chances of success based on data applicable to their own individual status, the data on the relationship between ethnicity and IVF outcome is limited. In the literature, a scarce number of reports were published on the relationship between ethnic background and IVF outcome. Self-identified Asian infertile women in the USA were reported to have lower clinical pregnancy and live birth rates compared with white women.<sup>1</sup> Other authors in the

USA have also reported that white women had more biochemical pregnancies and live birth rates compared with women from ethnic minorities, including Hispanic, Asian and Afro-Caribbean women.<sup>2–7</sup>

In the UK, two studies that were published in the mid and late 1990s reported differing observations in relation to women of South Asian Indian background undergoing IVF compared with white European populations.<sup>8,9</sup> In two separate studies, again in the USA, lower live birth rates were reported in South Asian Indian women compared with white women, despite their younger age and lower basal follicle stimulating hormone (FSH) levels.<sup>10,11</sup> Less than a handful of studies reported no differences in assisted

reproductive technology (ART) outcome between Hispanic and white women,<sup>12</sup> or between African-American and white women.<sup>13,14</sup> In a separate Spanish study using oocyte donation, differences in ART outcome were reported between black and white European women, but no difference was observed between South-East Asian and white European women<sup>15</sup>; however, no live birth data were reported. Whereas large studies, mostly from the USA, reported an association between race/ethnicity and ART outcome,<sup>16</sup> studies from outside the USA, especially from the UK, have reported conflicting results. The latter studies are mostly of small sample size and are more than a decade old, when success rates were lower compared with current success rates.

In this current study, we aimed to investigate the relationship between ethnicity and IVF outcome in a large IVF population receiving treatment over a period of 5 years between 2006 and 2011. The IVF outcome, including live birth rates between ethnic minority and white European groups, were compared. The different ethnic minorities were further subcategorised, and the differences in outcome between the subpopulation groups, such as South-East Asian, African-Caribbean, and Middle Eastern, were also studied.

## Methods

### Experimental design

In this observational cohort study we aimed to recruit all women undergoing their first cycle of IVF or intracytoplasmic sperm injection (ICSI) treatment. This study was performed in the UK at the Nottingham University Research and Treatment Unit in Reproduction (NURTURE), and included all women who met the above criterion between 2006 and 2011. All of them were undergoing their first cycle of ART. All couples were asked to complete their demographic profile, including their ethnic origin, following the policy of the unit. White women were identified as white Europeans. Other ethnic groups undergoing treatment were South-East Asians (from India, Pakistan, Bangladesh, and Sri Lanka), Middle-Eastern Asians, and African-Caribbeans. The study was approved by the institutional review board. The process of data extraction was consistent with the data protection rules.

### Treatment protocol

All participants underwent IVF/ICSI treatment using a standard long agonist or antagonist protocol, depending on ovarian reserve tests, as previously described.<sup>17</sup> For the long protocol, down-regulation with gonadotrophin-releasing hormone (GnRH) agonists [500 µg/day of buserelin (Suprefact®; Aventis Pharma, Kent, UK) or 800 µg/day of nafarelin (Synarel®; Pharmacia, Milton Keynes, UK)] was started in the midluteal phase of the menstrual cycle. Pitui-

tary desensitisation was confirmed 2 weeks later by an endometrial thickness of less than 5 mm and no ovarian activity evident on transvaginal ultrasound, in association with an estradiol level <200 pmol/L; ovarian stimulation was then commenced. In an antagonist protocol, ovarian stimulation is commenced on day 2 of the menstrual cycle by introducing antagonists (0.25 mg of cetrorelix; Cetrotide® [cetrolix acetate for injection, Merck Serono Pharmaceuticals Ltd, Feltham, UK]) from day 5 of ovarian stimulation. The starting daily doses of gonadotrophins [recombinant FSH (rFSH) or human menopausal gonadotrophins (HMGs)] were 150–450 iu, depending on the woman's age and ovarian reserve test.

The women were monitored for follicular development by a series of transvaginal ultrasound and serum estradiol measurements from the fifth or sixth day of stimulation. When there were three follicles measuring 18 mm or more in diameter, human chorionic gonadotrophin [hCG; 6500 iu Ovitrelle® (Merck Serono Pharmaceuticals Ltd, Feltham, UK) or 10 000 iu of Pregnyl® (Organon Laboratories Ltd, Cambridgeshire, UK)] was administered, and oocyte retrieval was performed 36 hours later. Transvaginal ultrasound-guided oocyte retrieval was performed under sedation or general anaesthesia. The oocytes retrieved were fertilised by IVF or ICSI treatment, depending on the results of the semen analysis or the quality of the semen obtained on the day of oocyte retrieval. For women with partners considered to have normal semen parameters, IVF was performed by mixing groups of collected oocytes with a sperm suspension containing 150 000 motile sperm/ml overnight in the incubator. For women having ICSI, meiotic maturity was assessed after denudation and only mature oocytes with a visible polar body were injected with one sperm following its mechanical immobilisation. Fertilisation as determined by the presence of two pronuclei (2 PN) was assessed at 18–20 hours after IVF or ICSI. Depending on the number of embryos that develop, a maximum of two embryos were transferred into the uterus at days 2, 3, or 5 after insemination by IVF or ICSI. Single embryo transfer was discussed with the women and offered in line with the normal practice of the clinic. From the day of embryo transfer, luteal phase support was started using progesterone pessaries (400 mg twice a day vaginally; Cyclogest®; Shire Pharmaceuticals Ltd, Basingstoke, Hants, UK), and the serum hCG level was measured 16 days later to determine the outcome (biochemical pregnancy). A transvaginal ultrasound was arranged 3–4 weeks later to confirm the viability of the pregnancy (clinical pregnancy) if the biochemical test was positive (hCG > 50 iu/L). A repeat ultrasound scan was also performed at 12 weeks of gestation to ensure that the pregnancy remained viable (continuing pregnancy). All pregnant women were followed-up to know the eventual outcome of their

pregnancies, and a live birth is thus defined as a viable infant born after 24 weeks of gestation. The miscarriage rate is calculated as the proportion of pregnancies lost before 24 weeks of gestation.

### Statistical analysis

Data recorded in a Microsoft EXCEL spreadsheet were analysed using SPSS 16 for WINDOWS (Statistical Package for Social Sciences; IBM, Chicago, IL, USA). The primary outcome was live birth. Secondary outcomes included clinical pregnancy rates, implantation rates, and ovarian response, as measured by the number of oocytes retrieved. The Levene test of homogeneity of variances and Kolmogorov–Smirnov test of normality were performed to choose the appropriate statistical test. Continuous data were analysed by a Student's *t*-test or by the Mann–Whitney *U*-test, depending on the data distribution. Chi-square and Fisher exact tests were performed to analyse the relationship between two categorical variables. When  $P < 0.05$ , the difference was considered to be statistically significant in all statistical tests. Logistic regression analysis was used to assess the association of ethnicity and other demographic variables with live birth rates. To estimate the independent contribution of ethnic minority group to treatment outcomes, multivariate logistic regression analyses were performed. Potential confounding factors found to be statistically significant in univariate analyses and others generally regarded as clinically significant were included in the models. Backward conditional elimination was used to generate the most parsimonious model.

## Results

Of the 1517 women who began ovarian stimulation treatment, 23 did not reach the egg-collection stage because of poor ovarian response, 11 developed an excessive response, and therefore embryo transfer was deferred, with the freezing of all embryos to reduce the risk of severe ovarian hyperstimulation syndrome (OHSS), five had no eggs collected at the oocyte retrieval stage, nine had no mature eggs, and therefore could not proceed with ICSI treatment, 39 had failed fertilisation, and 35 had failed cleavage or failed development of blastocysts. Eventually, 1395 women had embryo transfer.

Analysis was performed in a total of 1517 women, of which 1291 (85.1%) were white Europeans and 226 (14.9%) belonged to an ethnic minority group. Table 1 illustrates a comparison of the clinical, endocrine, and ultrasound variables between the two groups. Whereas pre-treatment ovarian reserve variables (mean age, basal FSH, and total antral follicle count) were significantly favourable in the ethnic group (Table 1), the stimulation characteristics (dose of gonadotrophins and duration of stimulation) and embryology data (number of eggs retrieved, fertilisation and cleavage rates, single and double embryo transfer rates, and blastocyst transfer rates) were similar in both groups (Table 2). However, the live birth rates were significantly lower in the ethnic minority group, as were the biochemical pregnancy rates, clinical pregnancy rates, and implantation rates (Figure 1A; Table 2). All these outcomes were calculated per cycle started.

**Table 1.** Comparison of baseline clinical, endocrine, and ultrasound characteristics between ethnic and white European groups (data presented as  $\pm$  SD and range or%)

Variables	Ethnic group ( <i>n</i> = 226)	White European group ( <i>n</i> = 1291)	<i>P</i>
Age	33.3 $\pm$ 4.5 (23–44)	34.4 $\pm$ 4.3 (21–45)	<0.001
Body mass index (kg/m <sup>2</sup> )	25.8 $\pm$ 4.2 (17.0–35.0)	24.3 $\pm$ 3.5 (18.0–36.0)	<0.001
Basal FSH (iu/L)	6.0 $\pm$ 2.4 (0.1–14.2)	6.6 $\pm$ 2.5 (0.9–14.9)	<0.01
<b>Cause of infertility</b>			
Male	92 (40.5%)	441 (34.2%)	<0.02
Female	57 (25.1%)	447 (34.6%)	
Combined	40 (17.7%)	152 (11.8%)	
Unexplained	37 (16.7%)	251 (19.4%)	
<b>Type of infertility</b>			
Primary	179 (71.9%)	932 (72.2%)	0.924
Secondary	64 (28.1%)	359 (27.8%)	
<b>Smoking</b>			
Non-smoker	223 (98.6%)	1180 (91.4%)	<0.001
Smoker	3 (1.4%)	111 (8.6%)	
Duration of infertility (months)	50.5 $\pm$ 36.5 (10–246)	42 $\pm$ 26.7 (2–240)	<0.001
Total antral follicle count	20.4 $\pm$ 12.4 (1–77)	17.7 $\pm$ 9.8 (3–91)	<0.01

**Table 2.** Mean  $\pm$  SD (range) values for the stimulation characteristics, embryology data, and outcome variables

Variables	Ethnic group ( <i>n</i> = 226)	White European group ( <i>n</i> = 1291)	<i>P</i>
Starting daily dose of gonadotrophins	247 $\pm$ 109.8 (75–450)	245.7 $\pm$ 68.5 (75–450)	0.828
Total dose of gonadotrophins used	2896.3 $\pm$ 1905.3 (750–6300)	2733.8 $\pm$ 1306.2 (900–7500)	0.178
Peak estradiol level (pmol/L)	7933 $\pm$ 4634.6 (11–21834)	7883.9 $\pm$ 5319.7 (79–74063)	0.906
Number of follicles aspirated	14.2 $\pm$ 7.6 (0–40)	14.5 $\pm$ 8.5 (0–59)	0.587
Number oocytes retrieved	11.5 $\pm$ 7.3 (0–50)	11.4 $\pm$ 6.4 (0–58)	0.777
Number of mature oocytes	9.4 $\pm$ 5.9 (0–35)	9.5 $\pm$ 5.5 (0–49)	0.771
Fertilisation rate (%)	63.3 $\pm$ 27.2	66 $\pm$ 25.1	0.147
Cleavage rate (%)	95.7 $\pm$ 14.9	95.7 $\pm$ 13.2	0.966
Blastocyst rate (%)	40.2 $\pm$ 18.7	42.9 $\pm$ 21.9	0.466
<b>Number of embryos transferred</b>			
1	66 (32.4%)	414 (34.8%)	0.656
2	138 (67.6%)	777 (65.2%)	
<b>Days of embryo transfer</b>			
2 or 3 days	166 (81.4%)	936 (78.6%)	0.367
5 days	38 (18.6%)	255 (21.4%)	
Over all implantation rate*	22.6%	37.4%	<0.01
Biochemical pregnancy rate	97 (42.9%)	712 (55.2%)	0.001
Clinical pregnancy rate	87 (38.5%)	619 (47.9%)	0.009
Live birth rate	79 (35.0%)	566 (43.8%)	0.013

\*Implantation rate is measured as the number of fetal hearts measured over the number of embryos transferred.

On univariate logistic regression analysis, ethnicity was an independent predictor of live birth rate (OR 0.688; 95% CI 0.513–0.924;  $P \leq 0.02$ ). Age and FSH were the other independent predictors of live birth among all the variables studied (Table 3). On multivariate analysis incorporating age, FSH, and ethnicity, after controlling for age and FSH, ethnicity remained as a significant predictor of live birth (OR 0.591; 95% CI 0.425–0.822;  $P \leq 0.01$ ; Table 3), with its association strengthened further as indicated by a shift of odds ratio from 0.688 to 0.591.

Within the ethnic minority group, three distinct subgroups were identified: South-East Asian ( $n = 182$ ); African-Caribbean ( $n = 30$ ); and Middle Eastern ( $n = 14$ ). The live birth rates in the South-East Asian, African-Caribbean, and Middle-Eastern populations were 38% (69/182), 23.3% (7/30), and 21.4% (3/14), respectively, in contrast to the live birth rates in the white European population (43.8%; 566/1291; Figure 1A,B). A pairwise comparison revealed similar live birth rates between the subgroups and white European population, although there was a trend towards decreased live birth rate in ethnic minority groups, particularly in the African-Caribbean and Middle-Eastern Asian populations. The relative risks for the South-East Asian, African-Caribbean, and Middle-Eastern populations were 0.86 (95% CI 0.71–1.05;  $P = 0.15$ ), 0.53 (95% CI 0.28–1.02;  $P = 0.06$ ), and 0.49 (95% CI 0.18–1.34;  $P = 0.16$ ), respectively. On regression analysis, ethnicity was not a significant predictor of successful IVF outcome (live birth)

when only the South-East Asian population (a single large ethnic minority group) was included in the analysis (OR 0.78; 95% CI 0.57–1.08).

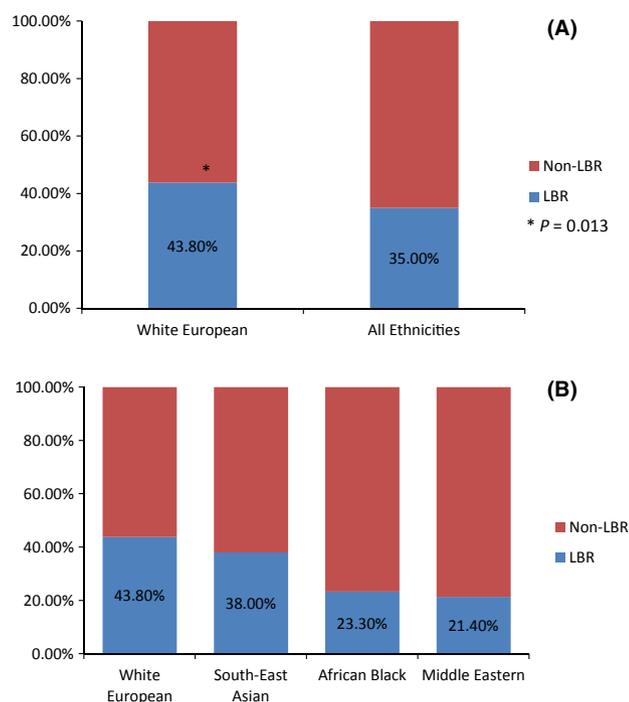
## Discussion

### Main findings

The data in this study indicate that live birth rates, clinical pregnancy rates, and implantation rates following IVF treatment are significantly lower in the ethnic group compared with white European women, and it proves that ethnicity may be a major determinant of live birth following IVF treatment. Upon subgroup analysis, the success rates were lower in the South-East Asian, African-Caribbean, and Middle-Eastern populations, in descending order; however, the live birth rates in these different subgroups were not statistically different from the live birth rates in the white European population, possibly because of the small sample sizes of each subgroup. In this work we tried to narrow down the category of the Asian population to South-East Asians and Middle-Eastern Asians so that the analysis reflects a more homogeneous population, who are more likely to respond uniformly to ART treatment.

### Strengths and limitations

As this study used a consecutive unselected population, there were differences observed in the demographic profile between the groups with most factors (age, smoking status,



**Figure 1.** Live birth rates (LBRs): (A) white European women versus women from all ethnic minorities ( $P = 0.013$ ); (B) white European women versus women from South-East Asian, African-Caribbean, and Middle-Eastern Asian groups.

**Table 3.** Logistic regression analysis of the baseline characteristics, for the prediction of live birth.

Parameters	Odds ratio	95% CI	P
<b>Univariate analysis</b>			
Age	0.937	0.915–0.959	<0.001
Body mass index (kg/m <sup>2</sup> )	0.977	0.940–1.017	0.254
Basal FSH	0.933	0.881–0.989	<0.02
Smoking	0.605	0.342–1.068	0.083
Duration of infertility	0.997	0.992–1.002	0.259
Total antral follicle count	1.012	0.998–1.026	0.087
Ethnicity	0.688	0.513–0.924	<0.02
<b>Multivariate analysis of all the significant variables of univariate analysis</b>			
Age	0.944	0.915–0.974	<0.001
Basal FSH	.939	0.886–0.995	<0.05
Ethnicity	0.591	0.425–0.822	<0.01

and antral follicle count), favouring the ethnic minority groups. Despite this, IVF/ICSI success rates were lower in the ethnic minority group. Besides using a consecutive unselected population analysed only for the first treatment cycle, another major strength of our study is that we have reported on live birth rates rather than just the pregnancy

rates. The major aim of all couples undergoing any fertility treatment is to achieve a healthy baby, and the results from this study will help us to counsel couples from the ethnic minority groups appropriately, as their success rates may match the overall success rate of the unit. Furthermore, our study population, with 85.1% white Europeans and 14.9% from ethnic minorities, reflects the typical UK population (85.4% white Europeans and 14.6% ethnic minorities), according to the Office for National Statistics in the UK.<sup>18</sup> Although the sample size of the South-East Asian population ( $n = 182$ ) in our study was moderate, the corresponding sizes of the African-Caribbean ( $n = 30$ ) and Middle-Eastern ( $n = 14$ ) populations were very small for providing meaningful data on subgroup analysis for counselling women from those ethnic backgrounds, and a larger data set is needed for this purpose.

### Interpretations

The data in this study agree with most other publications, and notably with the work by Purcell and colleagues reporting a significantly low live birth rate compared with the white population in the USA.<sup>1</sup> Although this study reported results for the Asian population as a whole, we have also individually reported the results for the South-East Asian and Middle-Eastern Asian populations separately. Whereas there are other reports comparing success rates in South-East Asian and white populations in the UK,<sup>2,8,9,19</sup> two have reported significantly lower pregnancy rates in the South-East Asian population,<sup>9,19</sup> with the other two reporting similar pregnancy rates.<sup>2,8</sup> Whereas the study by Palep-Singh et al.<sup>19</sup> exclusively looked at a selected population with polycystic ovary syndrome (PCOS), the other studies reported on smaller sample sizes. In contrast, our study used unselected women with a larger sample size, and included only the first cycle of IVF/ICSI treatment, which would have limited potential selection and treatment bias.

Observed differences of treatment outcome in the ethnic minority group may be reflective of true biological differences, which may primarily be related to lifestyle factors, socio-economic status, or some unknown factors. Whereas genetic background is a potential determinant of quantitative and qualitative ovarian reserve, and subsequent IVF outcome, variation in environmental exposures and lifestyle and cultural factors could be influencing the reproductive outcomes. It is interesting to note that ovarian response, as assessed by the number of oocytes retrieved, and peak estradiol levels, fertilisation rate, embryo cleavage rate, blastocyst development rate, and the number of embryos transferred were similar between the ethnic and white European groups. However, the implantation rate was significantly lower in the ethnic minority group, and this was consequently reflected in the live birth

rates. The reason for the reduced implantation rate and subsequent reduced outcome in the ethnic minority group is unclear, although this points to a need for further investigation, specifically into endometrial receptivity. It is extremely unlikely that genital infections, such as tuberculosis, which are more prevalent in Asian and African countries, may have played a role in the reduced endometrial receptivity, as most of the ethnic minority population are first or later generations, and therefore have very limited exposure to such infections. There may be other reasons, with an increased prevalence of certain pathologies such as PCOS and uterine fibroids in the ethnic population, as these pathologies are known to adversely influence endometrial receptivity. In summary, the strong association between ethnicity and IVF outcome may be related to various factors; however, a true direct causal effect of ethnicity on IVF outcome is difficult to establish until a large prospective observational study, controlling for lifestyle factors, socio-economic status, and other possible factors, including various pelvic pathologies, demonstrates a strong consistent association.<sup>20</sup>

Although there is a reduction in live birth rates in the ethnic minorities compared with their white European counterparts following IVF treatment, the results are not favourable for Asians following intrauterine insemination (IUI) either. In a study on IUI following ovarian stimulation, Lamb et al.<sup>21</sup> showed that Asian women had a 2.8% reduction in pregnancy rate compared with their white counterparts: 40% of the women who sought treatment had more than 2 years of infertility, whereas only 26.7% of white women had a duration of more than 2 years of infertility. Hence Asian women in general should be motivated to seek treatment earlier to improve their pregnancy rates, as age is a well-established determinant factor for treatment outcome. It is reassuring to note that fecundability and spontaneous conceptions were similar between Asian and white populations in one study.<sup>22</sup> This may indicate that reproductive physiology and implantation are not different in natural cycles, in contrast to superovulated and supra-physiological cycles during ART.

## Conclusion

The data in this study indicate that live birth rates, clinical pregnancy rates, and implantation rates following IVF treatment are significantly reduced in the ethnic group compared with white European women, which suggests that ethnicity is a major determinant of live birth following IVF treatment. Upon subgroup analysis, success rates remain lower in the South-East Asian, African-Caribbean, and Middle-Eastern populations, in descending order, than in the white European population, but these differences were not statistically significant, possibly because of the

small sample sizes. Patients undergoing subfertility treatment have various emotions, ranging from hope and cautious optimism to anxiety and frustration. Hence it is important that women are well informed about their realistic probabilities of a positive outcome with fertility treatment. Meticulous data collection and analysis for each ethnic group in each fertility unit can help provide appropriate counselling to women from ethnic minority groups. Further research is needed to estimate the degree of variation in success rates of IVF treatment from a very large database. Modifications in clinical strategies to bring about equivalent success rates among all ethnic groups can be achieved after the relationship between ethnicity and IVF outcome is better understood.

## Disclosure of interests

The authors declare that they have no competing interests.

## Contribution to authorship

K.J. analysed the data, interpreted the results, and wrote the article. D.P. prepared and discussed the data. J.H. generated the clinical and laboratory data. B.K.C. discussed aspects of reproductive physiology and edited the article. W.E.M. conceived the project, interpreted the results, and wrote the article. All authors read and approved the final version of the article.

## Details of ethics approval

Approval for this study of the relationship between ethnic background and clinical outcome after ART was obtained on 18 June 2012 from the Research Ethics Committee of the East Midlands, UK (ref. no. 12/EM/0202).

## Funding

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## Commentary on 'Effect of ethnicity on live birth rates after *in vitro* fertilisation or intracytoplasmic sperm injection treatment'

Major differences in fertility exist between breeds within the same livestock species. In humans, large variations in sperm count have been described for different ethnicities. With all the morphometric and genetic variation between ethnic groups, is it not likely that fertility might also vary significantly between different populations, despite all living humans belonging to one single species? Would not such variation also affect the chance of live birth after *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI)?

The setting of a single IVF centre treating infertile couples with different ethnic backgrounds but with a similar environmental exposure constitutes a putatively ideal playground to tackle the issue of differences in IVF outcome between ethnicities. In the current issue of *BJOG* Jayaprakasan and colleagues report an elaborate analysis of a cohort of 1517 women undergoing their first IVF or ICSI cycles. Within this cohort 1291 (85%) women were classified as white European, whereas 182 (12%), 30 (2%), and 14 (1%) women were classified as being of South-East Asian, African-Caribbean, and Middle-Eastern origin, respectively. The authors conclude from their analysis that ethnicity is independently associated with the likelihood of live birth after IVF treatment. The confounding factors assessed were female age, body mass index (BMI), basal follicle stimulating hormone (FSH), smoking, duration of infertility, and antral follicle count (AFC).

Observational studies draw inferences about the effect of an exposure on subjects, where the assignment of subjects to groups is observed rather than manipulated (e.g. randomised). Therefore, observational studies can rarely convincingly

demonstrate cause-and-effect phenomena because of the issue of confounding. For the critical reader it is therefore mandatory to always scrutinise the results from observational research to determine whether alternative explanations for the study results exist.

In the present analysis, differences between groups in socio-economic background, promiscuity, previous genital tract infections, incidence of genital tuberculosis, drug abuse, consanguinity, number and type of previous (less costly) conservative treatment attempts, etc. are all potential confounding factors of the likelihood of live birth. These confounding factors could not be assessed. Is it possible that such confounding could – at least partly – also account for the finding that African-Caribbean and Middle-Eastern women had a much worse outcome compared with South-East Asian and white European women?

From a methodological point of view it is noteworthy that the sample sizes are not well balanced between the groups compared, and that the numbers of subjects in the ethnic minority groups are rather small. This prevents the generation of precise estimates of effect sizes. Accordingly, statistical significance is only achieved when all ethnic minority groups are pooled as if they were one group, and when the analysis is artificially limited to a single comparison (e.g. all white European women versus any women from ethnic minorities), despite major differences in outcomes between individual ethnic groups.

So is belonging to an ethnic minority within an industrialised western European setting indeed causal for worse IVF outcomes, independent of other anamnestic, socio-economic, and general health factors? This question unfortunately remains open, but Jayaprakasan and colleagues have provided an important contribution to this field of research and have, hopefully, stimulated others for further investigation. Consistency in findings observed by other IVF groups in other industrialised countries with different samples would certainly fortify the concept of causality in this context.

### **Declaration of interests**

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