Epidemiology and management of infertility: a population-based study in UK primary care

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\textbf{Background.} Our current knowledge of the epidemiology of infertility is limited and outdated. Health care provision for infertility in the UK attracts public interest because of restrictions on access to services.

\textbf{Objective.} To describe the incidence, prevalence, referral patterns and outcomes of infertile couples, presenting in general practice in UK.

\textbf{Methods.} A population-based retrospective observational outcome study of infertile couples from general practices in Northumberland, Tyne and Wear, UK (population 1 043 513). Outcome data at 1 year were collected on all couples who presented to their GP between the 1st January 2005 and 30th June 2006 with a fertility problem.

\textbf{Results.} Thirty-four per cent of general practices in the study area contributed data (population 404 263). The incidence of infertility was 0.9 couples per 1000 general population. The average age of women was 31 years, and the average time attempting conception was 18 months. Treatment end points for half of all couples were \textit{in vitro} fertilization (IVF) or intracytoplasmic sperm injection (ICSI). Over half of the couples in the study were not eligible for National Health Service (NHS) fertility treatment on social criteria. At 12 months, 27\% of all couples in the study achieved a pregnancy spontaneously and a further 9\% with treatment.

\textbf{Conclusions.} Infertile women present to their GP later in life compared with 20 years ago, and after a shorter period of infertility. Half of the couples required treatment with IVF or ICSI. Adopting the British Fertility Society recommendation of allowing couples, where one or both partners has a child in a previous relationship, will result in an additional 26\% of infertile couples becoming eligible for NHS fertility treatment.

\textbf{Keywords.} Epidemiology, family practice, infertility, primary care.

\section*{Introduction}

In the UK, \(~1\) in 7 couples (14\%) will experience difficulty in conceiving.\textsuperscript{1–3} Comparable societies report rates between 8\% and 20\%.\textsuperscript{4–6} The annual incidence of infertility is estimated at 1.2 couples per 1000 total general population.\textsuperscript{1} For an average general practice with 6000 patients, this equates to \(~7\) couples presenting with a fertility problem each year.

Common causes of infertility are male infertility, ovulatory disorders, tubal disorders and unexplained infertility. Male infertility is identified as a cause in 19–57\% of all infertile couples.\textsuperscript{1,4,7,8} Estimates of the prevalence of ovulatory disorders vary from 21\% to 32\%, 14\% to 26\% for tubal disorders and 5\% to 6\% for endometriosis.\textsuperscript{1,4,7} Estimates of the prevalence of unexplained infertility vary from 8\% to 30\%.\textsuperscript{9} One-third of infertile couples have both male and female contributory causes.\textsuperscript{1,4}

Previous UK epidemiological studies of infertility include a specialist clinic-based study\textsuperscript{1} and two population postal questionnaire studies.\textsuperscript{2,3} Because of selection bias and response bias, respectively, these studies are likely to present an incomplete picture. The
specialist referral system in the UK requires patients seeking medical help for infertility to consult their GP in the first instance. GP records therefore contain correspondence from specialist consultations, as well as primary care consultations and investigations. The aim of this study was to describe the incidence and causes of infertility and the treatments offered to infertile couples presenting to their GP in Northumberland and Tyne and Wear in North-east UK.

Methods

Design and setting
This was a retrospective observational study of the patients of 58 general practices in Northumberland and Tyne and Wear. It was nested within a stratified cluster randomized controlled trial evaluating the use of open access hysterosalpingography in the initial management of infertility in primary care.10

Participants and sampling
With the help of practice administration staff, we extracted completely anonymous data on-site from the computerized GP clinical record on all infertile couples (both partners) who presented to their GP over 18 months between the 1st January 2005 and 30th June 2006. Each couple was followed up for 1 year. Data retrieved from the clinical record were the age of the female, length of time trying to conceive, female and couple fertility status, referral patterns, diagnoses from hospital letters, first-line treatments offered and pregnancy rates. Infertility was defined as failure to conceive after regular unprotected intercourse for at least 12 months, in line with National Health Service (NHS) treatment thresholds for further investigation.11

Outcomes and analysis
Descriptive statistics were examined using parametric and non-parametric tests where appropriate. Dichotomous variables were compared using chi-square and 95% confidence intervals (CIs) presented. A P value of 0.05 or less was considered significant.

Results

Of 173 practices invited to join the study, 71 (41%) agreed to take part. Four practices subsequently withdrew from the study and a further nine practices denied the research team access to their records at the end of the study citing an inability to release practice administrator time. This left 58 practices contributing to the final analysis.

In the 58 practices, 797 infertile couples consulted their GP over the 18-month period seeking advice on their fertility status. In all, 116 couples had been trying to conceive for <12 months at their first consultation and were excluded from the study. The remaining 681 prevalent cases from a population of 72 182 women aged 16–42 years gave an annual prevalence of 6 per 1000 women. Of the 681 infertile couples, 534 couples presented for the first time from a combined total GP list size of 403 263 patients from 58 practices over the 18-month period. These couples represented an annual incidence of 0.9 infertile couples per 1000 total general population. The characteristics of these participants are shown in Table 1.

Infertility diagnoses
A diagnosis was recorded in the GP clinical record at 12 months follow-up for 64% (344/534) of couples (Table 2). Ovulatory and semen problems were equally present but for a significant proportion of cases (38%) infertility was diagnosed as ‘unexplained’. Twenty-four couples (7%) had >1 diagnosis recorded contributing to their infertility. Six per cent (19/344) of diagnoses were made in primary care with the remaining diagnoses made following referral. The place of diagnosis is shown in Table 2.

Patterns of referral and management of infertility
Most infertile couples, 403/534 (75%), were referred for specialist help; 209/403 (52%) being referred to Human Fertilization and Embryology Authority (HFEA) licensed fertility units, 174/403 (43%) being referred to non-HFEA licensed fertility units and 20/403 (5%) referred privately (Fig. 1). Non-HFEA licensed fertility units were equally likely to receive referrals of couples with semen and/or tubal disorder compared to HFEA licensed fertility units [57/174 versus 77/209, chi-square = 0.7, odds ratio (OR) = 0.8, 95% CI 0.5–1.3, P = 0.4]. Sixty-four of 178 couples (36%) who required in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) as a first-line

<table>
<thead>
<tr>
<th>TABLE 1 Characteristics of the study participants</th>
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<tbody>
<tr>
<td>n = 534 incident cases</td>
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<tr>
<td>Age of female</td>
</tr>
<tr>
<td>Years: mean (SD)</td>
</tr>
<tr>
<td>31 (6)</td>
</tr>
<tr>
<td>Trying to conceive</td>
</tr>
<tr>
<td>Months: median (IQR)</td>
</tr>
<tr>
<td>18 (12–24)</td>
</tr>
<tr>
<td>Primary infertility</td>
</tr>
<tr>
<td>Female, n</td>
</tr>
<tr>
<td>292 (55)</td>
</tr>
<tr>
<td>Couple fertility status</td>
</tr>
<tr>
<td>Primary infertility same union: n</td>
</tr>
<tr>
<td>238 (45)</td>
</tr>
<tr>
<td>Secondary infertility same union: n</td>
</tr>
<tr>
<td>153 (29)</td>
</tr>
<tr>
<td>Tertiary infertility: female primary, male</td>
</tr>
<tr>
<td>secondary: n</td>
</tr>
<tr>
<td>52 (10)</td>
</tr>
<tr>
<td>Female secondary, male primary: n</td>
</tr>
<tr>
<td>45 (8)</td>
</tr>
<tr>
<td>Both secondary other union: n</td>
</tr>
<tr>
<td>44 (8)</td>
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<td>SD, standard deviation; IQR, interquartile range.</td>
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</tbody>
</table>
treatment strategy were initially referred to a non-HFEA licensed fertility unit.

Half of the couples, 177/344 (51%), who reached a diagnosis in this study were offered or received IVF or ICSI as a first-line treatment (Table 3). Couples with a diagnosis of semen and/or tubal disorder were significantly more likely to be offered ICSI/IVF compared with couples with all other diagnoses (109/137 versus 68/207, chi-square = 72.0, OR = 8.0, 95% CI 4.7–13.7, P < 0.001). A quarter, 91/344 (26%), were offered ovulation induction with clomifene of which 8/91 (9%) were initiated by the GP. A significant proportion of patients with a diagnosis of unexplained infertility (39/132) were offered no treatment until their infertility had lasted 3 years.

**Pregnancy outcome**

Thirty six per cent (190/534) of all couples achieved a pregnancy at 1 year. Of these couples, 75% (142/190) were independent of treatment (Fig. 2). Pregnancy outcome for all couples at 1 year is shown by place of referral, diagnosis and treatment (Table 4). Women diagnosed with an ovulatory disorder alone were significantly more likely to achieve a pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Primary care</th>
<th>Secondary care</th>
<th>Tertiary care</th>
<th>Private care</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovulatory disorder</td>
<td>3</td>
<td>51</td>
<td>31</td>
<td>2</td>
<td>87</td>
</tr>
<tr>
<td>Tubal disorder</td>
<td>3</td>
<td>32</td>
<td>24</td>
<td>2</td>
<td>61</td>
</tr>
<tr>
<td>Semen disorder</td>
<td>0</td>
<td>25</td>
<td>53</td>
<td>7</td>
<td>85</td>
</tr>
<tr>
<td>Unexplained</td>
<td>13</td>
<td>41</td>
<td>74</td>
<td>4</td>
<td>132</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Twenty-four couples had >1 diagnosis.

**TABLE 2**

Diagnoses of 344 couples by referral destination: number (%)

243 couples had >1 diagnosis.

**FIGURE 1**

Referral routes of couples requiring IVF/ICSI (n = 534). *Secondary care: non-HFEA licensed fertility treatments available (ovulation induction only). Tertiary care: HFEA licensed units with a full compliment of fertility treatments available
compared with women with all other diagnoses at 1 year (30/72 versus 62/272, chi-square = 10.4, OR = 2.4, 95% CI 1.4–4.3, \( P = 0.001 \)). Women with a menstrual cycle >6 weeks were more likely to receive ovulation induction with clomifene as a first-line treatment strategy (31/52 versus 42/334, chi-square = 34.8, OR = 4.7, 95% CI 2.6–8.5, \( P < 0.001 \)). Only 6% (31/534) of all couples in the study had not completed their investigations at 1 year and 10% (55/534) of couples withdrew from investigation or treatment (Fig. 2).

Discussion

Main findings
Three quarters of couples presenting for the first time to their GP with a fertility problem were referred for specialist help. Primary care referrals to HFEA licensed fertility units and non-licensed tertiary fertility units were approximately equal but one-third of couples referred to the latter required onward referral for IVF or ICSI. Of all, 55% of couples had a child in the current or a previous relationship. This is the most common social exclusion criterion for withholding of treatment applied by Primary Care Trusts in the UK.\(^{12}\) Of the 534 couples in the study, 190 achieved a pregnancy of which 75% were independent of treatment. Of those couples who reached a diagnosis, half (51%) were offered or received IVF or ICSI as a first-line treatment. A quarter (26%) were offered ovulation induction with clomifene, which in a small number of cases was initiated by a GP.

Strengths and weaknesses
The data for this study were extracted from GP clinical records, which tend to be a complete record of an individual’s health care over time. Records in secondary and tertiary care services were not accessed, though correspondence from fertility clinics was available in the GP clinical record. Only one practice failed to fully computerize the clinical patient record necessitating a search of the manual records. A third of all practices in Northumberland, Tyne and Wear, participated in the study with a representative mix of small and large, rural and urban practices. One of the difficulties in generating epidemiological estimates is choosing an appropriate numerator and denominator for any rate. For the incident rate, the numerator of women aged 16–42 represents a reasonable fertile population similar to that used by Hull et al.\(^{1} \) The youngest woman in this study was aged 19 years. The denominator of total general population was chosen to give comparable statistics with the landmark work

![Diagram](https://academic.oup.com/fampra/article-abstract/26/4/269/534703/Downloaded-by-guest-on-08-November-2018)
of Hull et al., as well as a workload estimate for general practice.

Comparison with existing literature
Women in this study were older, with a shorter duration of infertility, than those in a 1985 survey (31 years versus 28 years; 23 months versus 29 months), suggesting that British women are delaying the start of their families and are then seeking help sooner. The annual incidence, however, has remained stable over this period at one couple per 1000 total general population, as has the lifetime prevalence of 14%. Patient referral patterns and outcomes for infertile couples presenting to GPs in the UK have not been previously described. However, three studies have described the clinical practice of GPs in the initial assessment of infertility, each demonstrating that they investigate approximately half of all couples that present. Our finding that ovulatory disorders and semen problems each accounted for one-quarter of all cases, with tubal problems accounting for one-fifth and unexplained infertility for one-third, is comparable with earlier studies. A large proportion of couples required treatment with IVF or ICSI, reflecting the previously reported 3-fold increase in the use of IVF and ICSI over the last decade, though NHS access to assisted reproduction remains variable throughout the UK.

Implications for future research and clinical practice
The British Fertility Society has recommended that NHS treatment be extended to same sex couples and couples where one partner has a child in a previous relationship. If these recommendations were adopted, an additional 26% of all infertile couples would be eligible for assisted reproduction (Table 1).

At the same time, there is evidence of inefficient use of services with patients being misdirected to HFEA licensed fertility units (tertiary care) that do not require IVF/ICSI and conversely patients to non-HFEA licensed fertility units (usually secondary care) with blocked tubes and semen problems that do require IVF/ICSI (Fig. 1). Referral pathways, to either HFEA licensed fertility units or non-HFEA licensed fertility units, are currently driven by commissioning arrangements and not the needs of the infertile couple. These ‘misdirected’ referrals by GPs are compounded by widespread lack of access to tubal assessment in primary care and limited interest among GPs in managing the infertile couple. Additionally, only 5% of couples in this study were referred privately by GPs despite our knowledge that 70% of IVF cycles in the UK are performed privately, suggesting that a significant proportion of ineligible couples are referred from general practice ‘inappropriately’ into NHS fertility services. Nevertheless, GPs could play a significant role in infertility management, initiating a more comprehensive initial assessment including open access tubal assessment and directing referrals more efficiently to the service required by infertile couples.

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Declaration

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Conflicts of interests: none declared.

References