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Factors associated with subfertility among women attending an antenatal clinic in Hull

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Abstract

Objectives—To identify lifestyle factors associated with subfertility (time to pregnancy >12 months) among women attending an antenatal clinic, and to determine whether this changed from 2001 to 2007.

Methods—Waiting-room surveys administered in 2001 and 2007.

Results—There were significant changes in lifestyle factors between 2001 and 2007, including such factors as previous contraceptive use and obesity, smoking, alcohol and caffeine intake of both partners. All changes were in the direction favourable to health and fertility. However, despite these health improvements, there was no overall decrease in the prevalence of subfertility in the antenatal population. Mathematical modelling showed that even if the entire population had improved their lifestyle this would have made little difference to the proportion of subfertile couples.

Conclusions—A modest improvement in lifestyle over a period of 6 years in couples trying to conceive a pregnancy did not lead to any reduction in the incidence of subfertility and even substantial changes would not have made a significant difference.

Keywords

Infertility; subfertility; time to pregnancy; reproductive and sexual health

Introduction

It is estimated that 10–15% of couples experience impaired fertility at some point in their reproductive lives (Hull et al., 1985; Healy et al., 1994). Subfertility is clinically defined as 12 months of unprotected intercourse during the fertile period of the menstrual cycle without a resulting pregnancy (Evers, 2002). The relationship between lifestyle factors and fertility has been studied from differing methodological approaches, in a variety of contexts (Grodstein et al., 1994a,b; Buck et al., 1997; Curtis et al., 1997; Hakim et al., 1998; Bolumar et al., 2000; Eggert et al., 2004; Hassan & Killick, 2003, 2004b; Kelly-Weeder & Cox,

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2006; Rostad et al., 2006; Chavarro et al., 2007; Homan et al., 2007). Commonly studied individual and lifestyle-related risk factors for subfertility include age, smoking and obesity.

This study investigates relationships between lifestyle factors and impaired fertility among a population of pregnant women attending an antenatal clinic in Hull, United Kingdom, in 2001 and 2007. The goals of the study were to identify which lifestyle factors are associated with subfertility (time to pregnancy (TTP) greater than 12 months) or severe subfertility (defined here as TTP greater than 24 months), and whether there were any differences from 2001 to 2007 in the prevalence of subfertility in this population, the distribution of factors potentially associated with subfertility and the relationships between lifestyle factors and subfertility.

Methods

Data were collected in Hull in September 2000 to May 2001, and again in February to May 2007, using the same survey instrument. Consecutive women attending the antenatal clinics were asked to complete a questionnaire inquiring about TTP (the interval of exposure to unprotected intercourse from discontinuing contraceptive use until conception), contraceptive use, pregnancy planning, history of pregnancies and fertility problems, gynecological disease and individual and lifestyle factors including age, height, weight, coffee and tea intake, smoking (own and partner's), alcohol use (own and partner's), recreational drug use (own and partner's) and the couple's coital frequency. The questionnaires were anonymous and contained no personal identifying information.

The survey was validated prior to its use in 2001 by an independent assessor, who interviewed 10 women in the clinic after they had completed the questionnaire, to ensure that they understood what information was required for each question. Minor changes were made to the wording of some questions as a result of these interviews. Another group of 10 was asked to complete the questionnaire on two occasions, 2 weeks apart, to ensure that their answers were consistent. There were no inconsistencies of response; although on the second occasion, three individuals were able to respond to questions they had originally not answered, hence reducing the proportion of missing data.

The response rate during the study was exceptionally high because patients had no objection to completing the questionnaire while waiting in the antenatal waiting room and was calculated as 98% from the total number of antenatal patients attending the antenatal clinic during the study months. The initial sample for both years combined was 3,114. Our analysis excludes those respondents for whom the outcome variable (TTP) is missing (n = 220, 7.1% of cases). We also excluded those whose pregnancy resulted from contraceptive failure or contraceptive non-compliance (n = 608, 19.7%) for two reasons. First, the definition of TTP in the survey (having intercourse without using any form of contraception) is not relevant to this portion of the sample, so the outcome variable cannot be meaningfully interpreted. Second, we assume that these women were, to some degree, attempting to avoid pregnancy and therefore would not be comparable to the rest of the sample. These restrictions resulted in a final sample size of 2,317 (1,558 in 2001 and 759 in 2007).

Data were analysed using Stata/SE 10.1. The outcomes of interest were subfertility (TTP >12 months) and severe subfertility (TTP >24 months). Logistic regression models were used to examine the relationships between medical history, lifestyle and demographic variables and subfertility. Separate models were estimated for planned and unplanned pregnancies, as preliminary analyses indicated that the factors associated with TTP may operate differently for these two groups of women (TTP was longer for women with unplanned pregnancies than for those with planned pregnancies, perhaps due to underlying

fertility problems in the former group). The initial, unrestricted models (not shown) included all relevant variables that were measured in the questionnaire (Table I). Our goal was to find the most parsimonious model capturing the association between the outcome and the predictors. Therefore, the final models presented here were restricted to include only variables that were significantly related to the outcome. Categories of independent variables were collapsed when no meaningful difference in odds ratios (ORs) between categories was detected.

Missing data were a concern in our analysis, as complete-case analysis resulted in an unacceptably high reduction in sample size (39.3% of cases were lost, reducing the sample size from 2,317 to 1,406). The problem cannot be solved simply by adding a category 'missing' for each variable in our models because the resulting effects estimates will be biased (Allison, 2001). To address the challenge of missing data, we employed multiple imputation with 10 imputation cycles, using the ICE and MIM commands in Stata (StataCorp, College Station, TX) (Carlin et al., 2008). Deleting incomplete cases, in addition to reducing sample size, will result in unbiased effects estimates only if data are completely missing at random (probabilities of response do not depend on any data values observed or missing); multiple imputation requires a less stringent requirement that data are missing at random (missing data values carry no information about probabilities of missingness). We found that in our logistic regression models significance level and magnitude of effect were comparable across the imputed data and the original data for all variables except one (partner's age) (results not shown).

Approval for the study was obtained from the Hull and East Yorkshire Research Ethics Committee. There are no conflicts of interest.

Results

Descriptive statistics are shown in Table I. There were no significant differences in the proportion of women with TTP >12 months or TTP >24 months between 2001 and 2007 among either subgroup (planned or unplanned pregnancies). There were, however, significant differences in the distributions of some variables potentially associated with TTP. Among women with planned pregnancies, we found significant differences between the two data collection periods in the distribution of age, BMI, contraceptive method used before the period of unprotected intercourse leading to the current pregnancy, number of previous pregnancies, history of reproductive problems (menstrual disorders, PID or Chlamydia and markers of hormonal imbalance), caffeine intake, alcohol use (own and partner's) and partner's smoking. Among women with unplanned pregnancies, we found differences by year in the distribution of BMI, contraceptive use, history of PID or Chlamydia, markers of hormonal imbalance, caffeine intake, history of drug use, partner's age and partner's smoking.

Factors associated with TTP among women with planned pregnancies

As seen in Table II, TTP >12 months among women with planned pregnancies significantly increased with women's age when controlling for other factors, when compared with women younger than 20, the odds of subfertility were six times as high for women aged 20–34, and 13.6 times as high for women 35 or older. BMI was also significantly associated with subfertility, as women who were overweight or obese (BMI 25) experienced odds of subfertility 1.7 times those of women of normal or low body mass index (BMI < 25). Certain reproductive history variables were also associated with subfertility. Women with no previous pregnancies had nearly twice the odds of subfertility of women with at least one previous pregnancy, and those with a history of menstrual problems experienced more than double the odds of subfertility of those with no such history. In addition, compared with

women who used condoms or IUDs, users of no contraceptive method experienced a 23.5fold greater odds of subfertility (in 2001), while odds for users of Depo-Provera were 20.7 times greater (in 2001) and odds for users of other hormonal methods were 2.6-fold greater. The effect of prior Depo-Provera use was reduced by 82% in 2007 (compared with 2001), and the effect of use of no method was reduced by 60%. Two partner-related variables emerged as significantly associated with subfertility: the odds of subfertility among women with partners aged 45 or older were 3.8 times those of women with younger partners, and the odds of subfertility among women whose partners smoked more than one pack of cigarettes per day were 1.5 times those whose partner smoked less than one pack, or not at all.

In addition to identifying factors associated with the standard, clinically-defined level of subfertility, we also estimated models to identify factors associated with more severe subfertility, TTP >24 months. As seen in Table III, women with a planned pregnancy were significantly more likely to experience a TTP >24 months if they were aged 30 or more (OR = 2.3). Women who were overweight or obese experienced twice the odds of severe subfertility as normal-weight or under-weight women. We found that similar reproductive history variables predicted TTP >12 and TTP >24: women with no previous pregnancies were twice as likely to experience severe subfertility as those with at least one past pregnancy (OR = 1.9), and women with a history of menstrual difficulties had more than twice the odds of severe subfertility of those without previous menstrual problems (OR =2.2). When considering history of contraceptive use, we found that the only significant distinction overall was between use of no contraceptive method and any contraceptive method; women who reported having used no method experienced 14.6-fold higher odds of severe subfertility than did women who had used any form of contraception (regardless of which specific method they identified). Although the effect of prior use of specific types of contraceptives did not differ, women whose prior method was hormonal (regardless of type) experienced only half the odds of severe subfertility in 2007, compared with women who used hormonal methods in 2001. Finally, we found that the only significant partner-related variable for TTP >24 was age; the odds of severe subfertility for women whose partner was 45 or older were four times those of women with younger partners.

Factors associated with TTP among women with unplanned pregnancies

As seen in Table IV, only three factors were associated with TPP >12 months or TPP >24 months among women whose pregnancies were unplanned: BMI 25, no use of contraception before the pregnancy, and a history of menstrual problems. Compared with women of normal or low weight, overweight or obese women experienced 1.8 times the odds of subfertility (TTP >12) and severe subfertility (TTP >24). Women using no contraceptive method experienced nearly 3-fold higher odds of waiting more than 12 months to become pregnant, and six times the odds of TTP >24 months as those who had used any method. The final significant predictor of subfertility among women with unplanned pregnancies in our model was any history of menstrual disorder, and we found that women who had experienced menstrual problems in the past had 1.7 times the odds of subfertility and 2.2 times the odds of severe subfertility as those who had not experienced such problems.

Discussion

The results of the study confirm the findings of our previous analyses of this population and also of previous studies of other populations by showing that the risk of significant degrees of subfertility in couples trying for pregnancy is influenced by the age and lifestyle habits of both partners.

We interpret the finding that a previous lack of contraceptive use was associated with a much reduced fertility as indicating that a significant fraction of this group were aware of their reduced fertility and hence chose not to use contraception, whether they were planning pregnancy or not. Depot medroxyprogesterone acetate injectables for hormonal contraception are known to induce prolonged amenorrhea in some individuals and hence increase the mean TTP after cessation in the group that uses them. The increased TTP in other hormone contraceptive users has been discussed in a previous publication of our 2001 cohort (Hassan & Killick, 2004a).

Our intention in repeating the study after a 6-year gap was to determine if a general increase in living standards and an increasing public awareness about reproductive health in our local population (Hull City Council 2008) would have translated into a reduction in the prevalence of subfertility. However, we found no difference in the prevalence of subfertility between the two survey years.

To a certain extent, the public health message seems to have been appreciated by our population as our group of pregnant women were less likely to be obese and drank less alcohol and caffeine in 2007 compared to 2001. Their male partners also drank less alcohol and smoked less in 2007. That this was a conscious improvement in lifestyle decisions on the part of the couples is suggested by the fact that the changes are much more marked in the group that planned their pregnancy. Indeed, there was no change at all in the unplanned pregnancy group in terms of alcohol intake or partner's alcohol intake. One notable exception to the improvement in lifestyle between 2001 and 2007 is that there was no difference in the prevalence of smoking by the pregnant women pre-conception.

These lifestyle improvements appear modest and, crucially, have not resulted in any improvement in the prevalence of subfertility in our local population. We ran simulations to predict whether the probability of subfertility would change in the 2007 sample if the lifestyle variables that were significantly associated with subfertility were held at their 2001 levels. When BMI and partner's smoking were held separately at the distribution found in the 2001 sample and all other factors held at 2007 levels, there would be less than one percentage point increase in the predicted probability of subfertility. If both BMI and partner's smoking are held at 2001 levels, there would be a 1.4% point increase. We might have expected to see a profound difference in the predicted probability of subfertility if we applied the 2001 distribution of contraceptive use to the 2007 sample, given that the interactions between survey year and use of injectable contraception and the use of no contraceptive method are strong and significant (the effect of using Depo-Provera is reduced by 82% and the effect of using no method is reduced by 60%). However, we found that holding the distribution of contraceptive use at 2001 levels decreased the predicted probability of subfertility by only 2.9% points.

We also wanted to know what the greatest possible change in the probability of subfertility might be if negative lifestyle factors were reduced to zero. When the overweight/obese BMI category and partner's heavy smoking (a pack a day or more) are held at zero and all other factors held at their 2007 levels, the predicted probability of subfertility is decreased by only 3.4% points. We therefore conclude that even if all individuals in this population eliminated the lifestyle factors that are associated with an increased likelihood of subfertility, there is not a particularly large scope for improving the probability of subfertility.

The limitations of our study include the fact that we only examined resolved subfertility. Those couples who remained infertile and were still trying to achieve pregnancy were not identified by our methodology.

Conclusion

Our study shows a small self-imposed improvement in lifestyle over a period of 6 years in couples trying to conceive a pregnancy. However, this has not led to a reduction in the incidence of subfertility. Simulations show that even major improvements in these lifestyle factors would yield only a modest improvement in the risk of subfertility.

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Table I

Distribution of factors potentially associated with subfertility in 2001 and 2007.

		Planned p	regnanci	es	n	nplanned	pregnano	ies
	2001	2007	Total	<i>p</i> -value	2001	2007	Total	<i>p</i> -value
TTP >12 months	20.3%	19.9%	20.1%	0.848	34.5%	29.8%	32.8%	0.271
TTP >24 months	9.6%	11.2%	10.1%	0.310	18.6%	14.3%	17.1%	0.202
Age				0.001				0.323
<20	3.7%	4.4%	3.9%		13.0%	16.1%	14.1%	
20-<25	15.5%	21.1%	17.3%		27.1%	27.6%	27.3%	
25-<30	37.0%	35.9%	36.7%		25.4%	24.8%	25.2%	
30-<35	30.9%	23.0%	28.4%		22.0%	15.5%	19.8%	
35+	13.0%	15.6%	13.8%		12.4%	16.1%	13.7%	
BMI				0.003				0.002
<18.5 (Underweight)	2.8%	4.2%	3.2%		2.3%	7.6%	4.2%	
18.5-<25 (Normal)	43.1%	51.5%	45.8%		39.6%	50.0%	43.2%	
25-<30 (Overweight)	37.0%	26.9%	33.8%		40.1%	23.8%	34.4%	
30 (Obese)	17.2%	17.4%	17.2%		18.1%	18.6%	18.2%	
Contraceptive use				0.000				0.034
Condom or IUD	22.0%	14.4%	19.6%		13.8%	12.2%	13.2%	
No method	10.6%	16.3%	12.4%		27.5%	25.2%	26.7%	
Injectable	2.8%	4.5%	3.3%		1.5%	7.0%	3.5%	
POP, COC, other hormonal	64.7%	64.7%	64.7%		57.2%	55.7%	56.7%	
Coital frequency				0.336				0.176
Fortnightly or less	7.4%	7.7%	7.5%		18.9%	17.3%	18.3%	
Once/week	21.5%	18.6%	20.6%		17.4%	16.9%	17.2%	
2-4 times/week	60.6%	60.9%	60.7%		51.4%	46.3%	49.6%	
5 times/week	10.5%	12.9%	11.2%		12.3%	19.5%	14.9%	
Previous pregnancies				0.036				0.097
None	25.5%	29.1%	26.7%		28.3%	36.5%	31.1%	
1	37.9%	31.6%	35.9%		24.9%	25.1%	25.0%	
2	36.6%	39.3%	37.5%		46.9%	38.4%	43.9%	
Age at menarche				0.338				0.050

		Planned p	regnanci	ss	n	nplanned	pregnano	ies
	2001	2007	Total	<i>p</i> -value	2001	2007	Total	<i>p</i> -value
<12	18.1%	20.2%	18.8%		20.3%	28.9%	23.9%	
12	81.9%	79.8%	81.2%		79.7%	71.1%	76.1%	
History of menstrual problems				0.000				0.054
Yes	22.6%	33.4%	26.1%		32.3%	40.7%	35.3%	
No	77.4%	66.6%	73.9%		67.7%	59.3%	64.7%	
History of PID or Chlamydia				0.001				0.031
Yes	7.3%	12.3%	8.9%		10.4%	16.8%	12.7%	
No	92.7%	87.7%	91.1%		89.6%	83.2%	87.3%	
History of problems with reproductive organs				0.083				0.194
Yes	15.5%	18.7%	16.5%		13.1%	17.2%	14.5%	
No	84.5%	81.3%	83.5%		86.9%	85.4%	85.5%	
History of problems with hormonal imbalance				0.010				0.000
Yes	6.6%	10.1%	7.7%		1.8%	9.6%	4.5%	
No	93.4%	89.9%	92.3%		98.2%	90.4%	95.5%	
Smoking				0.263				0.057
None	80.9%	77.9%	80.0%		61.6%	53.4%	58.8%	
1–19 per day	16.6%	19.9%	17.6%		29.4%	39.5%	32.8%	
20 per day	2.5%	2.2%	2.4%		9.0%	7.1%	8.4%	
Caffeine				0.000				0.000
None	11.5%	16.0%	12.9%		6.2%	20.8%	11.4%	
1-6 cups/week	80.7%	80.5%	80.7%		80.2%	69.4%	76.4%	
7 cups/week	7.8%	3.5%	6.4%		13.6%	9.8%	12.2%	
Alcohol use				0.000				0.311
None	54.1%	68.3%	58.5%		64.0%	66.0%	64.7%	
1-9 drinks/week	42.6%	27.7%	38.0%		34.9%	31.2%	33.6%	
10 drinks/week	3.4%	4.0%	3.5%		1.1%	2.8%	1.7%	
Drug use				0.244				0.000
Ever	2.7%	3.7%	3.0%		4.0%	15.2%	7.9%	
Never	97.3%	96.3%	97.0%		96.0%	84.8%	92.1%	
Partner's age				0.791				0.017

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		Planned p	regnanci	es	Ũ	nplanned	pregnano	ies
	2001	2007	Total	<i>p</i> -value	2001	2007	Total	<i>p</i> -value
<40	91.9%	91.0%	91.6%		94.1%	88.3%	92.1%	
40-<45	6.1%	7.0%	6.4%		4.2%	4.9%	4.4%	
45	2.0%	2.0%	2.0%		1.7%	6.8%	3.5%	
Partner's smoking				0.000				0.000
None	60.3%	64.2%	61.6%		43.5%	41.2%	42.7%	
1–19 per day	18.4%	24.4%	20.3%		20.9%	41.3%	28.1%	
20 per day	21.3%	11.4%	18.1%		35.6%	17.5%	29.2%	
Partner's alcohol use				0.000				0.339
None	17.5%	26.4%	20.3%		31.2%	37.5%	33.4%	
1-19 drinks/week	78.3%	65.8%	74.3%		60.5%	56.0%	58.9%	
20 drinks/week	4.3%	7.8%	5.4%		8.4%	6.5%	7.7%	
Partner's children from previous relationship				0.344				0.266
Any	15.0%	16.8%	15.6%		20.3%	24.6%	21.8%	
None	85.0%	83.2%	84.4%		79.7%	75.4%	78.2%	

Table II

Factors associated with time to pregnancy (TTP) >12 months among women with planned pregnancies.

	OR	<i>p</i> -value
Age		
<20	Ref	Ref
20-<35	5.9	0.000
35	13.6	0.000
BMI		
<25 (Underweight or normal)	Ref	Ref
25 (Overweight or obese)	1.7	0.000
Contraceptive use		
Condom or IUD	Ref	Ref
No method	23.5	0.000
Injectable	20.7	0.000
POP, COC, other hormonal	2.6	0.000
History of menstrual problems		
No	Ref	Ref
Yes	2.4	0.000
Previous pregnancies		
None	1.9	0.000
One or more	Ref	Ref
Partner's age		
<45	ref	ref
45+	3.8	0.001
Partner's smoking		
None or <pack day<="" td=""><td>Ref</td><td>Ref</td></pack>	Ref	Ref
Pack/day +	1.5	0.021
Survey year 2007 * No method	0.40	0.003
Survey year 2007 * Injectable	0.18	0.008

Table III

Factors associated with time to pregnancy (TTP) >24 months among women with planned pregnancies.

	OR	p-value
Age		
<30	Ref	Ref
30	2.3	0.000
BMI		
<25 (Underweight or normal)	Ref	Ref
25 (Overweight or obese)	2.0	0.000
Contraceptive use		
Any method	Ref	Ref
No method	14.6	0.000
History of menstrual problems		
No	Ref	Ref
Yes	2.2	0.000
Previous pregnancies		
None	1.9	0.002
One or more	Ref	Ref
Partner's age		
<45	Ref	Ref
45+	4.0	0.002
Survey year 2007 \star any hormonal method	0.46	0.013

Table IV

Factors associated with time to pregnancy (TTP) >12 months and >24 months among women with unplanned pregnancies.

	TTP >	12 months	TTP >	24 months
	OR	<i>p</i> -value	OR	<i>p</i> -value
BMI				
<25 (Underweight or normal)	Ref	Ref	Ref	Ref
25 (Overweight or obese)	1.8	0.003	1.8	0.041
Contraceptive use				
Any method	Ref	Ref	Ref	Ref
No method	2.9	0.000	6.0	0.000
History of menstrual problems				
No	Ref	Ref	Ref	Ref
Yes	1.7	0.004	2.2	0.003