BMJ Open

Mental health in women 20–23 years after IVF treatment: a Swedish cross-sectional study

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To cite: Vikström J, Josefsson A, Bladh M, *et al*. Mental health in women 20–23 years after IVF treatment: a Swedish cross-sectional study. *BMJ Open* 2015;**5**: e009426. doi:10.1136/bmjopen-2015-009426

▸ Prepublication history for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2015-009426).

Received 20 July 2015
Revised 15 September 2015
Accepted 6 October 2015

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ABSTRACT

Objective: To assess self-perceived mental health in women treated with in vitro fertilisation (IVF) 20–23 years previously, while comparing them to a reference group, and to determine any differences in mental health between those who had given birth, those who had adopted a child, those who had given birth and adopted a child and those who remained childless.

Design: A cross-sectional study.

Setting: A Center of Reproductive Medicine (RMC) at a Swedish University hospital.

Participants: 520 women who had undergone at least one IVF cycle at the University Hospital in Linköping between 1986 and 1989. 504 of 520 women (97%) were eligible for follow-up. While 34 women declined, 93 per cent (n=470) of the women agreed to participate. The reference group consisted of 150 women of the Swedish population included in a study that was used to validate the Symptom CheckList (SCL)-90.

Interventions: Follow-up was conducted in 2008–2009. The SCL-90 was used to measure the women's self-perceived mental health and a questionnaire specific for this study was used to retain demographic information.

Outcome measures: The SCL-90 assesses 9 primary dimensions; somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. There is also a global index of distress.

Results: Women who had previously undergone IVF treatment were at increased risk of symptoms of depression (p=0.017), obsessive-compulsion (p=0.02) and somatisation (p≤0.001) when compared to a reference group. In addition, the women who have remained childless are at increased risk of symptoms of depression (p=0.009) and phobic anxiety (p=0.017).

Conclusions: The majority of the women who have been treated with IVF 20–23 years previously appear to be in good mental health. However, women who remain childless and/or without partner after unsuccessful infertility treatment constitute a vulnerable group even later on in life.

Strengths and limitations of this study

- This is one of the few studies on the long-term mental health of women who have been treated with in vitro fertilisation.
- The follow-up period is exceptionally long at 20–23 years.
- The participation rate was very high at 93% (n=470). Unfortunately, possible confounding factors such as educational level and life events could not be controlled for.

INTRODUCTION

Infertility, as well as its investigations and treatment, can cause psychological distress,[1] such as symptoms of anxiety and depression.[2–4] The infertility treatment itself further adds to the strain created by the infertility.[5 6] In addition, childbirth is a known trigger for first-time episodes of psychiatric illness.[7 8] However, Ross *et al*[9] found in their review that there were no significant differences in the risk of experiencing symptoms of depression between those who had conceived spontaneously and those who had been treated with in vitro fertilisation (IVF).

Studies using self-reported symptoms as outcome measures when examining psychological well-being up to 10 years after IVF treatment have found that women who remain childless are at increased risk of anxiety,[6 10] depression[6 10 11] and stress[11] and have a lower sense of coherence,[10] self-esteem[11] and satisfaction with life[11 12] than those who had given birth after treatment. Women who give birth as a result of treatment show a more positive long-term emotional status.[4] Register-based studies using psychiatric diagnoses as outcome measures when examining risk of psychiatric illness after IVF treatment have varied in their results. Agerbo *et al*[13] found that there were no differences between those who had given birth or remained childless after treatment in regard to risk of psychiatric illness but that the risk was lower among those who had adopted children. Another Danish register-based study by Baldur-Felskov *et al*[14] found

that women who go through unsuccessful IVF treatment were at increased risk of hospitalisation due to most psychiatric disorders but that the risk of affective disorders were lower than for those who had given birth as a result of treatment. Meanwhile, Yli-Kuha *et al*[15] showed that the risk of depression was increased in those who had gone through an unsuccessful treatment.

In regard to long-term effects of infertility and its treatment, Gameiro *et al*[16] showed that women who had undergone infertility treatment 11–17 years previously suffered more mental health problems, when compared to the general population, and that a sustained child's wish negatively affected mental health. Meanwhile, studies have shown that most women come to terms with their parenthood goals.[16–18] This shows that reorientation and coping after unsuccessful IVF treatment is important[4 19–21] and that couples may be in need of counselling after unsuccessful IVF treatment to resolve the grieving process.[22] Twenty years after infertility treatment, the relationship quality in the couples who have previously undergone infertility treatment is good,[23] although a qualitative study on 14 women showed that they still suffered negative effects of the infertility which were especially great when the women were going through the grandparent phase.[24] Most studies have shown that childlessness does not influence psychological well-being in elderly individuals.[25–28] Thus, there are only a few studies on the mental health of women who have been treated with IVF from a long-term perspective. It is still unclear what effects infertility and its treatment has on women in a long-term perspective.

The aim of the present study was to assess self-perceived mental health in a group of women treated with IVF 20–23 years earlier. Second, we wanted to study possible differences in mental health between the four groups: those who had given birth, those who had adopted a child, those who had given birth and adopted a child and those who remained childless.

METHOD

Subjects

All women (n=520) who had received at least one IVF treatment cycle at the Center of Reproductive Medicine, University Hospital in Linkoping between 1986 and 1989 were, in 2008 to 2009, sent an introductory letter asking them to participate in the study. Six of the women were deceased and 10 women never received the letter; thus, 504 of 520 (97%) women were eligible for follow-up. Of these, 10 women returned the letter declining participation and 24 women did not answer. Thus, a total of 470 of 504 (93%) women eligible for follow-up agreed to participate. Of the 93% (n=470) of the women who agreed to participate, 55.1% (n=259) had biological children, 19.4% (n=91) had adoptive children, 5.3% (n=25) had both biological and adoptive children and 20.2% (n=95) had remained childless. As a reference group, we used score mean values for 150 women of the general Swedish population. These data were derived from a population-based study, through which the Symptom CheckList (SCL)-90 was validated, of women older than 40 years of age.[29 30]

Treatment procedures 1986–1989

The couples were given three or more publicly funded IVF treatments during this time period. Some of the couples might have had at least one child before entering treatment during this period. The upper age limit for the women was 38 years at the time of treatment. The waiting time from acceptance to treatment was approximately 3 years.

Outcome measures

The SCL-90 was used to measure the women's self-perceived mental health during the past week. The SCL-90 is an extensively used multidimensional psychological status symptom inventory consisting of 90 items.[29 30] It is an objective method for symptom assessment requiring individuals to rate their psychopathological problems and symptoms. These symptoms are then used to compute scores for depression and anxiety. The scale is a five-point Likert scale ranging from 'not at all' (0) to 'extremely' (4). The SCL-90 assesses 9 primary dimensions: somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism. The cut-off score for each primary dimension was set at the 95th centile of self-reported symptoms in the study population in order to indicate a severe level of symptoms.[31 32] Hence, >95th centile indicated 'Yes', meaning the occurrence of clinically relevant symptoms, and ≤95th centile indicated 'No'. There is also a global index of distress that can be used as a summary dimension. The cut-off score on the SCL-90 of <70 was used as an indicator of mental health.[29]

Demographics

Age, employment status, marital status, same/different partner since time of IVF treatment, number of children (biological and adopted), number of miscarriages and number of IVF treatments were assessed through a questionnaire specific for this study. Those with the same/different partner since time of IVF treatment thus constitute a subgroup to those who were married/cohabiting.

Statistics

Two-sided χ^2 tests were used to analyse differences between the subgroups in regard to background variables and self-perceived mental health. Student t test, also two sided, was used to compare mean scores between all women who had received IVF treatment and those in the reference group. Effect sizes, using Cohen's distance, were calculated in order to evaluate the magnitude of the differences of the mean scores between IVF-treated women and women in the reference group. p Values <0.05 were considered significant. All statistical

analyses were performed using IBM SPSS V.19 (IBM Corporation, Armonk, New York, USA).

RESULTS

Demographics

The distribution of demographics across the three groups is shown in table 1. The majority of the women were older than 45 years at the time of follow-up. Those who had remained childless and those who had adopted children were significantly (p≤0.001) more likely to be aged over 45 years than were those with biological children. While 41.5% (n=39) of the women without children were divorced or separated, the corresponding number for the women with biological children was 7.0% (n=18) (p≤0.001). Among those with adopted children, all women were married or cohabiting. Also, those with adopted children were the most likely to still be living with the same partner as they were at the time of IVF treatment (98.9%; n=90). Those without children (90%; n=54) who were cohabiting or married were more likely than those with biological children (70.6%; n=175) to have remained with the same partner (p≤0.001) (table 1).

The women had, on average, been through 2.7 (range=1–10) IVF cycles and 189 of the women had experienced 1–10 miscarriages (mean=1.9).

Self-perceived mental health

The women's own perceived mental health is displayed in table 2. Women who had biological or adoptive children were less likely to experience symptoms of phobic anxiety than women who had remained childless (p=0.017) (table 2). Also, women who had biological children were also significantly less likely than women who had remained childless to experience symptoms of depression (p=0.009). Women who were separated, lived alone or were unemployed showed more signs of depression, anxiety and obsessive-compulsive problems compared to women who were married and were gainfully employed. Women who were over 45 years of age also had more symptoms of mental illness. Women who had changed partner since the time of IVF had more obsessive-compulsive symptoms compared to women who still had the same partner, but there were no other differences between these two groups (table 2).

In regard to 'Global severity index' and 'Positive symptom total', the women who had experienced infertility within the couple and who had been through a number of IVF treatments 20–23 years earlier showed the same pattern as the reference group (table 3). Only on the 'Positive symptom distress index' did the IVF group have a higher score indicating that these women had reported experiencing more intense symptoms. In regard to the specific symptoms, the women who had previously undergone IVF treatment were at increased risk of depressive and obsessive-compulsive symptoms as well as having increased scores for somatisation (table 3).

DISCUSSION

Principal findings

The majority of the women who had been treated with IVF 20–23 years previously reported few mental health

Table 1 Demographic data for the women treated with in vitro fertilisation >20 years ago (n=470)

	Total		No children		Biological children		Adoptive children		Biological and adoptive children		
	n	Per cent	n	Per cent	n	Per cent	n	Per cent	n	Per cent	p Value
Employment status											
Employed	349	74.3	66	78.6	189	78.8	75	87.2	19	79.2	0.369
Missing	36	7.7	–	–	–	–	–	–	–	–	
Marital status											
Married/cohabiting	411	87.4	55	58.5	240	93.0	91	100.0	25	100.0	<0.001
Separated/divorced/other	57	12.1	39	41.5	18	7.0	0	0.0	0	0.0	
Missing	2	0.4	–	–	–	–	–	–	–	–	
Same partner											
Yes	343	73.0	54	90.0	175	70.6	90	98.9	24	96.0	<0.001
Missing	46	9.8									
Children											
No children	95	20.2	–	–	–	–	–	–	–	–	–
Biological children	259	55.1	–	–	–	–	–	–	–	–	
Adoptive children	91	19.4	–	–	–	–	–	–	–	–	
Biological and adoptive children	25	5.3	–	–	–	–	–	–	–	–	
Age at follow-up											
≥45 years old	289	61.5	75	78.9	136	52.5	63	69.2	15	60.0	<0.001

Significance level <0.05.

Table 2 The study group women's self-perceived mental health assessed by the Symptom CheckList 90

Sociodemographic factors in %*	Somatisation			Interpersonal sensitivity			Depression			Anxiety			Hostility		
	No	Yes	p Value	No	Yes	p Value	No	Yes	p Value	No	Yes	p Value	No	Yes	p Value
Employment															
Employed	80.4	80.0	0.962	81.2	69.0	0.108	81.8	65.8	0.017	81.8	59.3	0.004	80.5	78.6	0.860
Marital status															
Married/cohabiting	88.4	76.2	0.095	88.4	80.0	0.176	88.8	76.9	0.030	88.6	75.9	0.042	88.1	80.0	0.347
Separated/divorced/other	11.6	23.8		11.6	20.0		11.2	23.1		11.4	24.1		11.9	20.0	
Age at follow-up															
≥45 years old	60.7	77.3	0.119	61.5	61.3	0.981	60.0	77.5	0.030	60.7	73.3	0.168	61.7	56.3	0.661
Same partner															
Yes	81.1	75.0	0.541	81.5	70.8	0.197	81.2	77.4	0.609	81.3	73.9	0.381	81.3	66.7	0.203
Children															
No children	19.9	27.3	0.159	19.4	32.3	0.188	18.4	40.0	0.009	19.5	30.0	0.420	20.0	25.0	0.961
Biological children	56.0	36.4		56.0	41.9		56.7	37.5		55.9	43.3		55.3	50.0	
Adoptive children	19.2	22.7		19.6	16.1		19.3	20.0		19.1	23.3		19.4	18.8	
Biological and adoptive children	4.9	13.6		5.0	9.7		5.6	2.5		5.5	3.3		5.3	6.3	

Sociodemograpic factors in %*	Phobic anxiety			Paranoid ideation			Psychoticism			Obsessive-compulsive		
	No	Yes	p Value	No	Yes	p Value	No	Yes	p Value	No	Yes	p Value
Employment												
Employed	81.9	57.7	0.003	81.3	65.2	0.059	80.4	80.0	0.962	81.6	63.0	0.018
Marital status												
Married/cohabiting	88.4	77.8	0.100	87.8	87.5	0.961	88.4	76.2	0.095	88.6	75.9	0.042
Separated/divorced/other	11.9	22.2		12.2	12.5		11.6	23.8		11.4	24.1	
Age at follow-up												
≥45 years old	60.2	82.1	0.021	61.9	54.2	0.449	60.7	77.3	0.119	60.7	77.3	0.119
Same partner												
Yes	80.6	85.7	0.973	82.1	57.1	0.095	81.1	75.0	0.541	82.3	56.5	0.002
Children												
No children	18.8	42.9	0.017	20.4	16.7	0.693	19.9	27.3	0.159	19.1	36.7	0.099
Biological children	56.1	39.3		54.7	62.5		56.0	36.4		55.7	46.7	
Adoptive children	19.9	10.7		19.7	12.5		19.2	22.7		20.0	10.0	
Biological and adoptive children	5.2	7.1		5.2	8.3		4.9	13.6		5.2	6.7	

p Values derived from Pearson χ^2 statistic with significance level <0.05.
Cut-off for each primary dimension: Yes >95th centile (severe level of symptoms); No ≤95th centile.
*Percentage of individuals exhibiting the demographic factor for each category (Yes/No).

Table 3 The study group of 470 women compared to the reference group of 156 age-matched women

		IVF women n=463–470		Reference group age-matched sample n=156		Effect size Cohen's	
	Cronbach's α	Mean	SD	Mean	SD	distance	p Value
Somatisation	0.856	0.62	0.72	0.43	0.44	0.32*	<0.001
Obsessive-compulsive	0.864	0.57	0.68	0.49	0.52	0.13	0.020
Interpersonal sensitivity	0.884	0.41	0.68	0.42	0.47	0.02	0.763
Depression	0.921	0.62	0.80	0.52	0.58	0.14	0.017
Anxiety	0.870	0.49	0.70	0.43	0.48	0.10	0.079
Hostility	0.778	0.32	0.57	0.29	0.41	0.06	0.285
Phobic anxiety	0.746	0.13	0.41	0.11	0.26	0.06	0.303
Paranoid ideation	0.746	0.30	0.57	0.27	0.39	0.06	0.278
Psychoticism	0.762	0.15	0.41	0.14	0.24	0.03	0.599
Global Severity Index	0.975	0.41	0.60	0.38	0.38	0.06	0.291
Positive Symptom Distress Index	–	3.84	6.15	1.40	0.43	0.56†	<0.001
Positive symptom total	–	25.63	18.63	24.58	16.86	0.06	0.296

Significance level <0.05.
*Effect size Cohen's distance: ≥0.2 small.
†Effect size Cohen's distance: ≥0.5=medium.
‡Effect size Cohen's distance: ≥0.8=large.
IVF, in vitro fertilisation.

problems. However, women who had remained childless 20 years after infertility treatment reported negative psychological consequences to a greater degree than those who had since become mothers. Childless women reported more symptoms of depression than did those with biological children and symptoms of phobic anxiety than did the women who had biological or adopted children. Women who had remained childless were to a greater degree separated or divorced, a group which to a greater degree reported suffering from depressive, anxiety and obsessive-compulsive symptoms. When all women who had undergone IVF treatment were compared to a reference group, we found that the IVF women reported more depressive, obsessive-compulsive and somatisation symptoms.

Strengths and limitations

The major limitation in this study is that we do not have data on mental health and life events at the start of IVF treatment or during the 20 years that have passed for the participating women. We can assume that most of the women have experienced their share of difficulties related to one or more of the major life events such as illness, job loss, death in the family and even trauma, but these are unfortunately not factors we could control for. However, it is reasonable to assume that the reference group would be equally affected by such factors. Unfortunately, we have no information on educational level of the participants which might have influenced the results. Also, no additional information, for example, parental status or fertility problems, was available for the reference group.

A great strength of this study is the high participation rate of 93%. The reason for this surprisingly high rate might be that these women who were pioneers when IVF treatment was started in Sweden have a strong desire to be involved in studies concerning questions on health, IVF and childlessness. Another strength is the long period of observation.

Interpretation

In accordance with previous studies, the results of this study indicate that infertility treatment, especially when unsuccessful, might increase the risk of a negative psychological symptomatology.[10 12 24] Meanwhile, studies have shown that long-term psychological well-being is dependent on the ability to use coping skills[14 19–21] in order to overcome the grief process[22] and also on whether or not the woman still sustains a wish for biological children.[16] However, even if coping skills are successfully utilised, the grandparent phase, which the women of our study were just about to enter, might revoke the negative feelings that childlessness cause.[24] While some previous studies have shown that the difference in psychological symptoms depend on whether there are any children in the family, biological or adoptive,[12] others have shown only a positive influence of having biological children.[14] Also, Munk-Olsen and coworkers[13] found that adoptive parents were at reduced risk of psychiatric illness. We found that some symptoms were decreased in both groups with children while the risk of depressive symptoms was only decreased in those with biological children.

Mental health is an important issue to study in the clinics where infertility investigations are conducted. The mental health and the lifestyle of women and men can be an indicator of, and explanation for, the fact that some women have trouble getting pregnant. For instance, anxiety disorders and depression might interfere with the couple's relationship and sexuality in a

negative way, thus decreasing quality of life. It is often believed that emotional stress before trying to achieve pregnancy, naturally or through infertility treatment, will have a negative effect on pregnancy outcome. However, Boivin *et al*[33] showed, in a meta-analysis on 14 prospective studies, that pretreatment emotional distress did not negatively influence treatment outcome Owing to the limitations presented above, no firm conclusions regarding the long-term consequences of infertility treatment on mental well-being can be drawn. However, our results indicate that women who remain childless after IVF treatment might be at risk of experiencing negative psychological symptoms 20 years after treatment. In the future, we need to further explore the women who have a history of mental disorders or are vulnerable for mental ill-health in the IVF setting in order to not jeopardise their future mental health which could be negatively affected if the infertility treatment is unsuccessful. Also, for women who show signs of suffering from a mental disorder at the time of infertility investigation, counselling and treatment are important and medically correct actions need to be taken before starting infertility treatment. Moreover, women who remain childless after infertility treatment might be in need of follow-up and counselling to cope with their situation many years after infertility treatment.

Conclusion

In conclusion, the majority of the women who have been treated with IVF 20–23 years previously report few negative psychological symptoms. However, women who remain childless after unsuccessful infertility treatment constitute a vulnerable group that would most likely benefit from being observed in healthcare settings in order to prevent the evolvement of anxiety and depression symptoms and their side effects on somatic and psychological health.

Contributors JV participated in analysis, manuscript drafting and critical discussion and in the final preparation of the manuscript. AJ participated in analysis, manuscript drafting and critical discussion. MB participated in study design, execution and analysis. GS was involved in the research idea, design and execution, analysis, manuscript drafting and critical discussion. GS is the guarantor for the study.

Funding The study was supported by grants from The Health Research Council in the south east of Sweden.

Competing interests None declared.

Ethics approval The study has been approved by the Human Research Ethics Committee, in Linköping University (number 03–338, 9 September 2003).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The full data set and statistical code are available from the corresponding author at josefin.vikstrom@liu.se.

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